TARTU RIIKLIKU ÜLIKOOLI

TOIMETISED

УНЕНЫЕ ЗАПИСКИ
ТАРТУСКОГО ГОСУДАРСТВЕННОГО УНИВЕРСИТЕТА
ACTA ET COMMENTATIONES UNIVERSITATIS TARTUENSIS

589

CEREBROVASCULAR DISEASES

(EPIDEMIOLOGY, PATHOGENESIS, CLINICAL PICTURE AND TREATMENT)

СОСУДИСТЫЕ ЗАБОЛЕВАНИЯ ГОЛОВНОГО МОЗГА

(ЭПИДЕМИОЛОГИЯ, ПАТОГЕНЕЗ, КЛИНИКА И ЛЕЧЕНИЕ)

ТРУДЫ ПО МЕДИЦИНЕ

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ALUSTATUD 1893. a. VIHIK 589 ВЫПУСК ОСНОВАНЫ в 1893 г.

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ТАРТУ 1981

СОСУДИСТЫЕ ЗАБОЛЕВАНИЯ ГОЛОВНОГО МОЗГА.

В рамках советско-финляндского договора о сотрудничестве в области медицинской науки, здравоохранения и социального обеспечения договор о сотрудничестве в области неврологии и нейрохирургии между Тартуским госуниверситетом и Хельсинкским университетом подписан в ноябре 1973 года в г. Таллине. По этому договору в совместных научных исследованиях стали принимать участие клиника неврологии и нейрохирургии Тартуского госуниверситета (зав. проф. Э. Раудам), клиника неврологии (зав. проф. Э. Кивало) и клиника нейрохирургии (зав. проф. Х. Троупп) Хельсинкского университета. Согласно подписанному договору запланированы совместные исследования по согласованной программе по изучению распространения и факторов риска острых сосудистых заболеваний головного мозга в Эстонской ССР и в Финляндии, а также исследования ряда вопросов патогенеза, прогноза и лечения, в том числе и хирургического лечения этих заболеваний. С 1973 по 1980 год проведено всего 5 совместных симпозиумов в Таллине, Тарту и Хельсинки, где обсуждались результаты проведенных исследований, согласовывались программы дальнейших работ.

На III заседании смешанной советско-финляндской комиссии по сотрудничеству в области здравоохранения, медицинской науки и социального обеспечения, проходившем в сентябре 1978 г. в Хельсинки под совместным председательством заместителя Министра здравоохранения СССР Е. И. Новиковой и постоянного заместителя Министра социального обеспечения и здравоохранения Финляндии К. Пуро, с отчетами о проведенных совместных научных исследованиях по неврологии и нейрохирургии выступали проф. Э. Раудам (ЭССР), проф. Х. Троупп (Финляндия) и проф. О. Вальтимо (Финляндия). Комиссия решила, что сотрудничество по неврологии и нейрохирургии между Тартуским госуниверситетом и Хельсинкским университетом проводится успешно и плодотворно, получено много новой информации, полезной для развития теории и практики медицины как в СССР, так и в Финляндии. Результаты сов-

местных исследований в обеих странах опубликованы в более чем 20 статьях в местных и международных журналах.

Настоящий совместный сборник содержит 19 статей, в которых рассматриваются проблемы эпидемиологии, патогенеза, прогноза и хирургического лечения острых сосудистых заболеваний головного мозга.

Личные контакты специалистов обеих стран, ознакомление с клинической и научно-исследовательской работой лечебных учреждений Эстонской ССР и Финляндии способствуют лучшему взаимопониманию, развитию новых научных идей и улучшению лечебно-профилактической работы в обеих странах. Министерство здравоохранения СССР и Министерство социального обеспечения и здравоохранения Финляндии всячески поддерживали сотрудничество в области неврологии и нейрохирургии. От имени специалистов Эстонской ССР и Финляндии, принимающих участие в сотрудничестве, передаю искреннюю благодарность Министру здравоохранения СССР Б. П. Петровскому, заместителю Министра здравоохранения СССР Е. И. Новиковой, ректору Тартуского госуниверситета А. Я. Коопу, постоянному заместителю Министра социального обеспечения и здравоохранения Финляндии К. Пуро. Особо хочется отметить заслуги Генерального директора национального департамента здравоохранения Финляндии профессора Э. Кивало, который являлся инициатором и активным исполнителем программы нашего сотрудничества.

Сотрудничество специалистов Тартуского госуниверситета и Хельсинкского университета в области неврологии и нейрохирургии продолжится и в последующие годы в области сосудистой патологии головного мозга.

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Э. Раудам.

In the framework of the Soviet-Finnish agreement about cooperation in the field of medical science, public health and social maintenance, the agreement about cooperation in the area of neurology and neurosurgery between Tartu State University and Helsinki University was signed in Tallinn in November 1973. According to this agreement the Neurological and Neurosurgical Clinic of Tartu State University (Chief of the Clinic Prof. E. Raudam), the Neurological Clinic (Chief of the Clinic Prof. E. Kivalo) and the Neurosurgical Clinic (Chief of the Clinic Prof. H. Troupp) of Helsinki University started to participate in joint scientific investigations. In accordance with the agreement concluded and on the basis of an agreed programme, joint investigations were planned in the field of the distribution and the risk factors of acute vascular diseases of the brain in the Estonian SSR and in Finland as well as investigations concerning a number of problems of the pathogenesis, prognosis and treatment (including surgical treatment) of these diseases. In the period of 1974 to 1980 five joint symposia were held in Tallinn, Tartu and Helsinki, where the results of the conducted investigations were discussed and programmes of further studies were agreed upon.

At the third session of the mixed Soviet-Finnish comission on cooperation in the area of public health, medical science and social maintenance in Helsinki in September 1978 conducted under the joint chairmanship of the Deputy Minister of Public Health of the U.S.S.R, E. I. Novikova and the Permanent Deputy Minister of Social Care and Public Health of Finland K. Puro. Prof. E. Raudam (Estonian SSR), Prof. H. Troupp (Finland) and Prof. O. Valtimo (Finland) delivered reports on the joint scientific investigations carried out in the field of neurology and neurosurgery. The Commission decided that cooperation in the area of neurology and neurosurgery between Tartu State University and Helsinki University was being conducted with success and good results and that much fresh information had been obtained for the development of medical theory and practice both in the U.S.S.R. and in Finland. The results of joint investigations in both countries had been published in more than twenty papers of local and international journals.

The present joint collection contains nineteen reports dealing with the problems of epidemiology, pathogenesis, prognosis and surgical treatment of acute vascular diseases of the brain.

Personal contacts of the specialists of both the countries, acquaintance with the clinical and research work of the medical institutions of the Estonian SSR and Finland have contributed to a better understanding, to the development of new ideas and to the improvement of medical and prophylactic work in both the countries. The Ministry of Public Health of the U.S.S.R. and the Ministry of Social Care and Public Health of Finland have in every way supported the cooperation in the field of neurology and neurosurgery. On behalf of the specialists of the Estonian SSR and Finland, who have participated in this cooperation, I convey sincere gratitude to the Minister of Public Health of the U.S.S.R. B. P. Petrovsky, the Deputy Minister of Public Health of the U.S.S.R. E. I. Novikova, the Permanent Deputy Minister of Social Care and Public Health of Finland K. Puro, the Rector of Tartu State University A. J. Koop. In particular I would like to mention the merits of the General Director of the National Department of Public Health of Finland Prof. E. Kivalo, who was the initiator and active performer of the programme of our cooperation.

Professor, M.D. Chief of the Chair of Neurology and Neurosurgery of Tartu State University
E. Raudam

INCIDENCE OF STROKE IN THE ESPOO-KAUNIAINEN AREA, FINLAND, AND IN TARTU, ESTONIA, SOVIET UNION

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Cerebrovascular diseases (CVD) belong to the most common diseases in the developed countries. At present every eight European who dies has CVD as the principal cause of death (WHO, 1974). Data on the incidence of strokes, however, are scanty. In different studies the incidence varies between 90 and 260 per 100,000 annually, the average value being near 200 (Aho, 1975). Included in these figures are also those patients who already had had a stroke earlier and had a new attack of stroke during the study period. Comparison of the results of different studies is often hampered by the lack of age adjustment, and even if this has been performed, the standard population varies in different studies. In many studies the concept of stroke has also been deficiently defined.

In the present study we compared the incidence of stroke, defined by the same criterions, in the Espoo-Kauniainen area, Finland, and in the city of Tartu, Estonia, by using the population of Finland in the 1970 census as the standard population. Our aim was to clarify the starting-point in developing co-operation between the neurologic departments of Helsinki and Tartu universities in the research field of cerebrovascular diseases.

Material and methods

The diagnosis numbers 430—436 of the International Classification of Diseases were included in stroke exept number 435 — transient ischaemic attacks. In this way were included subarachnoid haemorrhage, intracerebral haemorrhage, embolic and thrombotic brain infarctions and acute non-specified cerebrovascular diseases. As a criterion for distinquishing transient ischaemic attacks from brain infarctions was the duration of symptoms and

signs: if these lasted less than 24 hours, the disease was regarded as a transient ischaemic attack; if they lasted longer, it meant a brain infarction. The type diagnosis of stroke was determined in both study areas by a neurologist who utilized the results of all examinations of the patients. In the Espoo-Kauniainen area the study was performed prospectively by the register method of the World Health Organization (WHO, 1971). All the persons in the study population who fell ill with a stroke during the years 1972 and 1973 were tried to be ascertained as completely as possible. The health care personnel of the study area was informed of the study and they were asked to enter in the register all cases, also those who were solely under treatment at home. The main stress, however, laid on an active search for cases: during the whole study period the hospitals of the study area were regularly visited and cases were asked for. The death certificates were checked every two weeks during the study period and one year after it. Registered were also those patients who already earlier had had a stroke and had a new one in the study period. In the present material, however, only those cases were included whose first stroke occurred in the study period. In counting the incidence figures the mean of the population in 1972 and in 1973 was used. The mean population was 113,100 persons. The method and results have been described in detail earlier (Aho, 1975).

In Tartu the study was performed retrospectively by surveying the files of the Outpatient Department and the Departments of Neurology and Neurosurgery of the Tartu Clinical Hospital from the years 1970 to 1973. Included were only those patients whose first stroke occurred in the study period. The Outpatient Department also supplied data on cases seen by doctors at home visits. The death certificates of the population under study were also surveyed. In counting the incidence figures the population of

Table 1

Age and sex distribution of the study populations in per cent

Age group (years)	Espoo-Kauniainen		Tartu	
	Males	Females	Males	Females
—19	35	32	32	25
20—29	21	21	19	17
30—39	17	16	16	14
40—49	13	12	13	14
50—59	7	9	9	10
60—69	5	7	7	10
70—79	2	3	3	7
80—	0.3	0.7	1	3
Total	100	100	100	100

Tartu on 1 January 1970 was used, when it constituted 90,459 persons. Also the results earlier published on Tartu (Zupping and Roose, 1976), were taken into consideration. The distribution of age and sex of the populations are presented in Table 1.

The population of Espoo-Kauniainen, especially the female population, is clearly younger than that of Tartu.

The direct method was used in age adjustment (Armitage, 1971). The standard population was the population of Finland in the 1970 census (males+females combined).

Results

In the Espoo-Kauniainen population 286 persons had a stroke during the two-year study period. Of them, 244 had not had a stroke earlier and they were accepted in the present study. In Tartu 667 persons had their first stroke during the study period

Table 2

Age and sex distribution of the cases

Age group (Years)	Espoo-Kauniainen			Tartu		
	Males	Females	Total	Males	Females	Total
20—29	5	2	7	2	2	4
30—39	2	9	11	6	1	7
40—49	13	13	26	21	10	31
50—59	23	17	40	27	26	53
60—69	43	27	70	62	73	135
70—79	21	40	61	70	170	240
80—	11	18	29	46	151	197
Total	118	126	244	234	433	667

Table 3

The distribution of the different types of stroke in per cent

Diagnosis	Espoo-Kauniainen (N-244)	Tartu (N-667)
Subarachnoid haemorrhage	17	6.5
Intracerebral haemorrhage	17	13.5
Brain infarction	61	80
Acute, nonspecified stroke	5	—
Total	100	100

of four years. The age- and sex-distributions of the materials are given in Table 2 and the diagnostic distributions in Table 3.

Two-thirds (66%) of the patients in Tartu while only one third (37%) of the patients in Espoo-Kauniainen were 70 years or older, that reflects the difference in the age structure of the two study populations (Table 1).

338 (51%) of the patients in Tartu and 95 (39%) of those in Espoo-Kauniainen died during the first three months after the onset of the stroke. Figure 1 depicts the age-depended incidence of stroke in males and in females in the populations studied. Table 4 presents the total incidences of males and of females in the study populations as age-adjusted.

Table 4

Total incidence of the first attack of stroke per 100,000 annually in the study populations; the population of Finland in the 1970 census as the standard for age adjustment (males + females)

	Espoo-Kauniainen		Tartu	
	Not age-adjusted incidence	Age-adjusted incidence	Not age-adjusted incidence	Age-adjusted incidence
Males	108	202	145	190
Females	107	147	216	139
Total	108	169	185	157

Discussion

The age-adjusted total incidence, 169 in the Espoo-Kauniainen area and 157 in Tartu, was in both populations of the same magnitude as most earlier studies. It was especially close to the incidence in Rochester in 1955 to 1969, which was 164 per 100,000 annually (Matsumoto et al., 1973). Only the first attack of stroke was included in that study. In both populations the incidence of males was higher than that of females in most age-groups (Figure 1). Also the age-adjusted total incidence was clearly higher in males (Table 4). The same trend of sex difference has been evident also in the death statistics (WHO 1974) as well as in many other incidence studies although its significance has been belittled (Kurtzke, 1969). The sex difference, however, is minimal compared, for example, with that in the coronary heart disease, where the high incidence of males especially in the young age-groups is a characteristic feature.

The prospective study in Finland and a retrospective one in Estonia gave nearly identical results. The small existing diffe-

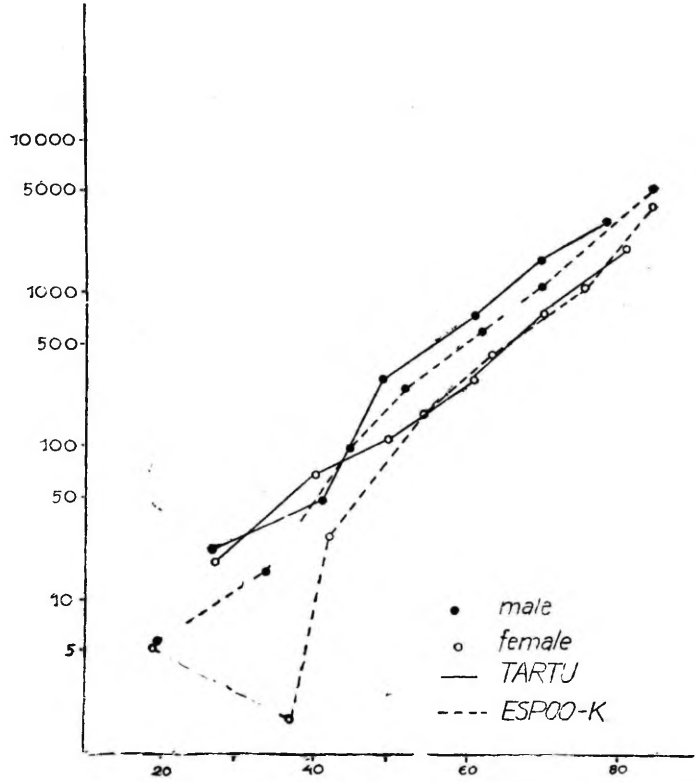

Figure 1. Age- and sex-dependent incidence of stroke in Tartu and Espoo-Kauniainen

rences may be explained even by methodological differences; it is more difficult to find very mild cases by the retrospective than by the prospective method.

Especially in the older age-groups the incidence seems to be of the same magnitude in both the study populations. In females under 50 years of age the incidence was higher in the Espoo-Kauniainen that in the Tartu population. This probably depends on the exceptionally high incidence of subarachnoid haemorrhage in Finland, which is also confirmed by the fact that 17% of the total material in Finland and only 6,5% in Estonia had subarachnoid haemorrhage. In earlier studies the incidence of subarachnoid haemorrhage has been 16.8 in Finland and 8.2 per 100,000 annually in Estonia (Pakarinen 1967, Raudam and Tomberg, personal communication 1974). Figure 1 also shows that 50- to 70-year old Finnish males have a little higher incidence than the Estonian males of the same age-groups.

The higher fatality rate during three months after onset of the disease in Estonian patients depends on the higher mean age of the patients since high age raises the fatality rate of stroke (Marquardsen, 1969). Despite small differences, we can conclude that the total incidence of stroke on both banks of the Gulf of Finland is very similar in magnitude. We stress, however, that differences in the study methods may have exercized an influence on the results.

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ЗАБОЛЕВАЕМОСТЬ ИНСУЛЬТОМ В ЭСПОО И КАУНИАЙНЕНЕ (ФИНЛЯНДИЯ) И В ГОРОДЕ ТАРТУ ЭСТОНСКОЙ ССР

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Резюме

Заболеваемость инсультом была установлена проспективно в Финляндии в городах Эспоо и Каунианнен в 1972—1973 годы и ретроспективно в городе Тарту Эстонской ССР в течение 4-х лет (1970—1973 гг.) В исследование включали лишь первичное заболевание инсультом.

За указанные периоды в Эспоо и Каунианнене заболели инсультом 244, а в г. Тарту 667 жителей. Стандартизованная заболеваемость инсультом в Эспоо и Каунианнене была 202

случая на 100000 населения для мужчин и 147/100000 для женщин, а в г. Тарту, соответственно 190/100000 среди мужчин и 139/100000 среди женщин. Эти данные хорошо соответствуют данным, полученным в других аналогичных исследованиях. По сравнению с Эстонской ССР несколько повышенная частота инсульта в Эспоо и Каунпайнене может быть связана с методическими разницами, влияющими на интерпретацию результатов.

Частота различных форм инсульта оказалась относительно сходной в двух исследуемых странах, за исключением заболеваемости субарахноидальным кровоизлиянием (САК). Последнее наблюдалось почти в 3 раза чаще в Финляндии, чем в Эстонской ССР. Возможно, что такая высокая частота САК среди финнов частично связана с более молодой структурой населения исследованных районов Финляндии.

Летальность за три месяца после начала заболевания была несколько более высокая в г. Тарту (51%), чем в Эспоо и Каунпайнене (39%), очевидно эта разница объясняется более высоким средним возрастом больных инсультом в Эстонской ССР.

CEREBROVASCULAR DISEASE IN TARTU, ESTONIA, USSR, 1970 THROUGH 1973; FREQUENCY, PROGNOSIS AND POPULATION SELECTIVITY

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In the last two decades cardiovascular diseases have been the subject of great common and scientific interest. The published reports and international epidemiologic studies have mainly dealt with the coronary heart disease. After the coronary heart disease and cancer, vascular diseases of the brain are now the third leading cause of death in most developed countries, account for a major amount of disability. Rehabilitation and treating of a stroke once it has occurred are obviously less rewarding than attempts at prevention. Differences in cerebrovascular epidemiology among various countries may suggest the existence of powerful environmental influences and can be used to formulate etiological hypotheses.

Epidemiologic data on cerebrovascular diseases (CVD) are far from complete. Until 1965 knowledge of the epidemiology of CVD was based mostly on retrospective studies, mortality data, autopsy or other often inadequate or nonrepresentative statistics. Only during the last decade have prospective population studies of the morbidity of CVD been performed[1, 2]. Population surveys provide the best available information on the incidence and relative frequency of the major types of CVD.

Some evidence suggests wide geographic variations in the incidence and mortality from CVD. The rates of death from stroke show wide variations between different countries and also within countries. Among countries Japan has a rate considerably higher, and Mexico considerably lower than the United States; Canada and Ireland have rates that are about the same as those in the white population of the US[2, 4]. In the US death from CVD is most common in the south central and south Atlantic states and least common in the south-western and the Rocky Mountain states[3, 4, 5]. It has been shown that the higher mortality from CVD

reported in the south-eastern states is due chiefly to a greater frequency of cerebral hemorrhage and hypertension [6]. A study of hospitalized stroke patients revealed that the incidence of stroke is higher in the high stroke death rate areas in the US [7].

Autopsy studies have also revealed geographic variations in the frequency of cerebral atherosclerosis. The highest frequency of cerebral atherosclerosis is found in the Japanese and Finnish populations and lowest in the Polish population; the Norwegian, Greek, Italian and Minnesota populations show frequencies between these extremes [8, 9]. The highest average involvement of the cerebral vessels is also found in the Finnish population [9].

So far, there have been only a few community-based studies on the incidence of CVD and the results of these do not show remarkable differences between different geographic areas [10, 11, 12, 13].

This study was undertaken to establish the incidence and mortality for various types of stroke in the population of Tartu, USSR. The Tartu Outpatient Clinic and the Neurological and Neurosurgical Departments of the Tartu Clinical Hospital provide essentially all of the neurological care for persons living in Tartu. Therefore, identification is assured of practically all Tartu residents in whom a serious illness has been diagnosed. This includes diagnoses made in the hospital, at the time of an outpatient clinic visit or a house call, or at autopsy for all medical care units in Tartu.

Methods

All medical records for the population of Tartu, which were kept at the Tartu Outpatient Clinic and Neurological and Neurosurgical Departments of the Tartu Clinical Hospital, were reviewed for the period 1970 to 1973, and those with a diagnosis of brain infarction, transient ischemic attacks (TIAs), cerebral hemorrhage or subarachnoid hemorrhage (SAH) were identified. Almost all patients were seen by a neurologist during the first day after the onset. The medical records were examined in depth to identify the presence of other significant diseases and the length of survival.

Patients who were residents of Tartu and who had an onset of their first stroke in the study period were included in the determination of incidence. Only the first stroke was considered when determining incidence. For mortality studies, patients were included who had a stroke and died during the stated years. Death certificates were reviewed to find any cases of stroke diagnosed for the first time at autopsy.

The diagnosis of the type of cerebrovascular disease was based on the information available in the clinical or autopsy records. Cerebral infarction was diagnosed in cases with a rapid onset of focal neurological deficit persisting for more than 24 hours and with a clear cerebrospinal fluid or without signs of meningeal irritation. No effort was made to distinguish between cerebral thrombosis and embolus.

TIA was diagnosed if there was a history of focal neurological dysfunction lasting for 24 hours or less. Attacks solely of aphasia, monoparesis, hemiparesis, hemihypesthesia and/or monocular visual loss were considered to be carotid attacks. Vertebrobasilar attacks were defined as consisting of two or more of the following symptoms: diplopia, dysphagia, dysarthria, vertigo, numbness of the face, and motor and sensory alterations in one or more limbs.

The diagnosis of a cerebral hemorrhage was based on some or all of the following symptoms: localizing neurological signs, disturbance of consciousness, meningeal irritation, bloody spinal fluid, and autopsy confirmation. SAH was distinguished from an intracerebral hemorrhage by the lack of localizing neurological signs or by autopsy.

For convenience, cerebral infarction, cerebral hemorrhage and SAH collectively will be referred to as cases of stroke. TIAs will be analyzed separately.

The data on the sex and age distribution of the population of Tartu were obtained from the census data on January 1, 1970. The total population in Tartu at the same time was 90,459.

Results

A total of 786 cases were included in the study; without the cases of TIA the number was 667. Forty per cent of the patients were hospitalized in the Neurological or Neurosurgical Departments. Cerebral infarction from all causes accounted for 80% of all cases of stroke, intracerebral hemorrhage accounted for 13.5% of the cases and SAH accounted for 6.5%.

Incidence

Table 1 shows the number and incidence rates for stroke according to age and sex for the population of Tartu.

The incidence rates for stroke were higher for men than for women in each age group over the age of 30. At the same time the rate was increasing significantly in each older age group. The rate of persons was 184/100,000 population per year.

The number of cases and average annual incidence rates for cerebral infarction are shown in Table 2.

Table 1

Number of Cases and Average Annual Incidence of Stroke per 100,000 Population, Tartu, 1970—1973 *

Age group (year)	Men		Women		Total	
	No.	Rate	No.	Rate	No.	Rate
20—29	2	6	2	6	4	12
30—39	6	22	1	3	7	13
40—49	21	97	10	35	31	62
50—59	27	197	26	131	53	158
60—69	62	579	73	372	135	445
70—79	70	1,520	170	1,268	240	1,329
80—89	40	3,020	136	2,760	176	2,839
90—99	6	6,250	15	3,440	21	3,950
Total	234	223	433	165	667	184

* Rates are based on the population on 1 January 1970.

Table 2

Number of Cases and Average Annual Incidence Rates for Cerebral Infarction per 100,000 Population, Tartu, 1970—1973 *

Age group (years)	Men		Women		Total	
	No.	Rate	No.	Rate	No.	Rate
20—29	1	3	1	3	2	3
30—39	3	11	1	3	4	7
40—49	11	51	4	14	15	31
50—59	20	146	13	63	33	98
60—69	47	440	53	270	100	324
70—79	62	1,349	145	1,077	207	1,149
80—89	31	2,345	120	2,600	151	2,435
90—99	6	6,250	14	3,210	20	3,760
Total	181	176	351	134	532	147

* Rates are based on the population on 1 January 1970.

The overall incidence rate for cerebral infarction was 147/100,000 population. It increased with age up to the oldest age group and was higher for men than for women.

Table 3 shows the number of cases and average annual incidence rates for cerebral hemorrhage and SAH.

The overall incidence rate for cerebral hemorrhage was 25/100,000 population and the one for SAH was 12/100,000 population. The rate for cerebral hemorrhage increased up to the age of 80—89 and the rate for SAH also increased up to the age of

Table 3

Number of Cases and Average Annual Incidence Rates for Cerebral Hemorrhage and Subarachnoid Hemorrhage per 100,0000 Population, Tartu, 1970—1973 *

Age group (years)	Cerebral hemorrhage		SAH	
	No.	Rate	No.	Rate
20—29	—	—	—	3
30—39	2	4	1	2
40—49	7	14	8	18
50—59	11	33	9	27
60—69	27	89	9	30
70—79	21	116	12	66
80—89	22	360	3	48
90—99	1	188	—	—
Total	91	25	44	12

* Rates are based on the population on 1 January 1970.

70—79. There were no significant differences in the rates for men and women.

The incidence rate for TIA was 33/100,000 population per year (Table 4).

Table 4

Number of Cases and Average Annual Incidence of TIA per 100,000 Population, Tartu, 1970—1973 *

Age group (years)	Men		Women		Total	
	No.	Rate	No.	Rate	No.	Rate
20—29	0	0	1	3	1	1
30—39	1	4	0	0	1	2
40—49	3	14	8	28	11	22
50—59	8	58	12	61	20	60
60—69	12	112	26	132	38	125
70—79	11	239	23	170	34	188
80—89	5	378	8	167	13	213
90—99	0	0	1	229	1	188
Total	40	36	79	33	119	33

* Rates are based on the population on 1 January 1970.

The rate of TIA was higher in men only in the older age groups. In 66% of the cases transient ischemia was in the carotid arterial system and in the vertebrobasilar arterial system in 34% of the cases. During the follow-up period of one to three

years completed stroke developed in 10% of cases, in most cases it occurred during the first year after the first attack.

Frequency of hypertension

The prevalence of hypertension (blood pressure values more than 160/95 mm Hg) in the total material was 46%. Hypertension was diagnosed in 44% of cases with cerebral infarction, in 15% of cases with TIA, in 65% of patients with cerebral hemorrhage and in 30% of patients with SAH.

Other associated diseases

The most common associated diseases in cases of cerebral infarction were atherosclerotic coronary diseases (33%), peripheral atherosclerosis (7%) and diabetes (4%). In patients with cerebral hemorrhage these diseases were diagnosed as follows: atherosclerotic coronary artery diseases in 13%, peripheral atherosclerosis in 7% and diabetes in 2% of all cases. A comparatively high prevalence of coronary artery diseases (25%) and peripheral atherosclerosis (12%) in the present material was established in patients with TIA. The prevalence of coronary artery diseases was lowest (11%) in the cases of SAH.

Survival

Probabilities of survival for the four years after the onset of various types of stroke are based on 1 to 4 year follow-up of the cases recorded during the years 1970 through 1973. The highest fatality rate for all types of stroke was found during the first month, after that period the fatality was much lower. The one-month survival for cerebral infarction was 54%, for cerebral hemorrhage 28% and for SAH 62%. One-year survival for cerebral infarction was 44%, for cerebral hemorrhage 25% and for SAH 58%. During the following four years the survival for all types of stroke decreased nonessentially.

Mortality rate

The mortality rate for stroke for this population was 98/100,000 per year.

Discussion

There are many reports on the frequency of stroke but only a few are useful for deriving estimates applicable to the whole

population. It is well known that estimates of the incidence of stroke from mortality statistics cannot be expected to correspond to those derived from morbidity surveys in the total population of a community. The information based on the data from a particular clinic may not be the same as that for the entire community because of the selection bias of the hospital. Therefore, only community-based studies can give us a true picture of the incidence of stroke and its subtypes among different populations.

The data of the incidence of stroke in various communities are given in Table 5.

Table 5

Incidence of Stroke in Different Communities

Community	Study period	Population of study area	Incidence	Age-adjusted incidence *
Rochester, Minnesota [14]	10	28250	194	190
Rochester, Minnesota [10]	15	32600	154	164
Middlesex, Connecticut [11]	1	83000	230	170
Carlisle, England [15]	7	71100	143	119
Mid-Missouri, USA [16]	1	78000	258	198
North Dakota and Moorhead, Minnesota [17]	2	94000	217	242
Espoo-Kauniainen, Finland [13]	2	113100	126	—
Hisajama, Japan [1]	4	6521	127	—
Tartu, Estonia, USSR	4	90459	184	168

* Age-adjusted incidence according to the population of the USA in 1960.

It is seen that the incidences of stroke in Rochester, USA, and in Tartu Estonian SSR, USSR, are very similar. In other communities, except for Carlisle, England, the Espoo-Kauniainen area of Finland and Hisajama, Japan, the incidence is a little higher. However, in these studies the number of unknown types of stroke is comparatively high, which makes one suspect that cases other than stroke also have been included in the study. The comparatively low incidence found in the Espoo-Kauniainen area of Finland might be explained by the young structure of this population. The studies in Hisajama and Carlisle, which assessed the lower incidence of stroke as well, have excluded the younger age groups of the population and the outpatient fatal cases of stroke.

It must be said, however that the data on the incidence rates in different communities are not exactly comparable because of the different age structure of the population studied. To overcome this, every investigator should reconstitute the series using the same standard population. The age-adjusted incidences of stroke are very similar in most communities (Table 5).

The incidence of TIA in Tartu is very close to the data reported from Rochester — 33 and 31 per 100,000 population per year [18], respectively.

The percentage of cerebral infarction among all strokes is similiar in Rochester, Framingham, Goulborn and Tartu (Table 6).

Table 6

Percentage Distribution of Various Types of Stroke in Different Communities

Community	Cerebral infarction		Cerebral hemorrhage	SAH	Unknown
	Thrombosis	Embolism			
Rochester, Minnesota [10]	75	3	10	5	7
Rochester, Minnesota [14]	79		10	6	5
Framingham, Massachussetts [2]	63	15	4	18	—
Connecticut, USA [11]	50		36		14
Hisajama, Japan [1]	63		25	6	6
Goulburn, Australia [12]	73		19	6	2
Espoo-Kauniainen, Finland [13]	61		16	15	7
Tartu, Estonia, USSR	80		13,5	6,5	—

The percentage of cerebral hemorrhage is lowest in Framingham. The relatively high percentage of SAH in the structure of stroke in Framingham and Espoo-Kauniainen is obviously partly associated with a younger population included into these studies.

In summary, the data concerning the incidence of CVD and its subtypes, dependence on age and sex, and the mortality rate in Tartu are close to the corresponding data reported so far from other countries.

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ОСТРЫЕ ЦЕРЕБРОВАСКУЛЯРНЫЕ ЗАБОЛЕВАНИЯ В ГОРОДЕ ТАРТУ ЭСТОНСКОЙ ССР В 1970—1973 ГГ.: ЗАБОЛЕВАЕМОСТЬ И ИСХОД.

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Резюме

Острые цереброваскулярные заболевания являются одной из основных причин смертности в большинстве развитых стран. Целью настоящей работы было установление частоты заболеваемости инсультом и его отдельными формами, а также летальности инсульта в г. Тарту с общей численностью населения 90459 жителей в 1970 году. В исследование включены все случаи инсульта в г. Тарту за 1970—1973 годы.

Выяснилось, что общая заболеваемость инсультом в г. Тарту составила 184 ± 14 случаев на 100000 населения в год, причём значительно чаще болели мужчины, чем женщины. Анализ структуры инсульта показал, что инфаркт мозга значительно превалировал над другими формами инсульта, составляя 80% случаев из них. Внутримозговые кровоизлияния равнялись 13,5% и субарахноидальные кровоизлияния — 6,5% из всех случаев инсульта.

Заболеваемость инфарктом мозга составляла 147 случаев на 100000 населения в год. В анамнезе у 26% больных инфар-

ктом мозга наблюдались атаки транзиторной ишемии головного мозга. Общая заболеваемость внутримозговым кровоизлиянием оказалась 25±5 случаев, а субарахноидальным кровоизлиянием — 12±5 случаев на 100000 населения в год.

В период наблюдения было диагностировано 119 случаев транзиторной ишемии головного мозга со средней частотой 33 случая на 100000 населения в год, причём 66% приступов были в системе сонных артерий и 34% — в вертебробазилярной системе. За 1—3-летний период наблюдения ишемическое размягчение головного мозга возникло в 10% случаев транзиторной ишемии в основном в течение года после первичной атаки.

Общая летальность инсульта в острый период заболевания составила 49±2%, отличаясь значительно при отдельных формах инсульта — 72±5% при кровоизлиянии в мозг, 46±2% при инфаркте мозга и 39±8% при субарахноидальном кровоизлиянии. За 4-летний катамнез существенно повысилась смертность среди больных, перенесших инфаркт мозга. В то же время общая летальность внутримозгового и субарахноидального кровоизлияний изменилась несущественно.

EPIDEMIOLOGY OF PRIMARY SUBARACHNOID HEMORRHAGES IN THE ESTONIAN SSR

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In the last decade cerebrovascular diseases have been the subject of epidemiologic studies, the majority of which have dealt mainly with the incidence and the mortality of stroke as a whole and the diagnostic distributions of stroke types as well. Less attention has been paid to the epidemiology of different subtypes of stroke.

Primary subarachnoid hemorrhages (SAH) have been the subject of several community-based studies, according to which they comprise 5—18% of the different types of stroke (1—6). In Tartu, the Estonian SSR, SAH were 6,5% of the total number of stroke (7). The earlier epidemiologic studies have revealed geographic variations in the frequency of SAH, the reported incidence varying between 5.5—19 cases per 100,000 population per year (6,8—13).

The purpose of the present study was to assess the incidence and the prognosis of primary subarachnoid hemorrhages among the population of the Estonian SSR.

Methods

The present series comprised all diagnosed cases of primary SAH among the population of two towns (Tartu and Pärnu) and 5 rural districts during an eight-year period, 1966—1973, inclusive. All medical records, which were kept at the Neurological and Neurosurgical Departments of the Tartu Clinical Hospital, the Tartu Out-patient Clinic, the Pärnu Hospital and District Hospitals as well as autopsy minutes from the Departments of Pathology and Department of Forensic Medicine and death certificates were retrospectively reviewed for the period from 1966 through 1973, and those with a diagnosis of primary SAH were identified. The cases of secondary SAH due to hypertensive intra-

cerebral hemorrhage, head injury, blood dyscrasias, brain tumors, etc., were omitted. Only the first hemorrhage was considered when determining the incidence. Our criteria for case-identification corresponded to those used by Pakarinen (11). The etiology of SAH was ascertained in 78% of cases by cerebral angiography and/or autopsy.

The data on the sex and age distribution of the study population were obtained from the census on January 1, 1970. The total population included in the study was 391, 403 individuals in 1970, which comprised about 30% of the population of the Estonian SSR at that time.

Results

The total number of identified cases of SAH during 1966–1973 was 274. The incidence of SAH for the town population (Tartu and Pärnu) was higher than for the rural population (Table 1), but this difference was not statistically significant. The rate per year did not vary significantly during the eight years studied.

Table 1

Number of cases and average annual incidence rate for SAH per 100,000 population in 1966—1973

Area	Incidence	
	No.	Rate
Tartu	84	11.6
Pärnu	46	11.4
5 rural districts	144	7.0
Total	274	8.7

Women predominated among the patients, but the incidence rate for women was only slightly higher than for men (Table 2). After the standardization of the data (indirect method, the age-specific incidence rate for the population of Tartu has been considered as a standard) in contrast, the incidence was higher in men than in women, although not significantly.

Table 2 shows also the increasing incidence rate for SAH in older age-groups of both sexes. The age-specific incidence rate in men achieved its maximum in earlier age-groups (50—59 years) than in women. 62.4 per cent of all the cases were between 40—69 years. The mean age was 52.9 years (49 years in men, 55 in women).

SAH was caused by the rupture of an aneurysm in 41% and by arteriovenous malformation in 3.7% of all cases in whom

Table 2

Age- and sex-specific annual incidence rate for SAH per 100,000 population of Tartu and Pärnu, 1966—1973

Age	Male	Female	Total
<20	0	0.6	0.3
20—29	5.5	3.1	4.2
30—39	10.7	5.3	7.9
40—49	14.6	9.9	11.9
50—59	42.6	20.0	30.5
60—69	17.5	30.6	25.9
70<	27.1	46.4	41.6
Total	10.7	12.2	11.5
Standardized rate	12.6	10.8	11.4

angiography or autopsy was performed. Localization of the aneurysms was as follows: anterior cerebral, anterior communicating artery — 29.4%, middle cerebral artery — 25.9%, internal carotid artery — 24.7%, vertebro-basilar system — 12%, non-differentiated localization — 9.4% of the cases. Multiple aneurysms were found in 7% of the cases.

Among the patients with SAH caused by a ruptured aneurysm persons of younger age predominated — 84% of the cases were younger than 60.

During the acute period of illness (8-week period) 46% of the patients died, 44% recovered well and 10% had some neurological deficiencies. Sudden death occurred in 32.5% of all the fatal cases, without these cases the case fatality rate was 31%. The case fatality rate depended on the etiology of SAH — it was much higher in patients with the rupture of an aneurysm (68%) than in patients with an arteriovenous malformation (12.5%) or in SAH cases of unknown causes (36%). The case fatality rate was also higher in cases of aneurysms of the vertebrobasilar system and of the middle cerebral artery, it was lowest in patients with internal carotid artery aneurysms.

The number of early recurrences of SAH was significantly higher in patients with a ruptured intracranial aneurysm (35%) than in others (13.5%). The incidence of recurrent hemorrhages increased within the second week of the disease. The case fatality rate in the case of a recurrent hemorrhage was 85% and in the initial hemorrhage — 35%.

During 1966—1973 altogether 134 patients had died from the first or the recurrent SAH. The mortality rate for SAH for our

total population was 4.3/100,000 per year without any significant differences between two sexes. The mortality rate was increasing in older age-groups, whereas it was remarkably higher in patients over 50 than in patients under 50 (9.6 and 2.1/100,000 per year, respectively).

Life-time table analysis gave a 86.5% probability for a year's survival, 80.1% for three-year survival and 77.4% for five-year survival.

Discussion

The results of this study show that the incidence of primary SAH in Estonia is remarkably similar to the frequency of SAH in other countries (Table 3).

Table 3

Incidence of SAH in different communities

Community	Study years	Population of study area	Incidence
Rochester, Minnesota [4]	1945—1954	30,425	10.6
Oslo, Norway [8]	1950—1954	400,000	6.0
Carlisle, England [14]	1955—1961	71,101	10.9
Netherlands [9]	1950—1962	400,000	7.8
Göteborg, Sweden [15]	1956—1959	—	9.0
Helsinki, Finland [11]	1954—1961	439,750	15.7
Iceland [12]	1958—1968	185,505	8.0
Pécs, Hungary [13]	1959—1968	136,556	5.5
Fargo, Moorhead and North Dakota, Minnesota [2]	1965—1966	94,037	17.0
Espoo-Kauniainen, Finland [6]	1972—1973	113,100	19.5
Estonia, USSR	1966—1973	391,403	8.7

However, the incidence of SAH in Finland as reported by Pakarinen (11) and Aho (6) and in the U.S. (2) is higher than in Estonia. A higher incidence of SAH among the urban than the rural population was found also in Iceland (12) and Hungary (13), which is probably due to some hypodiagnostic of the disease among the rural population.

The incidence of SAH increases with age, but in the present study the incidence rate in elderly age-groups was relatively higher than it has been reported from other countries, while, on the contrary it was lower in younger age-groups (11, 12, 14).

Our study revealed no clear sex difference in the incidence of SAH, but the age-specific incidence rates show that among men SAH occurs at a younger age than among women.

The frequency of arterial aneurysms in the present series was relatively low due to incomplete angiographic examinations — usually only unilateral or bilateral carotid angiography was per-

formed, but the percentage of arteriovenous malformations was in agreement with the earlier reports (8, 11).

Our material includes a large number of patients dying before admission to hospital, this explains a considerably high case fatality and mortality rate in the present series. The mortality is especially high during the initial period of SAH with a maximum in the first and the second week of the disease due to the frequent recurrences at that time. Although the risk of death decreases later, the estimated late mortality was also considerable.

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ЭПИДЕМИОЛОГИЯ СПОНТАННЫХ СУБАРАХНОИДАЛЬНЫХ КРОВОИЗЛИЯНИЙ В ЭСТОНСКОЙ ССР

Т. Томберг

Резюме

Целью данной работы являлось изучение распространения и прогноза спонтанных субарахноидальных кровоизлияний (САК) среди населения Эстонской ССР. Исследования проведены ретроспективно в 2 городах (Тарту и Пярну) и в 5 сельских районах Эстонской ССР в течение 8 лет (1966—1973 гг.). Всего зарегистрировано 274 первичных случаев спонтанных САК, что составляет в среднем 8,7 случаев на 100000 населения в год (11,5 случаев среди городского и 7,0 случаев среди сельского населения). Заболеваемость САК не отличалась по полу больных, но увеличивалась с возрастом, особенно после 50 лет. Отмечалась относительно высокая заболеваемость САК среди населения пожилого возраста. Этиологическими факторами САК в 41% случаев оказались артериальные аневризмы и в 3,7% случаев — артерио-венозные аневризмы.

Смертность от спонтанных САК составила 4,3 случаев на 100000 населения в год. Летальность в острой и подострой стадии САК была 46%, причем 32,5% числа умерших составляли случаи скоропостижной внебольничной смерти.

Ведущей причиной летального исхода САК являются ранние и поздние рецидивы кровоизлияния, которые чаще наблюдаются во второй неделе заболевания. Прогноз САК является значительно более неблагоприятным при разорвавшихся артериальных аневризмах, чем при САК другой этиологии. Методом вычисления таблиц смертности установлено, что вероятность выживания в течение первого года после острого периода САК составляет 86,5% и в течение пятого года — 77,4%.

RISK FACTORS IN STROKE

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Cerebrovascular diseases play an important role in the structure of morbidity, mortality and disability of the population. Despite of an increased understanding of the pathogenesis of brain lesions in stroke during the last decade, the results of treatment and rehabilitation of this disease show little improvement. The brain tissue is very sensitive to hypoxia and usually irreversible damage to the brain tissue develops far before any treatment can be initiated. The best answer to this devastating illness is a preventive approach. Epidemiological investigations have begun to identify highly vulnerable persons and the factors which predispose stroke. An epidemiological study for ascertaining risk factors may be retrospective and prospective. The former is more economical, quicker, furnishes a larger number of cases and the preselection of cases, lack of uniformly applied criteria and is less tedious to carry out. However, it suffers from the bias of an excess of incomplete, unplanned and unstandardized observations.

A prospective study is more cumbersome, costly and slow to yield results. Prospective studies allow planned observations and relate antecedent population characteristics to the development of disease many years later [1].

The purpose of this retrospective study was to assess the role of some factors which may predispose brain infarction. It was hoped that the investigation might give valuable information on the etiology of brain infarction in the Estonian population.

Methods

The study is based on 249 patients with brain infarction and 52 patients with cerebral hemorrhage admitted to the Neurological and Neurosurgical Departments of Tartu Clinical Hospital. The

diagnosis of each case was confined to history, to clinical and neurological examinations and in 20% of cases to cerebral angiography. Cases with proved cerebral embolism of cardiac origin in young patients were excluded. In the history of 34% of the patients were transient ischemic attacks. The study material consisted of 135 females and 114 males at an age of 35 to 96 years in cases of cerebral infarction, and 28 females and 24 males at an age of 33—79 years in cases of cerebral hemorrhage. The control group consisted of 190 persons without evidence of cerebrovascular disturbances in history and clinical examination. Most of them were hospitalized for the treatment of diseases of the peripheral nervous system. There were 103 females and 87 males at an age ranging from 31 to 81 years.

All the subjects under study were asked for the incidence of stroke in the family (parents, brothers, sisters) and cigarette habits. The arterial blood pressure, the height and weight were measured in all cases. Cholesterol, beta-lipoproteins, glucose and hemoglobin were measured in the blood. ECG was registered in all patients. The glucose tolerance test was performed in 31 cases with cerebral infarction and in 23 controls. Biochemical and metabolic evaluations were made during the third week of illness.

Results

The high blood pressure is clearly the most important risk factor in stroke. The percentage of cases with an elevated blood pressure (Table 1) among the patients with cerebral infarction

Risk factors in stroke

Table 1

Risk factor	Control	Cerebral infarction	Cerebral hemorrhage
Blood pressure $\geqslant$ 160/95 mm Hg	13±2	50±3*	52±7*
Systolic and diastolic blood pressure $\geqslant$ 160/95 mm Hg	5±2	29±3*	42±7*
Systolic blood pressure $\geqslant$ 160 mm Hg	3±1	13±2*	6±3*
Diastolic blood pressure $\geqslant$ 95 mm Hg	4±1	7±2*	4±3
ECG abnormalities	26±4	66±3*	53±7*
Blood sugar $\geqslant$ 120 mg %	6±2	23±3*	29±6*
Cholesterol $\geqslant$ 240 mg %	33±4	44±3*	54±8*
Beta-lipoproteins $\geqslant$ 55 u	38±4	48±3*	35±7
Hemoglobin $\geqslant$ 100%	14±2	36±3*	26±6*
female	3±2	20±3*	—
male	28±5	55±5	—
Stroke in the family	12±2	17±3	19±6
Cigarette habit	28±3	33±3	44±8
female	4±2	4±2	12±8
male	57±6	68±5	73±10
Overweight	48±6	38±4	40±8

* $P < 0,05$

and cerebral hemorrhage was considerably higher than in the control group, i. e. 50 ± 3% in cases of cerebral infarction, 52 ± 3% in cerebral hemorrhage and 13 ± 2% in the control group, respectively.

The difference was present in all age-groups. The mean values for the systolic and the diastolic blood pressure were also significantly higher in stroke patients compared to the controls (Table 2). In patients with stroke simultaneous elevation of both the systolic and the diastolic blood pressure and of the systolic pressure alone were revealed (Table 1).

Table 2

Mean values of risk factors in stroke

Risk faktor	Control	Cerebral infarction	Cerebral hemorrhage
Systolic blood pressure mm Hg	136±2	158±0*	165±6*
Diastolic blood pressure mm Hg	83±1	92±1*	97±3*
Blood sugar mg %	95±1	114±4*	115±7*
Cholesterol mg %	223±3	242±4*	244±8*
Beta-lipoproteins u.	52.3±1,3	58.3±1.4*	53.0±3.0*
Hemoglobin %	89,5±0.5	96.0±0.5*	93.0±1.0*
female	85.0±1.0	91.5±1.0*	—
male	94.0±1.0	101.5±8.5*	—

* $P < 0.05$

The ECG abnormalities were revaled in 66% of cases with brain infarction, in 53% of cases with cerebral hemorrhage and in 26% of the controls. (Table 1). Myocardiac ischemia and arrhythmia were more characteristic of patients with cerebral infarction, and left ventricular hypertrophy was typical of subjects with cerebral hemorrhage.

The percentage of cases with an elevated blood glucose level (above 120 mg %) was significantly higher in patients suffering from stroke, i.e. 23% in brain infarction and 29% in brain hemorrhage against 6% in the controls. (Table 1). A statistically significant increased mean blood glucose concentration was established in cases of stroke as well (Table 2). The disturbances of glucose metabolism were much more frequently revealed by the glucose tolerance test. An abnormal test was found in 46% of cases with cerebral infarction compared to 17% in the controls. ($P<0.05$).

Among the blood lipid abnormalities elevated cholesterol values (above 240 mg %) were more frequently observed in all stroke patients compared to the controls, while elevation of the lipoprotein content (above 55 u) in the blood was characteristic only of ischemic stroke (Table 1). There were no differences in

the lipid level between men and women and they were not correlated with the age of the patients. However, it must be noted that the percentage of elevated lipid values was quite high also in the control group. The mean values for blood cholesterol and beta-lipoproteins were also significantly increased in stroke patients compared to the controls (Table 2), both in men and women.

The percentage of an elevated blood hemoglobin content (above 100%) was significantly higher in patients with stroke (Table 1), i. e. 36% in cases of cerebral infarction, 26% in cases of cerebral hemorrhage and 14% in the controls. It was a characteristic finding in all the age-groups.

In families of patients with cerebral hemorrhage and infarction stroke occurred somewhat more frequently than in families of the control subjects, respectively, 17% in cases of cerebral infarction, 19% in cases of cerebral hemorrhage and 12% in the controls.

No significant differences were found in smoking habits and in the relative weight between the stroke and control groups.

Next, the frequency of various combined risk factors in cases of brain infarction was studied. The following factors were considered: hypertension, ECG abnormalities, blood glucose, beta-lipoproteins and hemoglobin. It was found that two or more factors occurred considerably more frequently in the patients with stroke than in the controls ($P<0.05$). Combination of three factors was observed almost 10 times and of four factors 30 times more often in patients with brain infarction than in the controls ($P<0.05$). Almost 40% of stroke patients had three or more associated factors whereas this was revealed only in 3% of the controls ($P<0.05$).

Discussion

This study has revealed a number of factors which are significantly associated with stroke. However uncertain the final answer is, certain precursors for stroke such as hypertension, ECG abnormalities, carbohydrate disorders, hyperlipidemia and an elevated blood hemoglobin level, are important. Of these factors hypertension is clearly the most important contributor to stroke [2, 3, 4]. It is known that hypertension, besides accelerating atherosclerosis, may precipitate strokes by impairing the cardiac function as well as an mechanically damaging diseased vessels or by reducing the cerebral blood flow.

Most victims of stroke are already ill with cardiac diseases, having several kinds of ECG abnormalities.[5] It has been established in the present study that coronary heart diseases and several kinds of arrhythmias mainly predispose subject to the development of ischemic stroke, whereas left ventricular hypertrophy,

usually caused by permanent hypertension, is most of all associated with cerebral hemorrhage. All these cardiac impairments, being the results of atherosclerosis and hypertension, weaken myocardiac action, diminish the cardiac output and the cerebral blood flow, contributing to the development of ischemic stroke. Atrial fibrillation and other dysrythmias are mainly associated with embolic stroke [1].

It has been established that impaired carbohydrate metabolism is associated with an increased risk of stroke [1]. Diabetes is clearly associated with the disease both large and small vessels [6], with multiple lipid abnormalities and with obesity and hypertension. Thus, it is not suprising that impaired glucose tolerance has often been observed in stroke patients, both in our material and in the reports of other investigators [7].

There is a good deal of evidence to link certain serum lipid patterns to atherosclerosis. However, studies of serum lipids in persons with cerebrovascular disease have not always shown higher serum lipid values [8, 9]. Our results, which established hyperlipidemia in stroke patients, are in agreement with many other reports [7, 10]. Strong association of lipids with cerebral infarction can be demonstrated only in those who are under 50 when the lipids were measured [11].

An elevated blood hemoglobin level may also be cited as a possible stroke precursor. Presumably it is the consequence of an increased propensity to thrombosis and hypertension, since the hemoglobin content of the blood influences its viscosity, dynamics of the flow, and its clotting characteristics. The result of both our investigations and several other studies confirm it [3, 12].

It seems reasonable to conclude from this and from other studies that at present the key to the prevention of stroke is early detection and control of hypertension and cardiac impairment. To assess the efficiency of correction of other risk factors in the prevention of stroke, some more data should be available. However, the magnitude of the problem compels us to evaluate the possibility of lowering the stroke incidence.

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ФАКТОРЫ РИСКА ИНСУЛЬТА

М. И.-Ф. Роозе

Резюме

Инсульт не является следствием одного патологического фактора, а результатом целого ряда длительно развивающихся патологических изменений в организме. Поэтому можно с уверенностью считать, что уменьшения заболеваемости инсультом можно достичь лишь путем ранней профилактики. Для этого необходимо выявить факторы риска, на основе которых можно установить лица, предрасположенные к инсульту.

В настоящей работе установлены факторы, связанные с инсультом среди населения г. Тарту. Всего исследовано 249 больных с ишемическим инсультом и 52 больных с внутримозговым кровоизлиянием. Контрольная группа состояла из 190 лиц, у которых в анамнезе и клинически расстройств мозгового кровообращения не выявилось.

Наиболее существенными факторами, статистически достоверно связанными с ишемическим инсультом, явились повышенное артериальное давление, расстройства сердечной деятельности, отражавшиеся в различных патологических изменениях ЭКГ, расстройства углеводного обмена, выражавшиеся в повышении уровня сахара крови и в пониженной толерантности к углеводам, нарушения липидного обмена, выявлявшиеся в по-

вышении содержания холестерина и бета-липопротеидов в крови, и повышенная вязкость крови, отражавшаяся в повышении уровня гемоглобина и числа эритроцитов в крови.

При изучении больных с кровоизлиянием мозга выявилось, что при геморрагическом инсульте были те же факторы риска, что и при инфаркте мозга, но отличались от последних лишь более высокими показателями артериального давления и более низкой частотой нарушений ЭКГ.

Результаты работы показывают, что при выработке и внедрении профилактических методов инсульта особое внимание следует уделять выявлению факторов риска инсульта среди населения, в частности в молодом возрасте.

PROGNOSIS OF STROKE

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In 1971 an international cooperative stroke register project was started under the auspices of the World Health Organization (WHO). The purpose of this project was to gain information about the incidence, course and prognosis of stroke in selected communities in different parts of the world. One of these stroke registers was that of Espoo-Kauniainen area in South Finland, where the register was active in 1972 and 1973. Two previous reports [1, 2] deal with the incidence and early prognosis of stroke patients in this register. The aim of the present study was to analyze the long-term prognosis of these patients.

Methods

A prospective study of all new stroke cases in the Espoo-Kauniainen area (population 113,100) in South Finland was carried out in 1972 and 1973 by the WHO stroke register method (for details see Aho and Fogelholm, 1974,[1] and Aho, 1975 [2]). Altogether 286 stroke patients could be established. The prognosis of these patients was evaluated. At the turn of the year 1976 to 1977, after a median follow-up period of four years, a questionnaire was sent to all surviving patients to elicit their state of health and/or disability. All patients could be traced. The chi-square test was used in statistical comparisons.

Results

Within the two-year registration time 286 stroke patients were found. The basic information concerning the type of stroke, age and sex distribution (Table 1), incidences (Table 2) and case fatality three months after the onset of stroke (Table 3), has pre-

Table 1

Type of stroke, median age and sex distribution (Aho 1975) [2]

Type of stroke	Male		Female		Total		
	Med. age	N	Med. age	N	Med. age	N	%
SAH	44	14	52	30	49	44	15
ICH	58	19	64	27	63	46	16
INF	64	93	71	82	67	175	61
NUD	70	11	71	10	70	21	8
All	64	137	69	149	66	286	100

Table 2

Incidences per 100,000 annually of different types of stroke (Aho 1975) [2]

Type of stroke	Study population			Age adjusted		
	Male	Female	Total	Male	Female	Total
SAH	12.9	25.6	19.5	14.1	33.1	23.9
ICH	17.5	23.0	20.3	24.1	35.0	29.7
INF	85.4	69.9	77.4	134.7	123.0	128.6
NUD	10.1	8.5	9.3	19.8	15.1	17.3
	125.8	127.0	126.4	192.7	206.2	199.5

Table 3

Case fatality three months after the onset of stroke according to age and type of stroke (Aho 1975) [2]

Type of stroke	< 65 years	$\geqslant 65$ years	Total
SAH	16/34 (47%)	3/10 (30%)	19/44 (43%)
ICH	16/26 (62%)	17/20 (85%)	33/46 (72%)
INF	4/65 (6%)	49/110(45%)	53/175(30%)
NUD	1/3 (33%)	8/18 (44%)	9/21 (43%)
All	37/128(29%)	77/158(49%)	114/286(40%)

viously been reported by Aho.[2] 61% of the patients belonged to the ischemic brain infarction (INF) group, and 15% and 16% to the subarachnoid hemorrhage (SAH) and intracerebral hemorrhage (ICH) groups, respectively, while in 8% of the cases the

type of stroke could not be specified (NUD). The incidence, age-adjusted to the population of Finland, was about 200/100,000/year. The three-month mortality in the age-group under 65 years, 37/128 (29%), was significantly lower than that of the age-group over 65 years, 77/158 (49%) ($P<0.05$). This was especially marked in brain infarction ($P<0.0005$). The highest mortality was found in old patients with an intracerebral hemorrhage and the lowest mortality, in young patients with an ischemic brain infarction.

After a median follow-up period of four years, 177 patients (78 men and 99 women) had died. Thus the four-year mortality was 62% (Table 4). The age was here an even more significant

Table 4

Case fatality after a median follow-up period of four years according to age and type of stroke

Type of stroke	<65 years	⩾65 years	Total
SAH	19/34 (56%)	7 /10 (70%)	26/44 (59%)
ICH	17/26 (65%)	17/20 (85%)	34/46 (74%)
INF	20/65 (31%)	83/110(75%)	103/175(59%)
NUD	1/3 (33%)	13/18 (72%)	14/21 (67%)
All	57/128(45%)	120/158(76%)	177/286(62%)

Table 5

Causes of death

	Before 3 months	After 3 months	Total
Cerebrovascular dis.	93	25	118
Cardiovascular dis.	18	22	40
Malignancy	1	6	7
Violent death	—	2	2
Miscellaneous	2	8	10
Total	114	63	177

($P<0.01$) determinant of mortality than in the three-month follow-up period. Here, 57/128 (45%) of those under the age of 65 had died, against 120/158 (76%) of the patients aged 65 years or older. Here too, the highest mortality was found among old patients with an intracerebral hemorrhage and the lowest mortality among young patients with an ischemic brain infarction. The mortality had changed very little in the group of intracerebral hemorrhages, but in the group of ischemic brain infarction it had nearly doubled the three-month mortality.

Table 6

ADL of the survivors after a median follow-up period of four years

Type of stroke	ADL category			Total
	1	2	3	
SAH	18	0	0	18
ICH	7	4	1	12
INF	50	13	9	72
NUD	2	2	3	7
All	77	19	13	109

ADL category: 1 = Fully independent
2 = Requires assistance in ADL
3 = Totally disabled

The causes of death are shown in Table 5. The primary cerebrovascular disease was the major cause of death within 3 months after stroke, but nearly an equal number of deaths vere due to cerebrovascular and cardiovascular causes thereafter.

After a median follow-up period of four years there were 109 survivors (59 men and 50 women). 71 had had their stroke before the age of 65, and 38 patients had been older than 65 at the time of stroke. The survivors were divided into three categories according to their activities of daily living (ADL): 1. Fully independent in ADL, 2. Those who required assistance in ADL, and 3. Totally disabled. The survivors' prognosis regarding ADL can be seen from Table 6. 71% of the survivors were fully independent; that is, all patients with previous SAH, but 69% of those with an ischemic brain infarction were also fully independent. 21% of the survivors had returned to work.

Discussion

The incidence of stroke in Finland is about 200/100,000/year, which is high compared with most other community studies.[3–5] The incidence of SAH in particular is much higher than has been reported from other countries. Pakarinen [6] in 1967 reported an incidence of SAH in Helsinki 16.8/100,000/year. In the present study this incidence is even higher: 23.9/100,000/year. Nearly two-thirds of the patients had a brain infarction, a fact which is common to most previous studies.

The mortality in the acute stage (within three months) was 40%. This is fairly low, but it does not differ markedly from earlier reports.[7–10] The low mortality may perhaps be due to the

young age structure of our material. Young age was especially favourable in connection with brain infarction, the difference in mortality between the younger and older age-groups being highly significant.

The mortality after a median follow-up period of four years was 62%. It had not changed much in the subarachnoid or in the intracerebral hemorrhage group, but it had doubled in the brain infarction group. This is in agreement with the results of Abu-Zeid et al. (1978) [10] based on a material of 1,484 stroke cases observed for 30 to 48 months in Manitoba, Canada. Most of the deaths in hemorrhagic stroke occurred during the first weeks, and if the patient survived, he would be considered to have passed the serious stage. The same was true of patients with SAH caused by a single intracranial arterial aneurysm.[11] Patients with brain infarction continue to run a risk of dying higher than the general population. In the present series, 31% of the patients under 65 years of age with brain infarction had died within 4 years. This is close to our previous series,[12] where 23% of the patients having a brain infarction and a verified unilateral occlusion of the internal carotid artery had died after a median follow-up period of 53 months. The median age was also low in this material: 53 years. However, in our previous series of middle cerebral artery occlusion and brain infarction [13] the 2.5-year mortality was 14%. This was most likely due to the fact that in this series the patients were quite young (mean age 44 years) and all had an occlusion of middle cerebral artery, which supplies only part of one hemisphere.

The causes of death within three months are mainly cerebrovascular, but after three months nearly as many patients die of cerebrovascular as of cardiovascular diseases. This was also reported in the previous series [12, 14, 15] and shows a close relationship of stroke and heart diseases.

The studies concerning functional recovery after stroke have shown that about half of the patients who survive become independent in self-care.

Summary

A prospective study of all stroke cases in the Espoo-Kauniainen area (population 113,100) in South Finland was carried out during 1972 and 1973 by the WHO stroke register method. 286 stroke patients could be found; 61% of them had a brain infarction, 16% an intracerebral hemorrhage and 15% a subarachnoid hemorrhage. The total incidence was 200/100,000/years after age-adjustment of the results to the population of Finland. Especially high was the incidence of subarachnoid hemorrhage, 23.9/100,000/year. The mortality within three months was 40% and that after

a median follow-up period of four year was 62%. The mortality was highest in old patients with an intracerebral hemorrhage and lowest in young patients with a brain infarction. The causes of death after the acute stage were cerebrovascular as often as cardiovascular. After four years, 71% of the survivors were fully independent in ADL and 21% had even returned to work, and about 10% need institutional care.[16, 17] In the present study, after a median follow-up of four years, 71% were fully independent in ADL and 21% of the survivors returned to work. This confirms to our previous results.[11–13] The most favourable result was seen among patients with a subarachnoid hemorrhage, which is in agreement with our previous series [11] and the worst, among patients with an intracerebral hemorrhage. It is conceivable that the good result in ADL is partly due to the fairly young age structure of our series. It can be concluded that the mortality of stroke is still high, but the survivors have a relatively good prognosis regarding their activities of daily living.

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ПРОГНОЗ ИНСУЛЬТА

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Резюме

В южной Финляндии в городах Эспоо и Кауниайнен в 1972—1973 годах по методу регистра ВОЗ было проведено проспективное исследование заболеваемости инсультом. Было установлено всего 286 больных инсультом, в том числе 61% больных с инфарктом мозга, 16% больных с внутримозговым кровоизлиянием и 15% больных с субарахноидальным кровоизлиянием. Общая заболеваемость инсультом равнялась 200 случаям на 100 000 населения в год (стандартизованная на возрастную структуру всего населения Финляндии). Особенно высокой оказалась частота субарахноидального кровоизлияния — 23,9 случаев на 100 000 населения в год. Летальность в течение первых 3-х месяцев после заболевания была 40% и через 4 года — 62%. Летальность оказалась наивысшей среди более старших больных с внутримозговым кровоизлиянием и наиболее низкой среди более молодых больных с инфарктом мозга. Причиной смерти в остром периоде заболевания были как цереброваскулярные, так и кардиоваскулярные заболевания. Через 4 года 71% больных, перенесших инсульт, оказались способными к самообслуживанию и не нуждались в посторонней помощи, 21% больных вернулся к прежней работе.

PROGNOSIS OF PATIENTS WITH INTERNAL CAROTID AND MIDDLE CEREBRAL ARTERY OCCLUSIVE DISEASE.

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The occlusive lesion of the cervical arteries and their main branches plays an important role in the pathogenesis of brain infarction. However, the severity of cerebrovascular disorders depends on various factors and may greatly vary in different cases [1–5]. So far, in the studies dealing with the prognosis of stroke, little attention has been paid to the survival and functional recovery of patients with internal carotid and middle cerebral artery occlusion.

The purpose of this study has been to analyze the short- and long-term prognosis of patients with verified internal carotid and middle cerebral artery occlusive disease.

Methods

We have analyzed the case histories of 83 patients with verified occlusive lesion of the internal carotid artery (ICA) or middle cerebral artery (MCA). All the patients had been admitted to the Department of Neurology, Tartu Clinical Hospital in 1967—1973. The clinical diagnosis of each case was confirmed by an angiographical examination or at autopsy. Out of the patients, 39 had occlusion and 16 — stenosis of the ICA near the carotid bifurcation, and 28 patients had occlusion of the MCA. Seven patients had a bilateral lesion of the arteries. The age of the patients at the onset of symptoms varied from 30 to 96 years. The mean age in women was 63 and in men — 53 years.

The median follow-up period was 6 years. Information about the follow-up period was obtained by means of a detailed questionnaire or at personal examination of the patients. The data were obtained in 50 cases of 60 survivors after the acute period of their illness. The patients were divided into four categories accor-

ding to prognosis: group I — fully independent in their activities of daily living (ADL), group II — persons requiring assistance in ADL, group III — totally disabled and group IV — died during the follow-up period. The probability of 5-year survival was estimated by means of a life-time table analysis.

Results

The age and sex distribution of the patients is presented in Table 1. Table 1 shows that men predominated among the patients, whereas the predominance of men was especially remarkable in the younger age-groups.

Brain infarction was present in 72 cases (in 69 cases in the territory of the MCA and in 3 cases in the territory of the anterior cerebral artery), 8 patients suffered from TIAs and 1 patient had no symptoms at all.

Table 1

Age and sex distribution of the patients with ICA and MCA occlusive disease

Age	Men	Women	Total
<20	—	—	—
20—29	—	—	—
30—39	9	1	10
40—49	9	2	11
50—59	19	5	24
60—69	16	11	27
70<	2	9	11
Total	55	28	83
%	66	34	100

The majority of the patients with TIAs had stenosis of the ICA only. During the acute period of cerebral infarction 23 patients died (34%). The casefatality rate was much higher in the case of MCA thrombosis compared with ICA thrombosis (48% and 27%, respectively). At the end of the acute period of disease the number of seriously disabled patients was similar in these two groups of patients (32% and 34%). 39% of the survived patients with ICA occlusion and 20% of the patients with MCA occlusion were free of symptoms. 13 patients of 16 subjects with ICA stenosis were well-recovered and only 3 had neurological signs.

The bilateral lesion of the carotid arteries or of their branches was associated with a more unfavorable short-term prognosis (out

of 7 patients with a bilateral lesion 5 patients died during the acute period of brain infarction).

An important role in the early prognosis seems to play the state of the collateral cerebral circulation as seen in the angiograms. In 78% of the patients who had died during the initial stroke, the collateral circulation was not seen from the angiograms.

There was a certain correlation between the age of the patients and their short-term survival rate. Among the patients under 60 years for men and 55 years for women the case fatality was 2.5 times lower than among the rest.

During the follow-up period 12 patients died: 6 of them during the first, 3 — during the second, 2 — during the third and 1 — during the fourth year after the initial stroke.

Causes of death were: a recurrent stroke in 9 cases and a progressive deterioration of the cerebral circulation and of the cardiovascular system — in 3 cases. 6 patients died of other causes — 2 of the coronary heart disease, 2 — of a malignant tumour and 2 — of some unknown causes.

The 5-year recurrence rate of stroke was 18%.

Table 2

Distribution of the survived patients with ICA and MCA occlusive disease according to prognosis groups

Group	n	%
I	9	18
II	12	24
III	11	22
IV	18	36
Total	50	100

Table 2 shows the distribution of the survivors according to prognosis groups.

Table 3

Distribution of the patients with hypertension (> 160/95 mm Hg) according to the prognosis group

Group	n	% *
I	2	22
II	3	27
III	5	27
IV	5	28

* Percentage of the total number of patients in each group.

The life-time table analysis gave an 89% probability of the survival of the first year and a 72% probability of that of the fifth year after ICA or MCA thrombosis.

Hypertension (< 160/95 mm Hg) was measured in 13 patients during their hospital stay. In the present material hypertension was of no prognostic value (Table 3).

The survivors were divided into 3 age-groups (<40, 40—59 and 60 < years). Table 4 shows the distribution of the patients according to age and prognosis.

Table 4

Distribution of the survivors according to the age and prognosis groups

Group	Age					
	<40		40—59		60<	
	n	% *	n	% *	n	% *
I	2	22	6	28	1	5
II	3	33	5	24	3	16
III	2	22	4	19	5	26
IV	2	22	6	28	10	53
Total	9	—	21	—	19	—

* Percentage of the total number of patients in each group.

The percentage of groups III and IV was higher among the patients aged 60 years or older compared with those younger than 60 years ($P<0.05$). The percentage of the group I decrease with increasing age with statistically significant differences between the age-groups under 60 years (< 40 and 40—59 years) and over 60 years ($P<0.05$).

Discussion

In the present series the patients had ICA or MCA occlusive disease in different degrees (unilateral stenosis or occlusion or bilateral lesion of the arteries), but the small number of the cases has not allowed us to analyze the longterm prognosis separately in each group of the patients. For that reason our results are not fully comparable with those based on an analysis of the highly selected material.

In the present study men prodominated among the patients, which agrees with previous reports [6, 7], but the mean age of our patients was much higher than has been reported earlier [6, 7]. The relatively old age-structure of the series may be partially responsible for the results obtained.

The case fatality rate in the acute stage was 34%, which is higher than has been found by other authors [6, 7]. The risk of death was associated with the degree of the occlusive lesion, it was higher in patients with a bilateral lesion of the arteries as well as in MCA occlusion where the possibilities of the collateral circulation are not favourable. The case fatality rate was lower and the functional recovery was better in patients with the stenosis or occlusion of the ICA.

Compared with the data of other investigators [3, 4, 8, 9] the probability of survival in the present series was relatively favourable. The life-time table analysis gave a 72% probability of surviving the fifth year. However, a similar probability of survival (78%) has been reported by Waltimo et al.[6] and Kaste et al.[7] in patients with ICA and MCA occlusion.

The main cause of death was cerebrovascular disease (a recurrent stroke) followed by coronary heart disease.

The functional recovery of the patients in this series was not so good as reported earlier [6, 7]. This might be due to the old age-structure of the patients studied. The results of this study indicate a more unfavourable outcome for the patients of older age: the percentage of the patients fully independent in ADL or requiring some assistance in ADL was significantly lower among the patients over 60 than in younger age-groups. The early and late case fatality rate among the patients over 60 years was also much higher than among the rest. It can be explained by the more adequate state of the cardiovascular system and by better possibilities to compensate for the functional deficiency at a younger age.

As stated by other authors [6], hypertension was of no prognostic value.

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ПРОГНОЗ БОЛЬНЫХ С ЗАКУПОРКОЙ ВНУТРЕННЕЙ СОННОЙ И СРЕДНЕЙ МОЗГОВОЙ АРТЕРИЙ

Т. Томберг

Резюме

С целью изучения течения и прогноза при верифицированных окклюзирующих поражениях внутренней сонной и средней мозговой артерий проанализированы клинические и катамнестические данные 83 больных, госпитализированных в неврологическом отделении Тартуской клинической больницы в 1967—1973 гг. Продолжительность катамнеза была в среднем 6 лет. Средний возраст у мужчин был 53, у женщин 63 года. 16 больных имели стеноз, 39 больных — закупорку внутренней сонной артерии, а 28 больных — закупорку средней мозговой артерии.

Клиническое течение острой стадии поражений магистральных артерий мозга оказалось наиболее благоприятным при стенозе внутренней сонной артерии и наиболее неблагоприятным — при окклюзии средней мозговой артерии и при двустороннем поражении артерий. Летальность в острой стадии тромбоза составляла 34%.

В отдаленный период заболевания 18% выписанных больных стали практически здоровыми, 24% больных имели стойкие остаточные явления средней тяжести и 22% больных оказались тяжелыми инвалидами, которые нуждались в посторонней помощи, 24% больных умерли из-за нового ухудшения мозгового кровообращения в разные сроки после первичного инсульта, а 12% больных умерли по другим причинам. Методом вычисления таблиц смертности установлено, что вероятность выживания в течение первого года наблюдения равняется 89% и в течение пятого года — 72%.

CEREBRAL GAS EXCHANGE AND CEREBROSPINAL FLUID ACID-BASE BALANCE IN PATIENTS WITH CEREBRO-VASCULAR DISEASE

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The main purpose of this paper is to give a review of the results gained in some rather extensive studies of various arterial and jugular venous blood concentrations and also investigations into the CSF parameters in patients with two common types of stroke. These results have formed the basis of several reports presented at the meetings of neurologists from the State University of Tartu and from the University of Helsinki. Furthermore, these data have been printed both in the Soviet scientific publications and abroad. Therefore, only the most important results are described here and very few details are given on the study material, methods, etc.

Material and methods

Investigations were carried out in a series of 54 consecutive non-selected patients with intracerebral hemorrhage and a similar group of 157 patients with an ischemic type of stroke, i. e. brain infarction. The patients' conditions showed various degrees of severity; during the acute stage of the disease 28 persons with intracerebral hemorrhage and 37 patients with brain infarction died.

The arterial (A) and internal jugular venous (VJ) blood samples were analysed for pH, pCO_2, bicarbonates and pO_2 by using the Radiometer electrodes and the Astrup technique. The CSF pH was measured with a Radiometer electrode; the CSF pCO_2 was derived by means of a modified Siggaard-Andersen nomogram for $pK=6.13$. The actual bicarbonate of the CSF was calculated with the help of the Henderson-Hasselbalch equation. All samples were also analysed for lactate and pyruvate con-

centrations. These analyses were performed with the colorimetric methods of Barker-Summerson and Friedemann-Haugen, respectively. Statistical processing was performed by the use of an electronic computer /cf. 1,2/.

Results

The data given in Table 1 indicate that the most common finding in these patients was a considerable decrease in CSF bicarbonate, pCO_2 and pH with a concomitant increase in both CSF lactate and pyruvate concentrations.

Table 1

CSF acid-base parameters and lactate-pyruvate values ($\bar{x} \pm m$)

	Control group	Cerebral hemorrhage	Brain infarction
pH	7.338±0.005	7.306±0.006**	7.337±0.003
pCO_2 mm Hg	46.3±0.6	41.1±0.8**	41.7±0.5**
HCO_3^- mEq/l	23.5±0.3	19.5±0.5**	21.1±0.2**
pO_2 mm Hg	41.2±1,4	39,1±1.7	41.5±1.3
La⁻ mEq/l	2.03±0.12	5.11±0.29**	3.12±0.15**
Py⁻ mEq/l	0.079±0.004	0.157±0.008**	0.110±0.003**
La⁻/Py⁻	26.0±1.2	33.0±1.3**	28.2±0.8

** $p < 0.01$

The CSF lactate increase was correlated to the decrease of CSF bicarbonate ($r = -0.631$ in cerebral infarction and -0.675 in brain hemorrhage) /3, 4/. In the patients with brain infarction the decrease of CSF pCO_2 was about equal to the drop in the HCO_3^- concentration and, therefore, the CSF pH remained unchanged. However, in the intracerebral hemorrhage group the decrease of the bicarbonate concentration substantially exceeded the shift of the CSF pCO_2 and this led to non-compensated metabolic acidosis, i. e. to a decreased pH. Repeated investigations showed that CSF lactacidosis was of the greatest intensity during the very first days of the disease; thereafter is gradually decreased, but the CSF lactate values were often considerably higher even at the end of the second week from the onset of the disease.

Table 2 gives the arterial and jugular venous blood acid-base values recorded in both groups of the patients investigated. These results indicate that a rather noticeable respiratory alkalosis was present both in the cerebral venous and in the arterial blood. The table gives the actual bicarbonate recordings whereas the standard bicarbonate and the lactate-pyruvate values were

Table 2

Arterial and jugular venous acid-base parameters ($\bar{x}\pm m$)

	Arterial				Jugular venous				
	pH	HCO_3^- mm Hg	pCO_2 mEq/l	pO_2 mm Hg	pH	pCO_2 mm Hg	HCO_3^- mEq/l	pO_2 mm Hg	$(A—V)O_2$ vol %
Control group	7.409± 0.003	40.0± 0.6	24.5±0.3 0.3	101.7± 1.9	7.360± 0.005	48.4± 0.7	26.2± 0.5	43.0± 1.0	6.15± 0.20
Cerebral hemorrhage	7.470± 0.006**	32.5± 0.8**	23.1± 0.5	81.0± 2.0**	7.408± 0.007**	38.8± 1.0**	23.0± 0.6**	36.5± 1.1**	7.23± 0.20**
Brain infarction	7.440± 0.003**	33.5± 0.6**	22.7± 0.3*	79.2± 1.0**	7.387± 0.004**	41.1± 0.6**	23.6± 0.4**	35.5± 1.2**	7.49± 0.10**

* $p < 0.05$

** $p < 0.01$

normal, i. e. there were no considerable non-respiratory changes in the general acid-base balance. Hence, arterial hypocapnia was of a primary respiratory origin, i. e. was caused by pulmonary hyperventilation. However, Table 2 indicates that the patients were moderately hypoxic. Although the absolute decrease of cerebral venous pO_2 was slightly less pronounced than in the arterial blood, the results of the studies suggest that venous hypoxemia was caused by an increased consumption of oxygen from the blood unit circulating through the brain vascular network, i. e. a remarkably reduced CBF. A drop in the mean cerebral venous pO_2 from 43 mm Hg in the control group to 35.5 mm Hg in the brain infarction group and to 36.5 mm Hg in the intracerebral hemorrhage group seems to be physiologically more important than the decrease of the arterial pO_2 from 101.7 mm Hg to the corresponding values of 79.2 mm Hg and 81.0 mm Hg. Furthermore, this conclusion derives also from the investigation of cerebral arteriovenous oxygen differences based on the manometric measurements of the total oxygen content, where the changes in the cerebral arteriovenous difference directly reflect the CBF alterations, although reciprocally /5—7/. Table 2 indicates that the decrease of the O_2 content was more marked in the cerebral venous than in the arterial blood. The A—V oxygen difference was, therefore, increased and this was especially noticeable in case of a good recovery.

The analysis indicated that the extent of changes in various values was in a close relation to the clinical course of the disease and to the severity of brain damage. CSF metabolic acidosis together with hypocapnia and hypoxemia of both the cerebral venous and the arterial blood were, in comparison with the survivors, remarkably more pronounced in patients with a fatal outcome. In the intracerebral hemorrhage group the mean CSF lactate concentrations were 4.29 ± 0.38 mEq/l for survivors and 5.88 ± 0.39 mEq/l for nonsurvivors, respectively. The corresponding values for patients with brain infarction were 2.90 ± 0.21 mEq/l and 3.58 ± 0.17 mEq/l. The highest CSF lactate values were recorded in deeply comatose patients with hemorrhagic strokes where the mean value was 7.74 ± 0.54 mEq/l.

The mean values for the whole series indicated that low cerebral venous pO_2 in patients with stroke was connected with an elevated CSF lactate concentration (Tables 1 and 2). However, a special analysis revealed the existence of an ambiguous relation between these parameters. If the cases with a relatively good condition and with a favourable outcome of the disease were analysed separately, the study revealed the existence of a considerable reciprocal correlation between the decrease of the cerebral venous pO_2 and the increase of the CSF lactate concentration ($r = -0.559$ in patients with hemorrhagic stroke and

r=—0.490 in the group of brain infarction). An entirely different situation was disclosed in the group of patients whose condition was grave due to an extensive damage to the brain. These patients were comatose and had a clear clinical picture of brain stem involvement. In this group a severe CSF lactacidosis coincided with a considerable increase in the cerebral venous pO_2 to hyperoxic values and with a remarkably reduced A—V oxygen difference (r=0.708 in patients with hemorrhagic stroke and r=0.711 in the group of brain infarction). In several cases there was a good correlation between the deteriorating course of the disease and the corresponding decrease of cerebral (A—V) O_2. The conclusion is that in this condition the metabolic demands of the brain decreased relatively more than the CBF, which led to a state of the "luxury perfusion". Another expression of the "luxury perfusion" is the increase of jugular venous pO_2 to supernormal values, i. e. more than 43 mm Hg. If this factor was kept in view, a special analysis revealed that the patients with intracerebral hemorrhage whose jugular venous pO_2 exceeded 43 mm Hg had the highest CSF lactate concentration (7.30 mEq/l) whereas the patients with JV pO_2 43—32 mm Hg had "only" 4.30 mEq/l lactate in their CSF. A quite similar trend was disclosed in the group of ischemic strokes /8,9/.

All these differences had a clear-cut clinical appearance in terms of the general condition, consciousness disorders, etc. This is indicated in Table 3.

Table 3

Dependence of some recorded parameters on the clinical condition of patients ($\bar{x}\pm m$)

	Control group	Moderately ill	Deeply comatose
CSF pH	7.338±0.005	7.322±0.006**	7.255±0.007**
CSF La⁻ mEq/l	2.03 ±0.12	3.97±0.36**	7.74 ±0.42**
JV pO_2 mm Hg	43.0 ±1.0	34.0 ±1.6**	43.5 ±1.8**
A pCO_2 mm Hg	40.0 ±0.6	34.9 ±0.4**	28.1 ±1.2**

** $p<0.01$

Table 3 indicates that CSF lactacidosis is substantially more pronounced in the severe group, i. e. in the patients who were in deep coma from the very onset until the fatal end of disease. Furthermore, it is seen again that profounced CSF lactacidosis coincides with a supernormal VJ pO_2, i. e. the "luxury perfusion", and also with pulmonary hyperventilation.

Comments

It has been concluded that CSF acidosis points to the presence of brain tissue hypoxic acidosis, whereas cerebral venous hypoxemia indicates an insufficient brain oxygen supply, and venous hypocapnia shows a restricted carbon dioxide production within the intracellular compartment /1, 2/. The results of earlier experimental works /10, 11/ indicate that a reduced oxygen supply leads to an anaerobic shift in glucose metabolism within the brain tissue. This results in the production of excessive amounts of lactate in the brain. The actual site of lactate production is the intracellular compartment. Due to a relatively slow diffusion rate, the extracellular lactate concentration will increase with a certain lag and give a relatively long-lasting extracellular (i. e. in the CSF) acidosis in brain /12/.

However, the presence of systemic respiratory alkalosis in these patients renders the "hypoxic" explanation of CSF lactic acidosis into a subject of a certain criticism. It has been established that an intra- and extracellular pH of the cerebral tissue is regulated not only by means of physical-chemical buffering reactions but also by metabolic adjustments. These are, at least in part, effective by means of modifications in the activity of aerobic glycolysis in the brain tissue, which is considered to be a pH-dependent process /13, 14/. Therefore, in order to analyse the possible role of systemic respiratory alkalosis in an increased output of lactate in the brain tissue, the above-mentioned material was subjected to a special analysis. This study revealed that CSF lactic acidosis was also present in the patients whose hyperventilation was very mild or completely absent. Therefore, the conclusion was that CSF lactic acidosis is first of all the result of a hypoxic damage to the brain and is only to a smaller extent dependent on systemic alkalosis in patients with brain damage /15/. Furthermore, the results of these studies indicate that the pathogenesis of respiratory alkalosis is ambiguous. Cerebral extracellular lactic acidosis is the most important factor which, alongside with the upper brain stem damage, leads to the development of pulmonary hyperventilation /1, 6/.

The presence of brain extracellular lactic acidosis coincides with several other biochemical disturbances within the cerebral tissure, viz. energy deficiency, disorders of the sodium pump, etc. /2, 10, 11/. These changes play their roles as secondary pathogenetic factors which considerably determine the extent of brain damage. Figure 1 gives a tentative scheme of the events leading to the formation of an ischemic focus within the brain. This scheme begins from occlusion but may as well start from ischemia, e. g. in cases of cerebrovascular insufficiency, in acute disorders of the systemic circulation and also in patients with a

greatly reduced cerebral perfusion pressure, viz. intracranial hematomas, cerebral edema, etc. Hence this scheme is valid for the explanation of the damage to the brain tissue in various clinical conditions where the leading cause of the disorder is hypoxia. The results of various investigations have revealed that the acidotic shift in the brain extracellular fluid pH may lead first

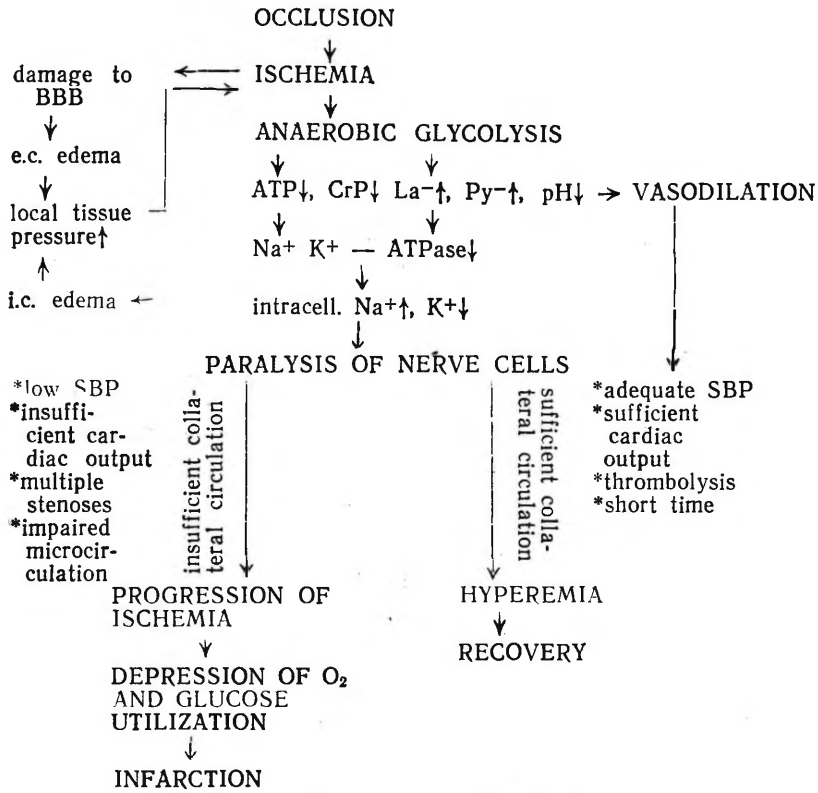

Fig. 1. Pathogenesis of brain infarction

to active vasodilation and thereafter — to vasoparalysis /2, 16—18/. The clinical investigations which form the basis of this paper suggest the conclusion that cerebral lactic acidosis with its reflection in CSF metabolic acidosis is the trigger mechanism for the luxury perfusion syndrome and also for such related events as brain swelling, etc. However, the vasoactive influence of hydrogen ions can also be realized by means of local neurogenic mechanisms, e. g. by altering the sensitivity of either smooth muscular or neural elements to some other messenger of information like active amines, potassium and calcium ions, etc. /19, 20/.

Conclusions

Cerebral ischemia, which is the main cause of brain infarction and the consequence of intracerebral hemorrhage, leads to brain tissue lactic acidosis. This is reflected in the long-lasting metabolic acidosis of the cerebrospinal fluid. Brain extracellular acidosis is the main cause of the secondary circulatory and metabolic disturbances within the affected cerebral tissue and thus plays an important role in the determination of the extent of neural damage.

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ГАЗООБМЕН ГОЛОВНОГО МОЗГА И КИСЛОТНО-ЩЕЛОЧНОЕ РАВНОВЕСИЕ ЛИКВОРА У БОЛЬНЫХ С СОСУДИСТЫМИ ЗАБОЛЕВАНИЯМИ ГОЛОВНОГО МОЗГА

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Резюме

Основной целью настоящей обзорной статьи является представление результатов исследований мозгового газообмена и кислотно-щелочных параметров ликвора у больных с инфарктом головного мозга и внутримозговым кровоизлиянием. Исследования были проведены у 54 больных с геморрагическим и у 157 пациентов с ишемическим инсультом.

Установлено, что при ишемическом инсульте в ликворе характерным сдвигом оказалось наличие компенсированного, а при геморрагическом инсульте — некомпенсированного метаболического ацидоза. Главной причиной ацидоза ликвора явилось накопление лактата. Установлено также, что причина лактацидоза ликвора — циркуляторная тканевая гипоксия головного мозга. Об этом свидетельствует выраженная венозная гипоксемия мозга и, особенно, — увеличение артерио-венозной

разницы мозга по O_2. Однако в части случаев инфаркта мозга и внутримозгового кровообращения, где были зарегистрированы сверхнормальные величины pO_2 венозной крови головного мозга и сокращение артерио-венозной разницы по O_2, повышение концентрации лактата в ликворе оказалось более выраженным, чем при низких величинах pO_2. Следовательно, гипоксический ацидоз головного мозга приводит к избыточной, превышающей метаболические потребности ткани, перфузии головного мозга. Предполагается, что внеклеточный ацидоз действует в две стадии: вначале развивается активная вазодилятация, при продолжении и углублении ацидоза состояние прогрессирует до вазопаралича с такими присоединяющимися нарушениями, как застой и полнокровие. Таким образом, гипоксический ацидоз играет большую роль в развитии отека мозга. Кроме того, ацидоз мозговой ткани обычно приводит к гипервентиляции легких. Последняя выражается в развитии существенного дыхательного алкалоза, который не связан с локализацией морфологического поражения в мозге.

ACTIVITY OF LACTATE DEHYDROGENASE OF THE CEREBROSPINAL FLUID AND OF THE BLOOD IN PATIENTS WITH BRAIN INFARCTION

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Earlier studies have revealed that any cause of hypoxia leads to a considerable acidosis of the cerebral tissue. The main reason for the development of the brain tissue metabolic acidosis is the accumulation of lactic acid which is formed in the process of anaerobic glycolysis in the intracellular compartment. Thereafter, the lactate is rather slowly diffused into the extracellular fluid and creates long-lasting metabolic acidosis of the cerebrospinal fluid (1). The present investigation was aimed at measuring the activity of the enzyme lactate dehydrogenase (LD), which is a catalyzer for the main reaction of glycolysis which hydrates pyruvate into lactate. The latter is the end product of the anaerobic breakdown of glucose in the mammalian tissues. Hence, the increased activity of the enzyme may be helpful for the diagnostics of hypoxia even before a pronounced lactic acidosis develops.

Material and methods

The investigations were performed in a series of 42 patients with ischemic stroke. The patients were investigated in a consecutive order; no special selection was made. All of them had brain infarctions which were limited to one of the cerebral hemispheres. Most of the patients were in a severe or median general condition and all had a pronounced neurological deficit. During the hospital treatment 12 of them died. The mean age of the patients was 68 years.

The control group of 10 subjects with the mean age of 52 years was composed of clinical patients in whom no evidence of central nervous system disease was found, but lumbar puncture was done for diagnostic purposes.

The activity of LD and of the isoenzyme LD_1 was determined in the CSF and in the arterial blood serum by means of the kinetic method. The analyses were performed twice — in the first and on the second week of the disease. The measurements were made by means of the Swedish reaction velocity analyzer (Reaction Rate Analyzer 2086) and the chemicals were obtained from Boehringer, Sigma (West Germany). The activity of the enzyme was determined at a temperature of 25 °C and the results were expressed in international units (I.U.).

Results

The results of the determinations are shown in Table 1. Both in the control group and in the diseased groups there was no relationship between the CSF LD activity and the protein or the cellular content of the CSF.

Table 1

The activity of LD and LD_1 of the CSF and blood in patients with brain infarction ($\bar{x}\pm m$ I.U.)

Studied groups	CSF		Serum	
	LD	LD_1	LD	LD_1
Brain infarction				
First week	71±7*	39±9*	251±12*	140±7*
Second week	95±33*	61±20*	315±39*	204±31*
Control group	24±2	13±1	171±10*	81±5

*$P<0,05$

The table indicates that the mean activities of LD and LD_1 of the CSF and the blood serum in patients with brain infarction considerably exceeded the corresponding control values ($P<0.05$). This was valid both for the first and for the second week of the disease. The correlation analysis revealed that the LD and LD_1 activity changes were fairly closely related both in the CSF ($r=0.680$) and in the serum ($r=0.460$).

Table 2

The activity of LD and LD_1 of the blood depending on the outcome of the disease ($\bar{x}\pm m$ I.U.)

Studied groups	First week		Second week	
	LD	LD_1	LD	LD_1
Survivors	233±11	136±7	236±19	152±30
Nonsurvivors	329±28*	188±21*	465±105*	288±74

*$P<0.05$

Table 2 gives the dependence of the blood serum LD and LD_1 activity on the outcome of the disease. The table reveals that the increased activity of the enzymes indicated a poor prognosis. This was especially noticeable during the second week of the disease. The activity of LD and LD_1 in the blood serum was remarkably higher in the cases with a fatal end of the disease ($P<0.05$). In the last subgroup of the patients the activity of LD even increased during the second week of the disease. However, due to a small number of cases this shift was only at the border of statistical significance. In the cases with a favourable end of the disease the enzyme activity did not change considerably during the second week of the disease.

The comparison of the CSF enzyme activity depending on the outcome of the disease also revealed a clear trend towards the increase of this parameter in nonsurvivors. The mean values for LD and LD_1 of the CSF were 64 ± 22 I.U. and 36 ± 9 I.U. in survivors versus 79 ± 30 I.U. and 44 ± 19 I.U. in nonsurvivors. However, this difference did not go beyond the limits of veracity.

Discussion

The earlier investigations of our group have revealed that arterial hypoxemia and respiratory alkalosis, which often develop in patients with brain infarction, considerably, enhance the already existing cerebral tissue hypoxia (2, 3). However, there are no considerable generalized metabolic acid-base disorders and the lactate concentration of the arterial blood remains normal in these patients (1). Nevertheless, the results of the present study still disclose the metabolic effect of some systemic hypoxia.

The cerebral tissue is rich in LD (4). A destructive process should therefore release the enzyme into the CSF. In acute brain infarction, the elevated enzyme activity depends on the temporal relationship between the incident and the removal of the CSF and the size of the infarct. Therefore, the increased activity of LD in the CSF should reflect the corresponding change in the cerebral parenchyma.

Oxygen deficit is the trigger for the LD activation and thus sets going the glycolytic pathway of carbohydrate metabolism. The resulting increase of the tissue lactate concentration in its turn activates the activity of the anaerobic isoenzymes LD_4 and LD_5 with a concomitant inhibition of the aerobic isoenzymes LD_1 and LD_2. In other words, hypoxia in itself leads to the anaerobization of the LD spectrum in the tissue fluids (5). The presence of a clear positive correlation between the alterations of the lactate concentrations and the activity of LD have also been established by other investigators (6, 7). From this point of view it is difficult to explain why the activity of the LD of the CSF

did not increase substantially in the fatal cases of this series. It has been established that the CSF lactate concentrations are high in these patients (1). It is possible that the relatively mild increase of the net activity of LD depended mostly on the anaerobization of the isoenzyme spectrum under the conditions of hypoxia.

A considerable increase in LD_1 an isoenzyme of predominantly cardiac origin, is most likely the reflection of the cardiac disease in these patients which is either a pre-existent disorder or develops after stroke. These hitherto preliminary results suggest that several secondary pathogenetic factors which are evoked by cerebral ischemia tend to maintain the pathologic conditions not only in the brain but also in the myocardium.

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АКТИВНОСТЬ ЭНЗИМА ЛАКТАТ-ДЕГИДРОГЕНАЗЫ ЛИКВОРА И КРОВИ У БОЛЬНЫХ С ИНФАРКТОМ ГОЛОВНОГО МОЗГА

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Резюме

Основной целью настоящего исследования явилось изучение энзима лактат-дегидрогеназы (ЛДГ), являющегося катализатором главной реакции гликолиза, в ходе которой пируват гидрируется в лактат.

Исследования были проведены у 42 больных с ишемическим инсультом. Установлено, что активность ЛДГ ликвора и артериальной крови при инфаркте головного мозга значительно превышала активность этих энзимов у лиц контрольной группы. Повышение активности энзимов является прогностически неблагоприятным признаком, свидетельствующим о существенной анаэробизации обмена глюкозы. Установлено, что кислородное голодание приводит не только к повышению активности ЛДГ, но и к анаэробизации спектра энзима.

CHANGES IN THE CEREBROVASCULAR TONUS RELATED TO THE PROGNOSIS OF CEREBRAL VASCULAR DISORDERS

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The prognosis of a cerebrovascular disease often depends not so much on its primary etiology as on the severity of secondary cerebral metabolic disturbances (hypoxia, lactacidosis, etc.) which are quite similar in different nosological entities and possibly are reflected in some similar changes in the cerebral vascular tonus, too. To support this hypothesis the rheoencephalographical (REG) changes comparable according to the clinical condition and outcome but different in etiology were analyzed.

Methods and Patients

The REG recordings (n=158) of 36 cases of an acute spontaneous subarachnoid hemorrhage (SAH) have been compared to the REG (n=129) of 48 cases of cerebral infarction (CI) in the middle cerebral artery supply area and to the REG of 50 healthy subjects at a medium and at an advanced age. The patients were divided into 4 groups according to the severity of their clinical condition: I — 21 cases of SAH, having only meningeal signs and a mild unilateral motor and/or sensory deficiency in some cases; II — 15 cases of SAH, being in a severe condition, with pronounced disorders of consciousness and brain-stem signs due to recurrent hemorrhages or cerebral ischemia; III — 31 cases of CI with a mild unilateral motor and sensory deficiency and a favourable course of the disease; IV — 17 cases of CI, having a severe extensive unilateral deficiency of cerebral functions.

A 4-channel rheograph with a working frequency of 100 kHz connected to an electroencephalograph has been used. Bilateral frontal-mastoidal (F-M), frontal-central (F-C), central-temporal (C-T) and occipital-mastoidal (O-M) recordings have been obtained (at the time constant 0.3 sec). In this paper the quantitative REG values are given only for F-M recordings.

The following REG parameters were estimated: a) the amplitude of the REG wave (A) in ohms, which characterizes the maximum oscillation of the cerebral pulsatile blood volume; b) the product of A multiplication to the heart frequency (A.f) reflecting the pulsatile blood volume in a minute; c) the ratio of the anacrotic part of the curve (α) to the heart cycle time (T), i. e. $\alpha/T\%$, reflecting the tonus of the cerebral arteries; d) indexes A_I and A_{II} proposed by Simonson (cit. by Eninya [1]), i. e. the percentage of the height of the REG wave's catacrotic part at 0.25 and 0.5 intervals from the amplitude peak to the end of the wave to A. It has been suggested that A_I reflects the tonus of the small cerebral arteries and arterioles, A_{II} reflects that of the cerebral veins.

The mean normal values of these parameters were: $A = 0.110 \pm 0{,}003$; $A.f = 7.48 \pm 0.5$; $\alpha/T\% = 15.2 \pm 0.6$; $A_I = 85.0 \pm 2.4$; $A_{II} = 49.0 \pm 2.1$.

Results

Both groups of patients with a mild neurological deficiency and a favourable course of the disease (I — SAH, III — CI) were characterized by a marked rise in the cerebral vascular tonus (I: $\alpha/T\% = 19.3 \pm 0.8$; $A_I = 102.5 \pm 3.5$ ($P < 0.01$); III $\alpha/T\% = 20.8 \pm 0.7$ ($P < 0.01$)), a decrease in the pulsatile blood volume (I: $A = 0.098 \pm 0.003$ ($P < 0.01$); III: $A = 0.082 \pm 0.004$ $A.f. = 5.69 \pm 0.34$ ($P < 0.01$)), sometimes together with a relative increase in the venous blood volume (I: $A_{II} = 59.5 \pm 1.$ ($P < 0.01$)). The REG changes were bilateral but more pronounced on the affected side.

In cases of SAH with a severe clinical condition (group II) the decrease of A and the rise of A_{II} were more marked ($A = 0.077 \pm 0.004$; $A_{II} = 68.5 \pm 2.9$ ($P < 0.01$)), but the rise of $\alpha/T\%$ and A_I were less than in group I ($\alpha/T\% = 17.5 \pm 0.7$; $A_I = 95.6 \pm 2.4$ ($P < 0.01$)). The REG changes were bilateral and diffuse. In cases of recurrent hemorrhage with the development of large intracerebral hematomas or in cases of a progressive deterioration of the patient's condition (deep coma) the combination of very small pulsatile blood volume oscillations with an extensive decrease in the arterial tonus were found regularly.

The REG signs of cerebral vascular hypotonia were also seen in cases of large CI (group IV), i.e. the rise of the pulsatile blood volume ($A = 0.128 \pm 0.015$; $A.f. = 8.87 \pm 0.92$ ($P < 0.05$)) was combined with a relatively low arterial tonus ($\alpha/T\% = 17.1 \pm 1.$ ($P < 0.05$)). These changes were bilateral and extensive, in most cases a significant interhemispheric difference of parameters was observed only in regional recordings (C-T).

Discussion

This study revealed that changes in the cerebral vascular tonus were quite similar regardless of different primary etiopathogenetic factors of cerebral affection. In cases when only signs of a mild unilateral hemispheric neurological deficiency occurred and the course of the disease was favourable, the most consistent finding was the diminuation of the oscillations of the pulsatile blood flow and a rise in the tonus of the cerebral arteries and arterioles. In cases of SAH it was obviously caused by the neurogenic and humoral vasoconstriction (arterial spasm) inducing a certain amount of cerebral hypoxia [2, 3], in cases of CI it was probably brought about by neurogenic changes in the systemic and cerebral blood flow induced by focal cerebral hypoxia and by some systemic hypocapnia and alkalosis [4, 5].

It has been demonstrated by several authors that regardless of the etiology in cases of a severe cerebral affection (especially with the brain-stem deficiency signs, coma, unfavourable or fatal outcome), there occurs progressively increasing cerebral lactacidosis. The lowering of the pH of the cerebral interstitial tissue induces paralytic cerebral vasodilatation and loss of the cerebral vascular tonus and the CBF autoregulation [6, 7, 8]. We suppose that the REG signs of cerebral vascular hypotonia in cases of SAH and CI with a severe clinical condition reflect this process and, consequently, they are indicators of the patient's severe condition and of an unfavourable prognosis.

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ИЗМЕНЕНИЯ ТОНУСА МОЗГОВЫХ СОСУДОВ В ЗАВИСИМОСТИ ОТ ПРОГНОЗА ОСТРЫХ СОСУДИСТЫХ ЗАБОЛЕВАНИЙ ГОЛОВНОГО МОЗГА

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Резюме

Методом реоэнцефалографии изучены изменения тонуса мозговых сосудов в зависимости от течения и прогноза при разных видах мозговых инсультов. Всего проведены 158 РЭГ исследований у 36 больных в острой стадии спонтанного субарахноидального кровоизлияния (САК), 129 РЭГ у 48 больных инфарктом мозга (ИМ) и 50 РЭГ у лиц контрольной группы. Больные с САК и ИМ были подразделены на 4 подгруппы по тяжести неврологической симптоматики.

По количественным данным РЭГ у больных с САК и ИМ при маловыраженной неврологической симптоматике и благоприятном течении заболевания наблюдалось выраженное повышение тонуса мозговых сосудов разного калибра и снижение пульсового кровенаполнения, иногда вместе с относительным увеличением венозного кровенаполнения. У больных с САК в тяжёлом состоянии отмечалось более значительное снижение пульсового кровенаполнения в сочетании со сравнительно менее выраженным повышением тонуса сосудов. При обширных ИМ имело место снижение тонуса мозговых сосудов вместе с повышением пульсового кровенаполнения.

По нашим исследованиям, независимо от этиологии заболевания, тяжёлое поражение головного мозга сопровождается появлением гипотонии сосудов головного мозга. Это, по-видимому, является выражением паралитической вазодилятации мозговых сосудов из-за развития прогрессирующего лактацидоза мозговой ткани.

REGIONAL CEREBRAL BLOOD FLOW IN THE ACUTE PERIOD OF ISCHEMIC STROKE

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Measurements of the regional cerebral blood flow (rCBF) in the acute period of cerebral ischemic stroke have been performed at this laboratory from the year 1974 onward. This paper briefly summarizes the main results.

Methods and Patients

The Xenon^{133} clearance method of the rCBF measurement elaborated by Ingvar and Lassen [1, 2] has been used. After an intracarotid injection of 0.2—1.0 mCi Xe^{133} in 2—5 ml of saline full 10-minute Xe^{133} clearance curves were recorded. The calculations of the rCBF were made on the basis of the height/area method according to the formula:

$$rCBF = \lambda \cdot \frac{H_0 - H_{10}}{A},$$

where λ is the diffusion coefficient of Xe^{133}, H_0 and H_{10} denote the intensity of gamma-activity immediately after the injection and after 10 minutes, A signifies the area under the clearance curve.

The recording device was the Soviet multidetector system "Xenon-1". The rCBF has been measured in three relatively large regions, viz. frontal, temporal and parietal.

This report gives the results of the rCBF measurement in 60 cases of acute cerebral hemispheric infarction: 58 of them in the supply territory of the middle cerebral artery an 2 in the territory of the anterior cerebral artery. The mean age of the patients was 64.4 ± 1.6 years and it varied from 37 to 84 years. 10 patients died in the hospital, the others were discharged with a more or less pronounced neurologic deficiency.

In most cases cerebral angiography, rheoencephalography (REG), the determination of pO_2, pCO_2, pH in arterial and cerebral venous blood were also performed.

In 15 cases rCBF was measured before and after the intravenous administration of 60 mg of papaverine hydrochloride and in 13 cases before and after the intravenous injection of 240 mg of aminophylline.

Results

1. The spontaneous rCBF

The mean hemispheric rCBF of the patients was 31.9±1.2 ml/100 g/min, i.e. significantly less than the normal rCBF at this age: 45—55 ml/100 g/min [1, 2, 3, 4, 5]. The mean rCBF values in the frontal (31.2±1.3), temporal (32.3±1.3) and parietal (30.5±1.4) regions did not differ significantly. However, in 19.5 per cent of the cases marked individual differences (over ±20%) from the mean CBF were revealed in different regions. Relative hyperemia was more often disclosed in the temporal region and relative ischemia in the parietal region.

The mean rCBF of the patients over 65 was significantly less than in the younger age-group (30.2±1.8 and 33.9±1.5 ml/100 g/min, respectively; $P<0.05$). However, since the correlation between the CBF and the age was low ($r=-0.1491$), one can presume that a decrease in the CBF did not depend directly on the age itself but on the origin of larger ischemic foci at an older age. The connection between the decrease of the CBF and the severity of infarction has also been confirmed by the fact that the rCBF in the group of the patients who died in the hospital was significantly less than in the group with a good recovery rate (27.0±2.2 and 33.3±1.7 ml/100 g/min, respectively; $P<0.05$). No significant difference of the mean rCBF was found during the first three weeks of the diseace (31.8±1.5 ml/100 g/min in the 1st week, 33.4±2.7 in the 2nd and 31.1±3.6 later).

The patients with arterial hypertension (the arterial blood pressure over 160/95 mm Hg) had to some extent a smaller mean rCBF than the normotensive patients (30.7±2.0 and 32.5±1.5 ml/100 g/min, respectively). Probably, this was also due to the origin of larger ischemic foci in the patients with prolonged hypertensive changes in the cerebral blood vessels. We could not reveal diffuse disturbances of the CBF autoregulation (with the dependence of the CBF on the level of the systemic arterial pressure). There was no correlation between the rCBF and the mean arterial pressure ($r=0.0273$). The mean rCBF of the patients with an increased blood viscosity (with the blood hemoglobin content over 15.2/100 ml, i. e. 95%) was significantly less than in the group with a normal blood viscosity (29.2±1.5 and 34.2±1.9 ml/100 g/min, respectively; $P<0.05$).

The increase of the arterial pCO_2 was correlated with some rise in the mean rCBF ($r=0.3603$). The moderate reverse correlation ($r=-0.3935$) between the mean rCBF and the cerebral arterial-venous pO_2 difference was revealed but there was no correlation between the rCBF and the arterial pH ($r=-0.2321$).

We could not find any significant correlations between the CBF and the main rheoencephalographic (REG) parameters: the amplitude (A) and the relative length of the anacrotic phase ($\alpha/T\%$). Therefore, we cannot confirm the possibility of evaluating the cerebral blood flow by the amplitude of the REG (A) value what is sometimes presumed in the rheoencephalographic studies. One can suppose that rheoencephalography is a valuable noninvasive method for the evaluation of pulsatile changes in the cerebral blood volume and of the tonus of cerebral vessels but not directly of the blood flow in the brain tissue.

2. Changes in the rCBF caused by vasoactive drugs

After the intravenous injection of 60 mg of papaverine hydrochloride (in 15 cases) a significant increase in the mean rCBF was observed: from 31.8 ± 1.7 to 38.9 ± 2.5 ml/100 g/min ($P<0.05$). However, in one case of a severe infarction the rCBF decreased in 2 regions and in 4 cases in 1 region. The relative increase of the rCBF (in %) was most pronounced in the temporal region (+34%). The relative increase did not correlate with the absolute value of the rCBF before the injection, with the mean arterial pressure, with the patient's age and had only a moderate reverse correlation with the blood hemoglobin content and with the severity of infarction. The absolute increase of the rCBF (in ml/100 g/min) was slightly more in the patients under 65 years, with the arterial blood pressure under 160/95 mm Hg, in the first 10 days of the disease, in the group with the rCBF over 30 ml/100 g/min before the injection.

After an intravenous injection of 240 mg aminophylline (in 13 cases) the decrease of the rCBF was common: the mean rCBF decreased from 32.1 ± 2.4 to 29.3 ± 1.5 ml/100 g/min. However, in 4 cases (all of them from the group with an unfavorable final outcome) the mean rCBF increased from 23.0 ± 3.0 to 30.0 ± 3.0 ml/100 g/min. When these cases were excluded from calculations, a significant decrease in the rCBF was revealed: from 36.1 ± 1.8 to 28.9 ± 1.8 ml/100 g/min ($P<0.02$). More remarkable changes (in both directions) were observed in the temporal region. The correlation of the changes (in %) to the patient's age and to the blood hemoglobin content was slight, to the mean arterial pressure and to the severity of infarction being moderately reverse. Regional differences of the rCBF were smoothed in most cases.

We could confirm the observations of other authors [6, 7] about paradoxical reactions of the CBF under the influence of vasoactive drugs. The "intracerebral steal" syndrome described by

Olesen and Paulson [6] was also observed in severe cases of cerebral infarction after the injection of the cerebral vasodilating drug papaverine hydrochloride and the opposite syndrome, i. e. the "Robin Hood syndrome" (Skinhoj a. Paulson [7]) was seen after the injection of the cerebral vasoconstricting drug aminophylline. These paradoxical reactions reflect the regional loss of the autoregulation of the cerebral blood flow due to severe metabolic disturbances in the area of large cerebral infarction. The above-described changes in the rCBF under the influence of papaverine hydrochloride and aminophylline match well with our electro- and rheoencephalographic observations on the influence of these drugs on the brain function, the brain vascular tonus and the pulsatile blood volume.

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РЕГИОНАЛЬНЫЙ ОБЪЁМНЫЙ МОЗГОВОЙ КРОВОТОК В ОСТРОМ ПЕРИОДЕ ИШЕМИЧЕСКОГО ИНСУЛЬТА

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Резюме

Исследование объёмного мозгового кровотока (ОМК) методом клиренса ксенона-133 у 60 больных инфарктом больших полушарий головного мозга показало, что их средний

ОМК (31,9±1,2 мл/100 г/мин) был значительно ниже возрастной нормы. Понижение ОМК соответствовало клиническому исходу заболевания. У больных старше 65 лет средний ОМК оказался существенно ниже, чем в более молодой возрастной группе. У больных с артериальной гипертензией выше 160/95 мм рт. ст. и у больных с содержанием гемоглобина в крови свыше 15,2 г/100 мл (95%) ОМК был значительно ниже, чем у больных, у которых эти параметры не достигали указанных пределов. ОМК имел умеренную корреляцию с артериальным парциальным давлением углекислого газа и умеренную обратную корреляцию с артерио-венозной разницей парциального давления кислорода в головном мозге. Корреляций ОМК с основными параметрами реоэнцефалограммы не было выявлено.

После внутривенного введения 60 мг папаверина (у 15 больных) наблюдалось увеличение ОМК (от 31,8±1,7 до 38,9±2,5 мл/100 г/мин; $P < 0,05$), после внутривенного введения 240 мг эуфиллина (у 13 больных) преобладало уменьшение ОМК (от 32,1±2,4 до 29,3±1,5 мл/100 г/мин). У некоторых больных с грубым инфарктом головного мозга отмечались парадоксальные реакции ОМК, которые были вызваны нарушением авторегуляции мозгового кровотока.

BLOOD VOLUME AND EXTRACELLULAR VOLUME DYNAMICS IN STROKE

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Patients with stroke have rather frequently cardiovascular decompensation and it is regarded as one of the risk factors of cerebral ischemia [1]. The volume and distribution of blood and the extracelluar space are the main regulating factors of the circulation of blood and the stability of the cardiovascular system [2].

This study was designed to determine whether the blood volume (BV) and the extracellular volume (ECV) is altered in patients with stroke and whether this alteration corresponds to the type of stroke, its severity and outcome, circulation disorders and to the patient's sex and age.

Material and methods

The study included 80 patients with cerebral infarction (CI) and 38 patients with cerebral and subarachnoid hemorrhage (CH). 42 of 80 CI patients (52.5% of the cases) survived with a slight and moderate neurological deficit, 26 (32.5%) — with a great neurological deficit and 12 (15.0%) — died within the first month of the illness. The data on CH were accordingly — 18 (47.4%), 6(15.8%) and 14(36.6%). The main risk factors for stroke were atherosclerosis, hypertension and cardiovascular decompensation.

ECV was measured by rhodanid in percentage of body weight [3]. The control values were 24.2±0.75% of body weight. Rapid plasma volume (PV) was determined by the use of radioiodinated serum albumin (RISA)[4, 5] in the first week of the illness. Evans blue (T-1824) [4] was used in repeated dynamical PV studies. The total blood volume and the red cell volume (RCV) were calculated from PV by the use of whole body hematocrit (Ht). The data of rapid BV, PV and RCV are represented in per-

centage of excess or deficit of the predicted normal BV and its components, determined according to the patient's sex, body type, weight and surface area [6]. In addition, Ht, serum sodium and potassium concentrations and total protein were routinely recorded.

Results

Both studied groups — cerebral infarction and cerebral hemorrhage — showed a decreased blood volume and its components (Table 1). In cases of CI the decrease of BV was dependent

Table 1

Blood volume and its components in the first week of stroke
$\bar{x} \pm$S.D.

Group	Number of patients studied	Age	Ht (%)	Deficit of BV (%)	Deficit of PV (%)	Deficit of RCV (%)
Cerebral **infarction**	80	67±8	46.8±0.41**	−18.6±0.94*	−21.6±0.85*	−17.1±1.11*
Cerebral hemorrhage	26	61±8	45.4±0.44	−18.9±4.8*	−20.5±4.2*	−18.3±4.6*

* — different from the controls, $P<0.05$
** — CI different from CH, $P<0.05$

on the predominant loss of PV. As a result of the PV decrease, there was a significantly higher mean Ht value compared to the controls and CH. In cases of CH the mean value of the total BV deficit was the same as in CI, but there was no predominant PV loss compared with the RCV loss.

BV and its components normalized only within 2—3 weeks of the illness in cases of stroke with good recovery; in fatal cases the positive dynamics of BV and of its components was absent.

Table 2 gives BV and its components correlated to the clinical outcome and the severity of brain damage.

There was a great difference in BV and its components' level in CI and CH patients, having a different outcome — recovery or lethality. No difference was mentioned when severely disabled and lethal CI patients' BV and the values of its components were compared.

In addition, BV, PV and RCV values were correlated to the corresponding cardiovascular decompensation (Table 3).

Table 2

Blood volume and its compoients correlated to clinical outcome and severity of brain damage
$\bar{x} \pm S.D.$

Group	Results of patients studied	Age	Ht (%)	Deficit of BV (%)	Deficit of PV (%)	Deficit of RCV (%)
Cerebral infarction survived with a slight neurological deficit	30	67±8	48.9±0.27*	—12.9±1.25*	—14.6±1.69*	—12.4±1.09
Cerebral infarction survived with a great neurological deficit	29	73±8	46.3±0.73	—23.9±1.49*	—25.7±1.37*	—25.7±1.29
Lethal cerebral infarction	12	64±4	47.1±0.84**	—25.2±2.07**	—28.7±3.92**	—28.2±2.27**
Cerebral hemorrhage survived with a slight and moderate neurological deficit	15	65±4*	45.3±0.40	—11.9±2.8*	—14.8±3.2*	—13.2±2.2*
Lethal cerebral hemorrhage	9	57±8	43.9±0.42	—22.3±3.8**	—25.4±2.8**	—12.1±1.8*

* — different from controls, $P<0.05$
** — lethal cases different from survived cases, $P<0.05$

Table 3

Blood volume and its components correlated to cardiovascular decompensation
$\bar{x} \pm S.D.$

Group	Number of patients studied	Age	Ht (%)	Deficit of BV (%)	Deficit of PV (%)	Deficit of RCV (%)
Cerebral infarction without cardiovascular decompensation	15	68±4	46.2±0.24	−20.0±3.03*	−19.2±3.80*	−16.2±2.65*
Cerebral infarction with cardiovascular decompensation	12	70±8	47.4±0.42**	−26.85±0.87**	−28.8±0.44**	−26.0±0.84**
Cerebral hemorrhage without cardiovascular decompensation	8	66±4	45.0±1.24	−18.6±2.33*	−14.0±2.33*	−19.8±3.42*
Cerebral hemorrhage with cardiovascular decompensation	8	60±8	44.2±0.82	−29.05±5.04**	−30.1±5.74**	−27.3±3.8**

* — different from controls, $P < 0.05$
** — stroke with cardiovascular decompensation different from stroke without cardiovascular decompensation, $P < 0.05$

Table 3 shows that the deficit of the blood volume and of its components was significantly higher in cases of CI and CH with cardiovascular decompensation. In CI cases there was a predominant PV loss compared to the RCV loss, which resulted in higher Ht values of these patients.

The blood volume values were correlated, in addition, to the patient's age and sex, but no correlations were found between patient's age and sex and blood volume.

Thus, in this group of patients with stroke, the decrease in BV and its components appears to be related not to the type of stroke but to the severity of the brain damage and the clinical outcome. Thus, patients with a great neurological deficit and a lethal outcome demonstrated the lowest blood volume, while those with a mild neurological deficit had only a slight BV deficit. On the other hand, BV values were influenced by cardiovascular decompensation.

In 34 patients with stroke the ECV was measured. Our data demonstrated an ECV deficit in cases of CI in the first week of the illness: $\bar{x} \pm S.D. = 21.1 \pm 1.0\%$ of body weight compared to the normal values — $24.2 \pm 0.75\%$ of body weight, $P < 0.05$ and to the mean values of ECV in CH — $26.2 \pm 1.6\%$ of body weight. In the 2—3 week of the illness the mean ECV value had normalized in cases of CI. In addition, ECV expansion in patients with a severe stroke ($28.5 \pm 1.0\%$ of body weight, $P < 0.05$) and ECV depletion in the patients over 75 years ($20.6 \pm 0.9\%$ of body weight, $P < 0.05$) compared to the controls was found. Also a positive correlation between BV and ECV was ascertained, but it was not significant because of a small number of patients simultaneously studied ($n = 12$).

Data analysis correlated to the topical neurological diagnosis of brain damage did not produce any differences.

Water-electrolyte balance studies were not performed in our cases. Blood serum sodium was elevated (146.8 ± 0.64, $P < 0.05$) and potassium decreased (3.82 ± 0.12, $P < 0.05$) in severe CI. In severe CH the data were accordingly for sodium — 148.4 ± 0.44 $P < 0.05$ and for potassium — 3.83 ± 0.14, $P < 0.05$. Hypernatremia was found in 25.2%, hyponatremia in 15.0%, hypokaliemia in 18.2% and hyperkaliema in 22.4% of the cases of stroke. The mean serum total protein values were elevated in both — CI and CH.

No correlations were found between BV and its components and arterial blood pressure values.

As it requires special attention, BV and ECV values were not correlated to the patients' infusion-transfusion therapy. But we have to mention that studies of the body water compartments were performed on patients with stroke in conditions of intensive care.

Discussion

The total blood volume of normal adults remains remarkably constant [2, 3, 4]. In conditions of disease the deficit of BV an especially circulating blood volume there occurs, causing hypoperfusion of tissues and disorders of metabolism [2]. It is reported that hypovolemia develops in acute brain damage (brain injury, brain operations [7]), less is known about its occurrence in stroke [8]. According to the present study there develops a moderate deficit of rapidly circulating BV in the first week of CI and CH. Furthermore, there is also an ECV deficit in the first week of CI. Several hypotheses about the pathogenesis of hypovolemia and dehydration in brain damage are discussed [9].

The brain is the control centre for the regulation of the body water compartments [9]. Therefore BV and ECV depletion occurs particularly in hypothalamic lesion [9]. On the other hand, hypovolemia develops frequently as a result of severe stress [10]. This seemed likely in our patients, in which the BV deficit was merely dependent on the severity of brain damage. In a severe stroke the following factors as hypoxia, high extrarenal losses, hyperthermia, tracheotomy, and tube feeding with high protein solutions may also account for hypovolemia and ECV dehydration [9]. But our severe stroke patients experienced ECV expansion which was associated with hypernatremia. In addition, a low ECV in CI compared to normal ECV was found in the first week of the illness. There occurs more frequent cardiovascular decompensation without edema before CI compared to CH, thus it is possible that extracelluar dehydration and hypovolemia of the PV deficit in CI had developed earlier. Both the above-mentioned pathological changes are possible causes of cardiovascular decompensation, which is counted as a risk factor of stroke and of cerebral hypoperfusion [1, 3, 4].

We were not surprised to find hypovolemia in cardiovascular decompensation, as has already been reported [2]. These both are frequently interrelated but their primary nature remains sometimes unsolved [2]. In hypovolemia and in cardiovascular decompensation rheological properties of blood worsen because of increased erythrocyte and platelet aggregation and hypercoagulability, resulting in a decrease of rapidly circulating BV and in a sequestrated BV [11]. Thus, the circulating blood volume is divided into three parts: rapidly and slowly circulating and congestive portions [5]. It may be the cause of circulating hypoxia [5]. The background of the above-mentioned mechanisms are, possibly, systemic vascular diseases — atherosclerosis and hypertension.

When hypovolemia develops, there occur compensatory mechanisms — vasoconstriction, water retention and transcapillary influx of interstitial fluid [2]. Transcapillary refill is diminished in

an ECV deficit [2]. As serial Ht did not significantly decrease in our CI patients, the mechanism may have been present. In contrast, in CH because of a normal ECV transcapillary refill occured, which resulted in lower Ht values compared to CI. In addition, two aspects of the present study deserve comment. The first is ECV expansion and hypernatremia in severe stroke, the second is ECV depletion in patients older than 75. Both these results agree with earlier studies [4, 9].

As we have mentioned before, there was no correlation between BV values and the arterial blood pressure in stroke. It was not surprising that in a BV deficit over 30% initial hypertension diminished but no remarkable hypotension developed. At the same time, on the basis of our findings and of those of other investigators [2, 3, 4], it is clear that there is no reliable way of assessing the adequacy of BV. The only way for the determination of the adequacy of BV are studies on the direct blood and extracelluar volume, which are needed especially for stroke intensive-care patients. The question that remains unanswered in the present study is how disorders of the body water compartments depend on the patients' infusion-transfusion therapy. Special studies may provide the necessary clues.

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ДИНАМИКА ОБЪЁМА ЦИРКУЛИРУЮЩЕЙ КРОВИ И ВНЕКЛЕТОЧНОГО ПРОСТРАНСТВА ПРИ ИНСУЛЬТЕ

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Резюме

В работе приводятся данные объема циркулирующей крови (ОЦК) и его компонентов, а также объема внеклеточного пространства (ОВП) в динамике у 80 больных с ишемическим (ИИ) и у 38 больных с геморрагическим инсультом (ГИ). Выяснилось, что у больных с инсультом, независимо от его формы, возникает умеренный дефицит ОЦК и его компонентов на первой неделе болезни. Гиповолемия была более выражена при тяжёлом поражении головного мозга, по сравнению с более лёгкими формами инсульта. ОЦК снижается в связи с преимущественным снижением объема плазмы (ОП) при ИИ, приводящим к повышению гематокрита. У больных с ИИ к тому же дефицит ОВП возникает на первой неделе болезни, так как у больных с ГИ вышеуказанная патология отсутствовала. Более тяжёлая гиповолемия и повышенный ОВП были отмечены при инсульте тяжёлой степени. Потеря ОВП была отмечена также у больных с инсультом свыше 75 лет, а дефицит ОЦК — в зависимости от сердечно-сосудистой недостаточности. В статье дискутируются вопросы патогенеза расстройств водных секторов организма и их значения при инсульте.

6 Заказ № 4081

INTRAVASCULAR PLATELET AGGREGATION IN STROKE

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Previous animal studies have shown that platelet-activating substances can produce platelet aggregates and, secondarily, cerebral ischemia and hypoxia [1]. It is therefore possible that brain damage with occurrence of platelet-activating substances (ADP, thrombin, catecholamines, free fatty acids, etc.) induces platelet abnormalities that promote microaggregate formation or vasoconstriction and thereby extend the area of the previously damaged brain.

The aim of this study was to determine whether acute cerebrovascular disease — transitory ischemic attack (TIA), cerebral infarction (CI) subarachnoid hemorrhage (SAH) and cerebral hemorrhage (CH) — is accompanied by intravascular platelet aggregation (IPA) in the cerebral venous blood and in the systemic circulation, and whether the increase of circulating platelet aggregates (CPA) has any significance and prognostic value in stroke.

Materials and methods

The study included fifty-two stroke patients: suffering from TIA (10), cerebral infarction (19), subarachnoid hemorrhage (11); in 5 of these cases suffering from the rupture of saccular aneurysms of the brain vessels and from cerebral hemorrhage (12). The mean age was for TIA $\bar{x} \pm S.D. = 58 \pm 4$, for CI — 67 ± 4, for SAH — 48 ± 4 and for CH — 58 ± 4 years. The study embraced 24 men and 28 women. The diagnosis of stroke was based upon anamnesis, neurological investigation and lumbal puncture. In addition, angiography, electro-, rheo- and echo-encephalography for diagnostic purposes were also made use of. In cases of TIA, cerebrovascular arterial insufficiency took place in the carotid system in 8 cases and in the vertebro-basilar system — in 4 cases. In 3 patients with TIA and in 3 cases of CI stenosis of the internal

carotid artery was found. The basis for cerebrovascular disease was atherosclerosis in 68±8% of the cases and hypertension in 24±8% of the cases. Cardiovascular decompensation was diagnosed in 20±8% (TIA), 52±8% (CI) and 50±6% (in SAH and CH) of the cases. Thromboembolic phenomena in CI were: myocardial infarction (3), pulmonary infarction (4), femoral artery occlusion (3) deep vein thrombosis (3), and in CH: pulmonary infarction (3) and renal infarction (1). In the first month of the illness 21±8% of the patients with CI and 27±8% — with SAH and 30±8% with CH had a fatal outcome.

The data of patients were compared to the data of 2 control groups: I — 20 healthy persons (donors), the mean age 24±8 years; II — 15 patients without symptoms of systemic vascular disease, but having neurosis and postconcussion headaches without a neurogical deficit, the mean age 64±8 years.

Platelet counts, intravascular platelet aggregation, i. e. circulating platelet aggregates according to Wu and Hoak [2] and the percentage of aggregated platelets were studied. The percentage of CPA was expressed as

$$\frac{(\text{platelet count EDTA} - \text{platelet count EDTA+formalin}) \times 100\%}{\text{platelet count EDTA}}$$

In addition to platelet studies, activation of the coagulation system were determined by a β-naphtol test [3]. All data were studied in 1—3, 4—7, 8—14, 15—21 and 22—28 days of the illness in the systemic venous, arterial (A) and internal jugular vein (IJV) blood samples. The IJV blood was derived by the puncture of the superior bulb of IJV. Siliconised equipment was used. As there was no difference in data on the systemic arterial blood samples compared to the systemic venous ones, only the mean values of the arterial blood are given in Table 1.

Results

According to our data (Table 1), intravascular platelet aggregation and coagulation system activation were absent in young healthy persons. Few platelet aggregates observed were dependent, possibly, on vessel puncture and sampling technique [2]. In patients with nonvascular brain diseases a slight intravascular platelet aggregation was found, without any difference between the systemic and the cerebral venous blood samples. In 12±4% of the cases, also activation of the coagulation system and free thrombin activity was observed according to the β-naphtol test. In contrast, there was a significantly higher IPA compared to the control groups of patients with stroke (Table 1). The percentage of circulating platelet aggregates were highest in cases of CH compared to the other patients with stroke. As a rule, CPA were statistically significantly higher in the IJV blood samples versus

Table 1

Intravascular platelet aggregation in stroke
$\bar{x} \pm 2S.D.$

Groups	Days of illness	Platelets·$10^3/\mu l$		% of aggregated platelets		β-naphtol test	
		A	IJV	A	IJV	A	IJV
I Control group		240.0±4.1	—	6.4±1.8	—	0	—
II Control group		238.2±6.2	239.1±4.8	13.6±2.2	13.7±2.2	0.13±0.02	0.13±0.02
TIA	1	240.0±14.8	251.0±25.4	30.0±2.4[1,2]	42.1±4.8[1,2,3]	0.50±0.4[1,2]	0.56±0.4[1,2]
	2—7	252.0±12.1	248.1±18.4	19.0±2.4[1,2]	22.0±4.8[1,2]	0.42±0.4[1]	0.50±0.4[1]
CI	1—3	194.0±6.4[1,2]	181.6±6.8[1,2,3]	62.8±3.3[1,2]	67.4±3.8[1,2]	1.56±0.2[1,2]	1.96±0.2[1,2,3]
	4—7	196.0±16.0[1,2]	177.0±13.1[1,2]	56.2±3.9[1,2]	61.6±3.2[1,2,3]	2.25±0.1[1,2]	2.17±0.8[1,2]
	8—14	192.0±10.0[1,2]	177.0±10.0[1,2,3]	30.1±2.9[1,2]	50.0±3.8[1,2,3]	2.80±1.0[1,2]	2.71±1.0[1,2]
	15—21	190.0±24.8[1,2]	190.0±28.0	30.0±3.0[1,2]	45.5±6.9[1,2,3]	2.00±0.8[1,2]	2.00±0.8[1,2]
CH	1—3	195.5±18.8[1,2]	188.0±18.1	67.8±1.5[1,2]	81.4±7.0[1,2,3]	1.40±0.1[1,2]	2.20±0.1[1,2,3]
	4—7	181.0±14.1[1,2]	170.0±9.0[1,2,3]	68.3±2.7[1,2]	76.5±7.2[1,2]	2.27±0.2[1,2]	3.50±0.2[1,2,3]
	8—14	172.0±17.5[1,2]	167.0±8.3[1,2,3]	55.9±5.8[1,2]	68.0±2.8[1,2]	4.00±0.001[1,2]	4.00±0.00[1,2,3]
	15—21	170.0±16.0[1,2]	164.0±10.8[1,2]	50.0±4.8[1,2]	62.8±3.8[1,2]	4.00±0.001[1,2]	4.00±0.00[1,2,3]
SAH	1—3	220.0±12.4	193.0±12.0[1,2,3]	42.0±4.1[1,2]	50.0±4.2[1,2]	0.5±0.4[1,2]	0.50±0.4[1,2]
	4—7	212.0±14.8	194.0±13.8[1,2,3]	30.0±4.7[1,2]	—	1.0±0.2[1,2]	1.82±0.1[1,2,3]
	8—14	200.0±20.0[1,2]	174.0±12.0[1,2,3]	22.0±2.0[1,2]	30.0±1.6[1,2]	1.5±0.4[1,2]	2.0±0.4[1,2,3]
	15—21	210.0±24.8[1,2]	170.0±14.8[1,2,3]	20.0±2.1[1,2]	20.0±2.1[1,2]	1.7±0.4[1,2]	2.0±0.4[1,2]

1 — different from I control group, $P<0.05$
2 — different from II control group, $P<0.05$
3 — different of IJV blood samples compared to arterial blood samples, $P<0.05$

Table 2

Relationship between clinical outcome and intravascular platelet aggregation in stroke
$\bar{x} \pm 2S.D.$

Groups	Days of illness	Platelets·$10^3/\mu l$		% of aggregated platelets		β-naphtol test	
		A	IJV	A	IJV	A	IJV
I Stroke with good covery	1—7	195.0±13.8[1]	178.0±12.1[1]	50.0±2.4[1]	55.0±6.0[1]	1.1±0.4[1]	1.3±0.4[1]
	8—14	230.0±25.4	221.0±28.1[1]	44.7±2.6[1]	50.0±4.8[1]	0.4±0.7	1.3±0.3[1]
	15—21	248.0±17.4	218.0±19.6	25.9±2.7[1]	44.7±2.6[1]	0.4±0.3	1.5±0.4[1]
II Severe and lethal stroke	1—7	169.0±14.6[1,2]	141.0±8.4[1,2]	80.7±3.6[1,2]	84.0±3.8[1,2]	1.6±0.4[1,2]	2.1±0.4[1,2]
	8—14	174.0±17.5[1,2]	156.0±10.0[1,2]	75.4±5.1[1,2]	80.7±3.6[1,2]	2.2±0.2[1,2]	2.5±0.2[1,2]
	15—21	182.0±18.8[1,2]	162.0±12.0[1,2]	48.1±4.8[1,2]	72.0±6.0[1,2]	2.5±0.3[1,2]	3.5±0.4[1,2]

1 — different from control groups, $P<0.05$
2 — different from I group, $P<0.05$

the systemic arterial ones. The β-naphtol test was positive in all types of stroke (Table 1). The high level of CPA correlated well with the β-naphtol test ($r = +0.68$, $P<0.05$). An increased IPA and activated coagulation lasted up to one week in TIA, up to two weeks in SAH and up to four weeks and more in patients with CH and CI. The severity and duration of IPA and activated coagulation correlated well with the severity of the neurological deficit and the clinical outcome of stroke. In Table 2 mean values of CPA and of the β-naphtol test are compared to the severity of stroke. I group: patients were with a slight and moderate stroke and a recovery without a disabling neurological deficit. II group: patients were with an outcome of a severe neurological deficit (disorders of consciousness, speech, hemiplegia, etc.) or death in the first month of the illness. As can be seen from Table 2, CPA and the β-naphtol test were more pronounced in patients with severe and lethal stroke compared to patients with good recovery.

In addition, there was a good correlation between the severity of IPA and the thromboembolic phenomena — myocardial, pulmonary and renal infarction, deep vein and peripheral arterial thrombosis (Table 3). In cases of stroke with thromboembolism, IPA and soluble fibrin according to the β-naphtol test were more increased than without these complications.

Table 3

Relationship between systemic intravascular platelet aggregation and thromboembolic complications in stroke $\bar{x} \pm 2$S.D.

Groups	Platelets $\cdot 10^3/\mu l$	% of aggregated platelets	β-naphtol test
I Stroke without thromboembolic complications	200.0 ± 12.0^1	50.0 ± 7.2^1	2.10 ± 0.5^1
II Stroke with thromboembolic complications	$108.0 \pm 10.0^{1,2}$	$72.0 \pm 4.0^{1,2}$	$3.60 \pm 0.2^{1,2}$

1 — different from control groups, $P<0.05$
2 — different from I group, $P<0.05$

According to our data, a relationship was established between IPA, activated coagulation and the severity of cardiovascular decompensation (Table 4) and the increased IPA and higher values of the β-naphtol test, as well as the more pronounced cardiovascular decompensation. So, also we found the highest IPA and soluble fibrin in cases of stroke with cardiovascular decompensation in II^b — III stage. There was no relationship between the intensity of IPA and blood coagulation system activation and topical diagnosis of brain damage and the patients' age and sex.

Table 4

Relationship between systemic intravascular platelet aggregation and cardiovascular decompensation in stroke $\bar{x}\pm 2S.D.$

Groups	Platelets $\cdot 10^3/\mu l$	% of aggregated platelets	β-naphtol test
I Stroke without cardiovascular decompensation	229.1±12.0	36.0±5.1[1]	2.2±0.4[1]
II Stroke with cardiocascular decompensation in stage II_a	198.9±20.0[1,2]	55.0±6.0[1,2]	3.5±0.7[1,2,3]
III Stroke with cardiovascular decompensation in stage II_b—III	177.9±15.0[1,2,3]	66.0±5.0[1,2,3]	2.6±0.6[1]

1 — different from control groups, $P<0.05$
2 — different from I group, $P<0.05$
3 — different from II group, $P<0.05$

Discussion

Thus, according to our results, there are activation of the coagulation system and the spontaneus circulating platelet aggregate formation in the blood, i. e. intravascular platelet aggregation in stroke. These findings were more pronounced in the blood derived from a damaged brain (IJV blood samples) compared with the systemic arterial ones. Recent data, not available when this study began, confirm platelet aggregate formation in all types of stroke — TIA [4, 5], cerebral infarction [4, 5, 6], subarachnoid hemorrage [4,6] and cerebral hemorrhage [6]. It has also been established that experimental cerebral ischemia produces platelet aggregates [7], and moreover, platelet aggregates have been found in recent cerebral infarction at human autopsies [8]. It has been reported that the size of the final cerebral infarction may depend on the adequacy or the failure of the collateral circulation [9]. Platelet aggregates may contribute to delayed postischemic hypoperfusion by obstructing the cerebral microcirculation or by stimulating vasoconstriction [9]. Moreover, substances released from platelet aggregates in contact with vascular endothelium may promote the formation of cerebral edema by increasing vascular permeability [10]. Just how cerebral ischemia and damage affect platelet function is yet unknown, but locally ischemic cerebral tissue can release catecholamines, arachidonic acid or thromboxane A_2 (TxA_2), substances that activate platelets [11, 12]. According to our data there also occurs activation of the intravascular coagulation

system with thrombinemia in stroke. The main factors producing intravascular coagulation in a damaged brain are release of brain thromboplastin (phospholipid) from a damaged brain tissue, stasis and hypodynamics from vascular spasms of the brain vessels, brain hypoxia with cerebral local lactacidosis and a local hemostatic response in SAH and CH. Platelet activation may be unopposed by prostaglandin I_2 (PG I_2), which is produced by a normal vascular tissue. PGI_2 inhibits platelet aggregation and opposes the vasoconstrictive action of TxA_2 produced by platelets. It is possible that the formation of PGI_2 in the brain is diminished during cerebral ischemia, the result might be to permit platelet aggregation and to increase the size of the damaged area [13].

In summary, transient platelet aggregation in cases of brain vascular damage may represent a hematological response to the brain tissue injury and, as it has been shown experimentally, circulating platelet aggregates may accumulate within the small blood vessels in the ischaemic cerebral hemisphere [7]. Platelet aggregation may thus contribute to the propagation of the brain damage. In addition, IPA accounts also for thromboembolic complications and cardiovascular decompensation in stroke. Due to the worsening of the rheological properties of blood it can also lead to serious hypoperfusion in the microvasculature of different organs causing multiple organ insufficiency. A pronounced IPA induces disseminated intravascular coagulation [14].

Thus the intravascular platelet aggregation is an important pathogenetic factor in stroke and a prompt use of the agents that effectively prevent this aggregation could be an important adjunct in the treatment of stroke.

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ВНУТРИСОСУДИСТАЯ АГРЕГАЦИЯ ТРОМБОЦИТОВ ПРИ ИНСУЛЬТЕ

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Резюме

Приводятся результаты динамического исследования внутрисосудистой агрегации тромбоцитов в системной артериальной и в мозговой венозной крови у 52 больных с инсультом. Выяснилось, что независимо от формы инсульта наблюдается повышенная внутрисосудистая агрегация тромбоцитов и активация свертывающей системы крови, превалирующие в мозговой венозной крови по сравнению с данными системной артериальной крови.

Вышеуказанная патология была больше выражена у больных с геморрагией головного мозга, по сравнению с больными с инфарктом головного мозга, с субарахноидальным кровоизлиянием и с предходящими нарушениями мозгового кровообращения.

Повышение внутрисосудистой агрегации тромбоцитов было пропорционально тяжести инсульта, тромбоэмболическим осложнениям и увеличению степени хронической сердечно-сосудистой недостаточности. Авторы считают внутрисосудистую агрегацию тромбоцитов доказанным компонентом патогенеза сосудистых заболеваний головного мозга, требующих соответственного лечения.

POLYACRYLAMIDE — GEL DISC ELECTROPHORESIS OF NATIVE CSF AND SERUM PROTEINS IN PATIENTS WITH CEREBRAL INFARCTION

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Diseases of the central nervous system are often characterized by a pathological composition of the cerebrospinal fluid (CSF). At normal or moderately raised total protein values some processes such as impairment of the blood — CSF barrier and immune reaction — cannot be diagnosed without electrophoresis (1), especially gel disc electrophoresis. This technique requires only a small quantity of sample and has a high resolution. Paper electrophoresis is 200-fold less sensitive than polyacrylamide-gel disc electrophoresis (2). CSF specimens have been analysed by this electrophoretic technique chiefly in patients with multiple sclerosis and infectious diseases, little informatsion has been obtained about the vascular diseases of the central nervous system. In the present study disc electrophoresis was applied to the fractionation of CSF and of serum proteins in patients with cerebral infarction.

Material and Methods

188 patients with cerebral infarction (age range 33—85 yr, mean age 64.3) were studied (Table 1). The patients were divided into two groups according to the severity of the brain damage: 156 protein samples were obtained from patients with light or moderate hemiparesis and without disturbances of consciousness, 32 protein samples were obtained from patients with deep hemiparesis or hemiplegia and with disturbances of consciousness. Lumbar punctures were carried out during the first days after the onset. Samples from 40 control subjects (age range 18—56 yr, mean age 30.7) were obtained from patients without organic diseases of the central nervous system.

In the present study the fractionation of CSF of serum proteins was performed by way of polyacrylamide-gel disc electro-

Table 1

Sex and age distributions

	Control group	Cerebral infarction		
		Total cases	Moderate brain damage	Severe brain damage
Males	25	90	77	13
Females	15	98	79	19
Total	40	188	156	32
Age range	18—56	33—85	33—85	38—82
Mean age	30.7	64.3	63.7	67.3

phoresis according to the method of Ornstein and Davis (1964). The CSF used was native, unconcentrated. Gel scanning was performed with a densitometer constructed in the Tartu State University. The densitometric trace was divided into 9 zones: pre-I-albumin, pre-II-albumin, albumin, α-globulin, transferrin, slow β-globulin, γ-globulin, α_2-macroglobulin and β-lipoproteid. Relative migration (R), defined as the ratio of the distance transversed by each protein zone to the distance of the whole front, was measured.

The total protein content of the CSF was determined by the method of Lowry.

The serum protein concentration was measured by a refractometer.

The lactic acid concentration in the CSF was determined by the method of Barker and Summerson.

Results

Table 2 presents the data obtained by estimating the content of the protein zones in CSF in mg/100 ml.

It can be seen that the mean values of all CSF protein zones and total protein were elevated. Especially increased values of γ-globulin and macroglobulins were noticed in patients with severe brain damage.

More information was obtained by the calculation of the relative concentrations of the protein zones of the CSF and of serum (Table 3).

A normal CSF contains pre-albumins 8.00, α-globulin 1.43, slow β-globulin 1.61 times relatively more than serum, γ-globulin 0.39, macroglobulins 0.28 times less than serum.

In patients with cerebral infarction the percentage of the pre-albumins and slow β-globulin decreased and γ-globulin increased, i. e. the protein composition of the CSF changed toward the protein composition of the serum, which depends on the severity of damage to the blood — CSF barrier (1, 3).

Table 2

Protein zones of CSF in patients with cerebral infarction
($\bar{x} \pm m$)

Protein zones (mg/100ml)	Control group	Cerebral infarction		
		Total cases	Moderate brain damage	Severe brain damage
Pre-I-albumin	3.30±0.11	3.81±0.08	3.64±0.08	4.64±0.25
Pre-II-albumin	0.24±0.01	0.98±0.09	0.77±0.06	1.97±0.40
Albumin	19.14±0.88	36.44±1.45	32.63±1.18	54.62±5.17
α-globulin	4.59±0.25	8.67±0.39	7.45±0.24	14.53±1.65
Transferrin	4.22±0.16	9.00±0.57	7.47±0.24	16.32±2.79
Slow β-globulin	2.70±0.13	5.01±0.23	4.36±0.13	8.14±1.04
γ-globulin	3.63±0.19	11.73±0.73	9.33±0.46	23.59±2.91
α_2-macroglobulin	0.28±0.03	0.89±0.11	0.59±0.04	2.02±0.51
β-lipoproteid	0.28±0.03	0.75±0.08	0.54±0.03	1.78±0.36
Total protein	78.85±1.15	78.35±3.66	67.15±2.09	131.93±15.75

Table 3

Protein relative concentrations of the CSF and of serum (CSF/Serum) ($x \pm m$)

Prtoein zones	Control group	Cerebral infarction		
		Total cases	Moderate brain damage	Severe brain damage
Pre-I + II-albumins	8.00±0.52	4.73±0.15	4.98±0.17	3.53±0.28
Albumin	1.14±0.03	1.18±0.02	1.18±0.02	1.14±0.06
α-globulin	1.43±0.09	1.50±0.03	1.51±0.04	1.43±0.07
Transferrin	1.06±0.07	1.03±0.02	1.02±0.02	1.11±0.06
Slow β-globulin	1.61±0.11	1.41±0.06	1.44±0.07	1.24±0.15
γ-globulin	0.39±0.02	0.53±0.01	0.49±0.01	0.71±0.05
Macroglobulins	0.28±0.03	0.35±0.02	0.32±0.01	0.50±0.05

This change is remarkable in patients with a severe brain damage.

Table 4 shows the data obtained by correlation between the content of the CSF protein zones and the CSF lactic acid concentration.

It can be seen that the content of pre-albumins, γ-globulin and macroglobulins in the CSF has a correlation with the lactic acid concentration in the CSF.

It is known that CSF acidosis indicates the presence of anaerobic glycolysis and acidosis in the brain tissue, and this occurs due to severe brain damage (4.5).

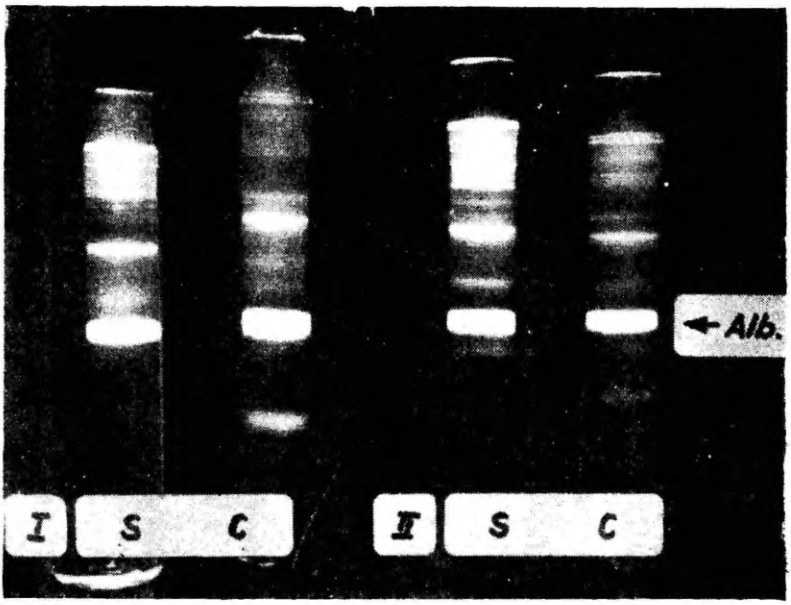

Fig. The patterns of polyacrylamide-gel disc electrophoretic proteins of normal composition (I) and of cerebral infarction (II). Abbreviations: S = serum; C = cerebrospinal fluid.

In the present study a close relationship was established between the severity of brain damage and the changes in the content of CSF protein zones in patients with cerebral infarction.

Table 4

Correlations between the CSF protein zones (expressed in percentage of total protein in mg/100 ml and in the ratio of the protein relative concentrations of CSF and serum) and the CSF lactic acid concentration

Protein zones	%	mg/100 ml	CSF % serum %
Pre-I-albumin	—0.027	0.479*	0.279
Pre-II-albumin	0.351	0.361*	0.279
Albumin	—0.320*	0.284	—0.260
α-globulin	—0.180	0.304	—0.200
Transferrin	0.447*	0.286	0.172
Slow β-globulin	—0.156	0.413*	—0.108
γ-globulin	0.462*	0.578*	0.590*
α_2-macroglobulin	0.445*	0.278	0.434*
β-lipoproteid	0.320*	0.388*	0.324
Macroglobulins	0.366*	0.478*	0.411*
Total protein	—	0.447*	—

* $P \leq 0.05$

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ЭЛЕКТРОФОРЕЗ БЕЛКОВ СПИННО-МОЗГОВОЙ ЖИДКОСТИ И СЫВОРОТКИ КРОВИ НА ПОЛИАКРИЛАМИДНОМ ГЕЛЕ У БОЛЬНЫХ С ИНФАРКТОМ ГОЛОВНОГО МОЗГА

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Резюме

Электрофорез белков спинно-мозговой жидкости (СМЖ) и сыворотки крови проводили на полиакриламидном геле по методу Davis и Ornstein (1964). Общий белок СМЖ определяли по методу Lowry, а лактат СМЖ по методу Barker и Summerson. СМЖ получили при люмбальной пункции.

Обследовано 188 больных с инфарктом головного мозга (ИМ) в течение первых двух недель заболевания. Среди них было 156 с лёгким и 32 — с тяжёлым поражением головного мозга. В качестве контрольной группы исследовали 40 лиц без признаков органического поражения головного мозга, у которых содержание общего белка в СМЖ было в пределах нормы.

Анализ полученных данных показал, что содержание общего белка СМЖ у больных с ИМ повышено. Характерным оказалось значительное повышение преальбуминов, γ-глобулинов и макроглобулинов, в особенности у больных с тяжёлым поражением головного мозга. Таким образом, состав СМЖ у больных с ИМ становится более сходным с составом сыворотки крови. Выявлена также корреляция между повышением лактата СМЖ и повышением преальбуминов, γ-глобулинов и макроглобулинов СМЖ у больных с инфарктом головного мозга.

VASOMOTOR EFFECTS OF THE STIMULATION OF VARIOUS SUBCORTICAL BRAIN STRUCTURES

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At the present time the role of extracerebral major arteries in the regulation of the blood circulation has been thoroughly investigated [1, 2, 3]. The regulatory role of the pial and cortical vessels has been studied to some extent [4, 5, 6]. At the same time the available data yield no information about microcircular reactions in the subcortical structures.

The aim of our work was to determine the subcortical structures, whose stimulation causes changes in the lumen of the cerebral microvessels, and the character of these changes.

Methods

Experiments were carried out on 155 adult rabbits. The regions under study were the following:

CT — *cortex temporalis*
CM — *cortex motorius*
VL — *nucleus ventralis lateralis thalami*
MD — *nucleus mediodorsalis thalami*
LA — *nucleus lateralis anterior thalami*
VA — *nucleus ventralis anterior thalami*
AHL — *area hypothalamica lateralis*
AHA — *area hypothalamica anterior*
HDM — *nucleus dorsomedialis hypothalami*
HVM — *nucleus ventromedialis hypothalami*
NHP — *nucleus hypothalamicus posterior*
AAA — *area amygdalaris anterior*
ACO — *nucleus corticalis amygdalae*
AME — *nucleus medialis amygdalae*
AC — *nucleus centralis amygdalae*
AL — *nucleus lateralis amygdalae*

AB — *nucleus basalis amygdalae*
HV — *pars ventralis hippocampi*
HD — *pars dorsalis hippocampi*
GP — *globus pallidus*
NFS — *nucleus fimbrialis septi*
NSL — *nucleus septalis lateralis*

The above-mentioned regions were separately subjected to monopolar electrical stimulation. The stainless steel electrodes (diameter 150 μ) covered (except of the 0.5 mm tip) with lacquer and organic glass insulation, being implanted stereotaxically, were used. A subcutaneous stainless steel spiral severed as the inactive electrode. Stimulation was carried out with rectangular impulses with the duration of 0.5 msec, frequency 60 Hz, potential 1 V. The duration of stimulation was 60×50 sec at 10 sec intervals.

At the last minute of stimulation the cerebral blood vessels vere fixed through a. carotis communis with 2 ml solution, the composition of what was: nigrosin 10%, gelatine 4.3%, phenol 0.9%, destilled water 84.8%.

At the same time 5 ml of saturated KCl solution was injected into the ear vein to stop heartbeat.

Experiments were carried out under urethan anesthesia (1 g/kg i. m.) together with local novocaine anesthesia. The blood pressure was measured with a Hg manometer through a catheter introduced into a. femoralis.

After the experiment the tissue round the electrode tip was coagulated in order to verify the electrode localization. The brain was removed and fixed in a 15% formalin solution during 48 hours. Then the brain was cut into 20—25 and 150—200 μ thick frontal sections on a freezing microtome. On cover-glass preparations coloured with thionine and haemolauc the lumen of the small blood vessels (starting with arterioles) was measured in all the above-mentioned structures with an ocular-scale microscope. Comparing the results of statistically analysed measurements with those of the check group we drew conclusions about the effect of stimulation of the above-mentioned structures on the microcirculation.

Results

The results of the experiments are given in the Table.

As there was no qualitative difference between the reactions in the different nuclei of one and the same structure, we shall present them below as one whole structure.

The stimulation of the thalamic nuclei caused a more or less expressed vasodilatation in all the investigated structures. Only in the case of stimulation of the MD the cortex vessels displayed

Lumen changes of the vessels (in ocular units) in the *cortex*, *thalamus*, *hypothalamus*, *septum*, *amygdala*, *hippocampus* and *globus pallidus* as caused by electrical stimulation (xx = P<0.01, x = P<0.05, (x) = P almost<0.05, — = not investigated)

Stimulated structures	Investigation regions of the microvessels						
	Cortex	*Thalamus*	*Hypo-thalamus*	*Septum*	*Amygdala*	*Hippocampus*	*Globus pallidus*
	Check lumen of the microvessels						
	2.02±0.08	1.78±0.03	1.79±0.03	1.81±0.08	1.89±0.04	1.85±0.11	1.83±0.12
	Lumen after stimulation						
Thalamus:							
VL	2.04±0.13	1.94±0.09	1.84±0.05	2.01±0.06	2.04±0.06	2.07±0.08	2.05±0.08
MD	1.83±0.15	2.05±0.09*	2.02±0.07*	1.99±0.10	2.02±0.06	2.06±0.06	2.10±0.06
LA	2.33±0.25	2.16±0.09*	2.11±0.10*	2.14±0.16	2.11±0.10(+)	2.08±0.05	2.14±0.05*
VA	2.02±0.15	1.99±0.10	2.10±0.14*	2.13±0.15	2.05±0.10	2.10±0.17	2.08±0.10
Hypothalamus:							
AHL ant.	3.10±0.40*	2.63±0.20*	2.28±0.13*	2.66±0.20*	2.82±0.13*	2.29±0.15(*)	2.70±0.24*
AHL post.	2.36±0.06	2.28±0.06*	2.15±0.05*	2.24±0.16*	2.15±0.07*	2.03±0.16	2.16±0.12(*)
AHA	2.24±0.14*	2.25±0.03*	2.20±0.04*	2.25±0.12*	2.22±0.04*	2.13±0.16	2.20±0.13*
HDM	2.20±0.24	2.18±0.03*	2.18±0.07	2.23±0.20(*)	2.28±0,09*	2.12±0.16	2.11±0.19(*)
HVM	2.27±0.16*	2.12±0.10	2.21±0.06	2.39±0.23	2.17±0.03*	2.09±0.17	2.23±0.19(*)
NHP	2.22±0.14*	2.21±0.03*	2.19±0.03*	2.32±0.24(*)	2.22±0.02*	2.09±0.10	2.36±0.14(*)
Septum:							
NFS	2.20±0.12	2.24±0.13(*)	2.12±0.13*	—	2.17±0.12	—	2.10±0.22
NSL	2.33±0.06(*)	2.18±0.15(*)	2.18±0.15*	—	2.22±0.13*	—	2.07±0.06
Amygdala:							
AME	1.86±0.12(*)	1.73±0.07	1.80±0,03	1.74±0.10*	1.73±0.07*	1.51±0.04	1.74±0.05
AL	1.78±0.19(*)	1.69±0.02*	1.74±0.03	1.72±0.06*	1.74±0.01*	1.61±0.05	1.64±0.10
AB	1.73±0.11*	1.78±0.05	1.74±0.03	1.64±0.06	1.82±0.02	1.65±0.10	1.62±0.10
AC	1.81±0.05*	1.76±0.14	1.70±0.03**	1.79±0.10*	1.71±0.03	1.76±0.14	1.75±0.11
Hippocampus	1.76±0.07(*)	1.99±0.10	2.04±0.13	2.07±0.06*	2.03±0.09	—	2.07±0.10
Gl. pallidus	1.99±0.03	2.04±0.23	2.18±0.26	2.06±0.04*	2.04±0.22	2.09±0.04	—

a tendency to constriction. The strongest vasodilating reaction over all the brain was caused by the stimulation of the LA.

The stimulation of the hypothalamic nuclei caused a distinct vasodilatation in all the investigated structures. In hippocampus it did not reach a statistically reliable level because of the great mean error (up to ± 0.17). The most considerable dilatation of the brain microvessels was observed when stimulating the anterior part of the AHL.

The stimulation of the septal nuclei caused vasodilatation in all structures. In the septum itself we could not estimate the lumen changes because of the large coagulation area arround the electrode tip. In the hippocampus we did not succeed in measuring the blood vessels in this series.

The amygdala was the only structure whose stimulation displayed no tendency to vasodilatation. The stimulation of the amygdalar nuclei either did not change considerably the lumen of the blood vessels or brought about some vasoconstriction.

The stimulation effects of the ventral and dorsal parts of the hippocampus were analogous. The blood vessels in this region were badly filled and the number of the measured lumens was relatively small, therefore the stimulation results of the HV and HD were considered together as a whole. In the cortex the stimulation of the hippocampus led to vasoconstriction. In all the other structures it caused vasodilatation.

The stimulation of the globus pallidus brought about vasodilatation in all the investigated structures with the exception of the cortex where practically no reaction took place. In the globus pallidus itself the blood vessels could not be measured due to the coagulation damage.

Discussion

The experimental data lead to the conclusion that a weak stimulation of subcortical structures causes vasodilatation in most cases, expressed to a greater or smaller extent. The exceptional case is the amygdala whose stimulation either did not change the lumen of the blood vessels or brought about to a constriction. Comparison of the other structures showed that the stimulation of more central (medial) structures, i. e. the hypothalamus, septum and to some extent also the thalamus, has a stronger vasodilating effect. That can be supposed as being related to their nonspecific activation system whose irritation state should activate also the cerebral circulation. The strongest vasodilatating effect in the stimulation of the hypothalamic nuclei was displayed by the anterior part of the AHL, in the stimulation of the nuclei of the septum — by the NSL, and in the stimulation of the thalamic nuclei — by the LA.

As far as it was possible to measure the blood vessels in the stimulated nucleus, it seemed that in comparison with the other cerebral regions the strongest reaction occurred in the nucleus itself.

The electrical stimulation of the structures studied did not bring about considerable changes in the general arterial pressure. Therefore the cause of the microcircular changes in our experiments should be attributed to some other mechanism, which will be explained in further experiments.

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СОСУДОДВИГАТЕЛЬНЫЕ ЭФФЕКТЫ СТИМУЛЯЦИИ РАЗЛИЧНЫХ ПОДКОРКОВЫХ СТРУКТУР ГОЛОВНОГО МОЗГА

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Резюме

Исследованию подвергалось действие электростимуляции различных ядер гипоталамуса, септума, амигдалы, гиппокампа и паллидума на внутренний диаметр микрососудов в тех же структурах и в новой коре. Опыты проведены на 155 кроликах

под уретановым наркозом. Во время стимуляции фиксировали прижизненно мозговые сосуды путем введения соответствующего раствора в общую сонную артерию и измеряли общее артериальное давление кровавым методом из бедренной артерии. Мозг резали на замораживающем микротоме. Сосуды исследовали на фронтальных срезах мозга.

Стимуляция большинства исследованных ядер вызывала вазодилятацию как в новой коре, так и в подкорковых структурах. Сравнительно бо́льшим вазодилятаторным эффектом обладала стимуляция гипоталамических, таламических и септальных ядер. Наиболее выраженная вазодилятация происходила при стимуляции переднелатерального гипоталамуса и переднего латерального ядра таламуса. Единственной структурой, стимуляции которой следовала вазоконструкция, была амигдала.

Так как в наших опытах никаких существенных изменений артериального давления не наблюдалось, причину вазодвигательных рефлексов следует искать в других механизмах.

INTRACRANIAL ARTERIAL ANEURYSMS IN CHILDREN

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Ruptured or symptomatic aneurysms in children are rare [1, 2, 4, 5, 8]. Yoshimoto [9] reported their frequency in the first two decades to have been 0,5% of the total number of patients with aneurysms, Nishioka [3] — 1.9%, Patel [4] — 1.3% and Sedzimir [5] — 4.6%. In 1967—1977 we studied altogether 1,095 patients with intracranial arterial aneurysms at the Neurosurgical Clinic of the University Central Hospital. 20 patients were from 0 to 16 years of age, i. e. 1.8%. The purpose of the present study is to find out the results of operative treatment and a late prognosis in this age-group compared with that of adults.

Material and methods

All survivors were invited for a personal checkup and a psychological test. One of the patients refused to come, she answered the questionnaire. Special attention was paid to the neurological deficits, the patient's working capacity and his education compared with that of his siblings and parents.

Age and sex

There were 11 girls and 9 boys. Only two of the patients were under 10 years of age. Three patients were from 10 to 13 years of age and the rest 15 patients were from 14 to 16 years.

Site of the aneurysms

More than half of the aneurysms, 12, were situated at the bifurcation of the internal carotid artery. Three patients had an

anterior communicating aneurysm ,two had a middle cerebral, one a posterior communicating, one a pericallosal and one a PICA aneurysm (Table 1).

Table 1

Location of aneurysms

Site	Number of cases
Carotid bifurcation	12
Anterior communicating	3
Middle cerebral	2
Posterior communicating	1
Pericallosal	1
Vertebral	1
Total	20

Treatment

16 patients were operated on. In 13 cases the neck of the aneurysm was clipped. In two cases, the first — an anterior communicating and the second a fusiform aneurysm of the pericallosal artery, proximal clipping was done. In one case only a wrapping of the aneurysm was performed. One patient was operated on during the first week after bleeding, 7 patients were operated on during the second, 5 patients during the third week and 3 patients still later.

Four patients were not operated on. Two because they were referred to the neurosurgical clinic more than six weeks after bleeding. One patient died 7 days after the SAH without regaining consciousness. One patient had not had a SAH and was investigated because of epileptic fits.

Results

Operated patients: There was one operative death. The patient in whom only a wrapping of the aneurysm was done, died two months after the operation of rebleeding. Out of the 14 survivors 10 were well, had had no neurological deficits, were either employed or were continuing their studies. All of them stated that their illness and operation had not prevented them from completing their studies or choosing the kind of job they had preferred. One patient had a slight residual hemiparesis which, however, did not disturb her studies.

Three patients were disabled. Two had a severe psychoorganic syndrome and epilepsy. The third patient was operated on at the

age of six months because of a ruptured middle cerebral aneurysm. She is retarded, not able to attend a normal school and has had epileptic fits.

Conservatively treated patients: Those two patients with a ruptured aneurysm not operated on have been well during the follow-up period of 9 and 10 years and have not had a rebleeding. The fourth patient with no subarachnoid hemorrhage has been well, has had a normal delivery and a healthy child and no bleeding during the follow-up period of 10 years.

Discussion

In children under 10 years of age aneurysms are unusual either because of the site or the size. This was also true for our two patients in this age-group. The middle cerebral aneurysm was situated in a distal branch of the middle cerebral artery. There was no evidence for an inflammatory origin of the aneurysm. The other patient had a fusiform aneurysm of the pericallosal artery.

Aneurysm ruptures in childhood seem to occur in the older age-groups from 12 to 16 years of age. The site of aneurysms differs from that in adults. More than a half of the aneurysms were situated at the bifurcation of the internal carotid artery — a location rare for adults. This has been the common location also in an other large series of childhood aneurysms [4,5] except that of Amacher [2]. The next commonest site is the anterior communicating artery. We receive all aneurysm patients from a certain geographical area. Thus the distribution of sites should be representative. The usual locations in adults — the posterior communicating and the middle cerebral artery — are rare in children. We had no multiple aneurysms. Neither did we observe any congenital malformations such as coarctation of the aorta or a polycystic kidney reported to be associated with childhood aneurysms [4, 6].

In 80% of the operated cases direct intracranial clipping of the neck of the aneurysm was done. There were no operative fatalities among the patients with aneurysms of the carotid bifurcation. They only operative death occurred in a patient with an anterior communicating aneurysm, who was still drowsy and desoriented at the time of the operation. He suddenly died two days after the operation. The autopsy showed that the clip was well in place and it did not occlude any artery. There was a wide infarction in the left cerebral hemisphere, opposite to the operative approach. If the operation had been postponed until the patient's level of consciousness had returned to normal, the result might have been better.

The majority of the patients surviving the operation had no

neurological deficit and were fully able to work or pursue their studies. One patient had a slight neurological deficit which did not interfere with her work or studies. Thus in 78% of the operated cases the results were good. Three patients were permanently disabled because of psycho-organic syndrome and epilepsy. It seems that children tolerate an operation better than adults. In a series of adult patients from this clinic the percentage of good results was 60% [7].

Two-thirds of the patients with a fatal outcome in Patel's and Sedzimir's series were either comatose or drowsy at the time of the operation, as was also our one operative fatality. Thus it seems clear that an operation should be undertaken only if the patient is fully alert and oriented. If the patient is comatose or drowsy, the operation should be postponed until the level of consciousness has returned to normal. The operative method of choice is direct intracranial clipping of the neck of the aneurysm. In selected cases a proximal clipping is advisable. The optimal time for the operation seems to be 7—10 days after bleeding. However, we have been able to follow this rule only in half of our cases.

Summary

A report on 20 children from 0 to 16 years of age with an intracranial arterial aneurysm. 19 patients had had a subarachnoid bleeding and one patient was investigated because of epileptic fits. Only two of the patients were under 10 years of age. More than a half of the aneurysms, 12, were situated at the bifurcation of the internal carotid artery. 16 patients were operated on. In 13 cases the neck of the aneurysm was clipped, in two cases a proximal clipping and in one case a wrapping of the aneurysm was done. There was one operative death. 10 of the operated patients were well, had no neurological deficits and were fully able to work or pursue their studies. One patient had a slight neurological deficit, not interfering with her work, and 3 patients had a disabling neurological deficit. An operation should be performed only if the level of consciousness is normal. Direct intracranial clipping of the neck of the aneurysm is the method of choice. The optimum time for operation is probably 7—10 days after the bleeding.

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ИНТРАКРАНИАЛЬНЫЕ АРТЕРИАЛЬНЫЕ АНЕВРИЗМЫ У ДЕТЕЙ

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Резюме

Приведены данные 20 детей в возрасте 0—16 лет, имеющих интракраниальные артериальные аневризмы. У 19 из них наблюдалось субарахноидальное кровоизлияние, один ребёнок был исследован по поводу эпилептических припадков. Лишь два из больных были моложе 10 лет. Больше половины аневризм (12) находились в области бифуркации внутренней сонной артерии. Шестнадцать больных были оперированы, в 13 случаях клипировали шейку аневризмы, в 2 случаях клипсы поставили проксимальнее от аневризмы. В одном случае было проведено закутывание мешка аневризмы мышцей. Имел место один случай послеоперативной смерти. Десять оперированных детей чувствовали себя хорошо, не имели никакой неврологической симптоматики, были способны работать и учиться. У одного больного осталась незначительная неврологическая симптоматика и у трех больных стойкий неврологический дефицит.

Из работы вытекает, что оперативное вмешательство при аневризмах у детей дает более хорошие результаты, если оперируют больных, не имеющих расстройств сознания. Наиболее оптимальное время для операции — 7—10 дни после кровотечения.

SURGICAL TREATMENT OF SACCULAR ANEURYSMS OF BRAIN ARTERIES

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Saccular aneurysms were first described on the basis of autopsies in the 18th century (5). Cerebral angiography introduced by Moniz in 1927 (3, 4) made it possible to diagnose aneurysms in patients.

The year 1930 marks a starting point in the diagnosis of aneurysms at the Neurosurgical Clinic of Tartu (7, 11). L. Puusepp wrote in 1939 (6) that arteriography was especially useful, being indispensable in the diagnosis of aneurysms just because it gives the exact size and location of an aneurysm. In 1939 a dissertation by G. Martinoff (2) on the clinical and angiographic diagnosis of the aneurysms treated at the Neurosurgical Clinic of Tartu was published. Up to 1939 three patients with a ruptured aneurysm had been surgically treated. Two of them underwent an internal carotid artery ligation on the neck, and one patient — a communicating carotid artery ligation. No complications occurred (2). In 1939 L. Puusepp removed an acute intracerebral hemorrhage from a lateral cerebral fissure (Sylvii). The patient recovered, but three weeks later there followed headache and weakness of the left hand. An aneurysm of the middle cerebral artery was diagnosed by means of carotid arteriography using thorotrast. When the internal carotid artery on the neck was ligated, the patient recovered (6).

When watersoluble contrast mediums became available, arteriographic diagnoses and the surgical treatment of aneurysms were reintroduced in 1957 at the Neurosurgical Clinic of Tartu (9).

Clinical material

In the years 1961 to 1978 eighty patients were surgically treated (see Table 1).

Table I

Age and sex of the patients operated on

Age of patients	0—9	10—19	20—29	30—39	40—49	50—59	60—69	70—79	Total
Men	1	—	7	11	9	8	4	—	40
Women	—	—	2	4	13	11	9	1	40
Total	1	—	9	15	22	19	13	1	80

Surgically treated aneurysms were located on the following cerebral arteries: internal carotid artery — 25 cases; anterior communicating artery and anterior cerebral artery — 33 cases; middle cerebral artery — 18 cases; posterior communicating artery — 5 cases.

Surgical method

Operations were carried out under general anaesthesia. They included: lateral frontal osteoplastic craniotomy performed in patients with anterior cerebral and anterior communicating artery aneurysms, unilateral osteoplastic frontotemporal craniotomy with subtemporal decompression in the internal carotid artery, in the posterior communicating artery and in the aneurysms of the middle cerebral artery.

For a better approach to the base of the skull in the intracranial phase of operation we used pulmonary hyperventilation with arterial pCO_2 within the limits of 25 mm Hg (10). Basal cisterns were then opened and the liquor was sucked. The method described allowed us access to aneurysms in the acute state of bleeding and in the brain oedema. Then there followed the aspiration of the hemorrhage, preparation of the aneurysm from adhesions and the clipping of the aneurysm, at the same time retaining the blood circulation in the cerebral arteries.

Surgical results

Of the 45 patients who were surgically treated after stilling the blood flow from a ruptured aneurysm and who were in a good general condition without any disturbances of consciousness, 42 (93.3 per cent) recovered. But of the 35 patients operated on in an acute state of bleeding only 11 (31.4 per cent) recovered.

Surgical treatment in an acute state was carried out on the patients whose consciousness progressively deteriorated. The cause of unconsciousness was subarachnoid rebleeding, intracerebral hemorrhage and brain oedema.

Out of the patients operated on in a good general condition without disturbances of consciousness, 3 died, the cause of death being accordingly rebleeding, cerebral infarction and pulmonary infarction. Of the 35 cases surgically treated in a state of unconsciousness, 24 died, 14 of them from brain oedema. 2 patients died from rebleeding, 3 from cerebral infarction, 4 from bronchopneumonia, 1 from cardiovascular insufficiency. 8 patients with an acute brain oedema died within 1—2 days after the operation, the others died within 5—74 days.

Table 2

Causes of death in the patients operated on

Cause of death	Patients operated on in a state	
	without disturbances of consciousness	of progressive deterioration of consciousness
Cerebral oedema	—	14
Rebleeding	1	2
Cerebral infarction	1	3
Pulmonary infarction	1	—
Bronchial pneumonia	—	4
Cardiovascular insufficiency	—	1
Total	3	24

Discussion

According to the data published in the literature on the neurosurgical treatment of saccular aneurysms of the brain arteries, the results of operations depended on the choice of patients. A. Konovalov's (8) data from the Institute of Neurosurgery in Moscow showed that the lethality of surgically treated patients with aneurysms of the brain arteries was 25—30 per cent until 1970, but later on lethality decreased to 5—8 per cent. A decrease in lethality was achieved by improving the surgical technique (including the microsurgical technique) and the principles of therapy.

The authors avoided operating on patients in a bad general condition except for those whose condition was caused by intracranial hemorrhage compressing the brain. Spasms of the cerebral arteries were not absolute contraindications for an operation.

In recent years the use of microsurgery has brought about fewer injuries to the brain arteries by a decrease in postsurgical arterial spasms as well as by better results of surgical treatment. Hollin, for example (1), with a selected contingent has obtained good results by using microsurgical methods in 84 per cent of 70

cases. His patients were operated on within 3—35 days of illness. He recommended to operate on patients 10 to 14 days after a subarachnoid hemorrhage.

There are neurosurgeons who prefer to operate on patients only in a good general condition with the aim of reducing postoperative lethality. Again there are others who operate on patients whose consciousness is progressively deteriorating with the aim of saving the patient's life and of preventing rebleedings in future. In view of the fact that a part of our patients operated on in a state of disturbances of consciousness recovered, an extraordinary surgical treatment is indicated.

In our opinion it is indicated that each patient with subarachnoid hemorrhage should within the first 24—48 hours undergo arteriographic investigation of both the carotid systems for the diagnosis of the location of an aneurysm and a study of the blood supply. After this the patient must be submitted to conservative therapy and a permanent neurological observation. The indication and the time for surgical treatment are determined according to the patient's condition. If he is losing consciousness (somnolence, sopor), he must be immediately operated on before falling into coma. In case of decreasing meningeal symptoms, and syndromes of unconsciousness, the patients with ruptured aneurysms must be operated on within 4—7 days to prevent subarachnoid rebleeding.

Conclusions

1) To make an accurate diagnosis of aneurysms, patients with subarachnoid hemorrhages must be immediately examined angiographically.

2) Patients with ruptured aneurysms must be operated on immediately, if they are losing consciousness. For recovering patients surgical treatment is indicated within 4—7 days to prevent subarachnoid rebleeding.

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ХИРУРГИЧЕСКОЕ ЛЕЧЕНИЕ МЕШОТЧАТЫХ АНЕВРИЗМ АРТЕРИЙ ГОЛОВНОГО МОЗГА

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Резюме

В Тартуской нейрохирургической клинике стали оперировать аневризмы артерий головного мозга в 1930 г. (Л. Пуусепп). В качестве метода операции применялась лигатура внутренней или общей сонной артерии. Начиная с 1961 г. применяется внутричерепное вмешательство, до 1978 г. прооперировано у 80 больных 81 аневризма. Локализация аневризм была следующей: внутренняя сонная артерия — 25, передняя соединительная артерия и передняя артерия мозга — 33, средняя артерия мозга — 18, задняя соединительная артерия — 5.

Из 45 больных, оперированных в хорошем состоянии, без расстройств сознания, поправились 42 (93,3%). Из оперированных в сопорозном или коматозном состоянии поправились 11 (31,4%).

Авторы считают необходимым немедленно после возникновения субарахноидального кровоизлияния проводить ангиографическое исследование обеих сонных артерий для определения аневризм и их топики. Больных с разрывом аневризм, у которых в результате применения консервативных методов лечения наступает улучшение, желательно оперировать на 4—7 день после кровоизлияния. Но при углублении расстройств сознания больного следует оперировать в экстренном порядке.

SURGICAL TREATMENT OF OCCLUSIVE LESIONS IN THE CAROTID ARTERIES

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Surgical material

In 1963—1978 of 47 patients with occlusive lesions operated on at the Neurosurgical Clinic of Tartu, 31 had internal carotid occlusions, 4 common carotid occlusions, 12 internal carotid stenoses.

According to clinical neurological findings, patients were divided into 3 groups:

1) 21 patients who had transient hemiparesis or weakness of one arm (lasting from a few minutes to some hours). Some of them had transient visual field defects of one eye (on the same side), speech defects. These symptoms recurred in an interval of some months to two years, but were persistent before the operation.

2) 5 patients whose hemiparesis developed progressively; right-sided hemiparesis was accompanied by speech defects.

3) 21 patients who had an attack of hemiparesis or paralysis; right-sided hemiparesis was accompanied by speech defects.

Arteriographic examination of the carotid system led to the conclusion that some patients with occlusive lesions in the internal carotid arteries had a fully developed collateral blood flow either through the ophthalmic artery or via the opposite internal carotid artery. The interval from the onset of the disease up to its arteriographic examination lasted from 3 weeks to 6 months. EEG studies showed a general dysrythmia of cortical bioelectrical activity; on the side of the internal carotid occlusion, groups of slow waves were detected in the frontotemporal territory, but seldom in the frontotemporal-parietooccipital territory. Compression tests of the carotid arteries were in most cases unilaterally, sometimes bilaterally positive (showing severe defects in the blood circulation in the internal carotid territory), in some cases negative (showing a good collateral blood supply).

Surgical methods and results

Surgical methods are given in Table 1. Of the 30 patients in whom were performed thrombendarterectomy, in 19 patients the blood flow was reestablished in the internal carotid artery (Table 2).

Table 1

Methods of operation

Operating method	Number of patients
Thrombendarterectomy of internal and common carotid arteries	30
Transplantation of external carotid artery into internal carotid artery	1
Sympathectomy of carotid arteries	16
Total	47

Table 2

Reestablishment of blood flow in internal carotid artery

Operating method	Number of patients	Blood flow in internal carotid artery	
		reestablished	not reestablished
Thrombendarterectomy	30	19	11
Transplantation of the external carotid artery into the internal carotid artery	1	1	—
Total	31	20	11

The blood flow was reestablished mainly in those patients who were surgically treated 10 to 18 hours after the onset of hemiparesis. This also occurred in the patients operated on later — in one case 2.5 weeks after the onset of the disease, in two cases after 2 months, in one case after 3.5 months. In those patients a segmentary occlusion or stenosis was noted at a length of 1 to 2 cm at the beginning of the internal carotid artery or at the level of the common carotid artery bifurcation. The reestablishment of the blood flow was unsuccessful in patients with occlusions of the internal carotid artery from its origin to the base of the skull. After the removal of thrombosis and the reestablishment of the blood flow the cutting of the artery was sutured (25 patients), or dilated and closed with a piece of the patient's vein (5 patients).

In one patient who had stenosis at a length of 4 cm in the internal carotid artery, the external carotid artery was transplanted into the internal carotid artery.

In 4 cases rethrombosis occurred after the operation. Of the thrombendarterectomized patients (Table 3), 18 recovered, 5 were discharged in an unimproved condition, 7 died. The last-mentioned patients suffered from severe cerebrovascular insufficiency before the operation, the arteriograms did not show any signs of a collateral blood flow. In three of them the blood flow in the internal carotid artery was reestablished, but after the operation cardiovascular insufficiency increased, in addition, one patient developed rethrombosis, both died in 3 days; one patient, surgically treated 5 weeks after the onset of hemiparesis, had a subarachnoid and intracerebral hemorrhage, and died on the third day.

Table 3

Results of thrombendarterectomy

Results	Number of patients
Recovered	18
Unimproved	5
Died	7
Total	30

In one case rethrombosis occurred 8 hours after the operation; the patient died 26 hours later. In one patient an occlusion of the vertebral artery developed on the third day after thrombosis in the internal carotid artery had been removed, which was diagnosed both on the clinical findings and at the section. In 2 patients whose blood flow failed to be restored a pre-operative sopor deepened, both died (Table 4).

Table 4

Causes of death of thrombendarterectomized patients

Cause of death	Number of patients
Cardiovascular insufficiency	2
Rethrombosis	1
Occlusio a. vertebralis	1
Cerebrovascular insufficiency	2
Subarachnoid and intracerebral hemorrhage	1
Total	7

16 patients were sympathectomized. They were operated on in 6 weeks to 2 years after the appearance of the symptoms of transient defects of the blood circulation (persistent before the operation: from 12 days to 4 months). When leaving the hospital (Table 5) 6 patients had normal neurologic findings, 4 recovered.

Table 5

Results of periarterial sympathectomy

Results	Number of patients
Recovered	6
Improved	4
Unimproved	1
Occlusio a. popliteae	1
Died	4
Total	16

The condition of one patient did not improve. One patient developed thrombosis of the popliteal artery, which was removed. 4 patients died, the causes of their death are given in Table 6.

Table 6

Causes of death in sympathectomized patients

Cause of death	Number of patients
Cardiovascular insufficiency	2
Acute laryngeal oedema	1
Cerebral infarction	1
Total	4

Catamnestic examination (4) up to 6 years after surgical treatment revealed that 7 patients of the group expressed no complaints, 5 patients of these worked in the field of their speciality. One patient had hemiparesis 15 months after the operation, 1 patient died from cardiovascular insufficiency.

Conclusions

It can be seen from our material that it is possible to reestablish the blood circulation in the internal carotid arteries 2 to 3.5 months after the first neurological symptoms. In our opinion surgical treatment can be indicated in internal carotid artery occlu-

sions unless the patient is in a comatose condition, or unless he suffers from cardiovascular insufficiency. In case the reestablishment of the blood circulation in the internal carotid arteries is impossible, periarterial sympathectomy can be made in the common and internal carotid arteries, or according to the data available in the literature (1, 2, 3) a microanastomosis between the branches of the temporal superficial arteries and the middle cerebral artery is indicated.

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ХИРУРГИЧЕСКОЕ ЛЕЧЕНИЕ ОККЛЮЗИРУЮЩИХ ПРОЦЕССОВ СОННЫХ АРТЕРИЙ

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Резюме

В 1963—1978 гг. в Тартуской нейрохирургической клинике оперировали 47 больных, из которых у 31 была окклюзия внутренней, у 4 — общей сонной артерии, у 12 — стеноз внутренней сонной артерии.

У 30 больных применили тромбэндартерэктомию внутренней и общей сонной артерий, у 16 периартериальную симпатэктомию сонных артерий. Причем у 19 тромбэндартерэктомированных больных восстановился кровоток внутренней сонной артерии. Восстановление кровотока было возможным и через 2—3,5 месяца после возникновения первых неврологических симптомов. Образование ретромбозов в послеоперационный период наблюдалось у 4 больных. Из тромбэндартерэктомированных больных относительно выздоровели 18, выписались без перемен — 5, умерли — 7. Из симпатэктомированных больных выздоровели 6, поправились — 4, выписались без перемен — 2, умерли — 4.

Авторы считают показанным оперативное вмешательство у больных с окклюзией внутренней сонной артерии, если у них не имеется сердечно-сосудистой недостаточности или ангиографически не установлено замедления кровотока мозга. Если не удается восстановить кровоток внутренней сонной артерии, показана периартериальная симпатэктомия общей, внутренней и наружной сонной артерий.

SURGICAL TREATMENT OF SPONTANEOUS INTRACEREBRAL HEMORRHAGES

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In many cases of a large intracerebral hemorrhage a conservative treatment has no effect, the patients die in some days after falling ill due to brainstem compression. If the surgical treatment is used in time, cases of death are not so frequent.

Surgical material

At the Neurosurgical Clinic of Tartu patients with an intracerebral hemorrhage have been treated surgically since 1957. Up to the end of 1978, 62 patients have been operated on. 36 of them were men and 26 women. For the age of the patients see Table 1.

Table 1

Age of patients

Age (in years)	Number of patients
10—20	2
21—30	5
31—40	5
41—50	13
51—60	19
61—70	15
71—80	3
Total	62

Etiological factors are given in Table 2. In most cases hemorrhage is provoked by some physical strain. The cause of intracerebral hemorrhages of the persons whose age was not more

than 40 years can be intracerebral arteriovenous aneurysms, which are diagnosed by the use of a serioangiograph; arteriovenous microaneurysms are diagnosed by studying the operation material histologically. The material of the last 10 years shows that chronical alcoholism is an etiological factor.

Table 2

Etiological factors

Etiological factors	Number of patients
Hypertension, arterial hypertension with atherosclerosis	43
Atherosclerosis	6
Arteriovenous aneurysm	2
Thromboangiitis	1
Chronical alcoholism	5
Unclear	5
Total	62

The location of hemorrhage was determined on the basis of neurological, echoencephalographical and angiographical investigations. Hemorrhage is most frequent in the temporal lobe (see Table 3). It is worth mentioning that the focus of the hemorrhage of the patients who suffered from chronical alcoholism was larger and was located in two lobes (in the area of the temporal and frontal or the frontal and parietal lobe).

Table 3

Location of hemorrhage in the brain

Location of hemorrhage	On the right side	On the left side	Total
Frontal lobe	3	3	6
Temporal lobe	17	18	35
Frontal and temporal lobe	4	5	9
Frontal and parietal lobe	3	2	5
Capsula interna	2	3	5
Cerebellum	—	2	2
Total	29	33	62

Out of 62 patients operated on by us, 31 were before the operation unconscious (see Table 4).

Table 4

State of consciousness before operation

State of consciousness	Number of patients
Coma	31
Sopor	20
Somnolence	6
Normal	5
Total	62

Surgical method and results

We performed a large craniotomy or trepanation with subtemporal decompression during the operation. The exact place of the hemorrhage was fixed by observation and palpation of the brain and by the puncturing of the hemorrhage. After puncturing the hemorrhage and aspiration of the fluid blood through a needle encephalotomy was made and the coagulated blood was rinsed out. A rubber tube tampon was left in the cavity of the hemorrhage for 24 to 48 hours.

The results of the operation depend on the state of the patient's consciousness (see Table 5).

Table 5

Results of operations

State of consciousness	Recovered	Died	Total
Coma	6(19.4%)	25(80.6%)	31(100%)
Sopor	17(85.0%)	3(15.0%)	20(100%)
Somnolence	4	2	6
Normal	5	—	5
Total	32(51.6%)	30(48.44%)	62(100%)

Of the 31 patients operated on in the state of coma, 6 recovered (19.4%), 12 patients (38.7%) recovered temporarily, they regained consciousness. They lived from 6 up to 117 days after the operation and died due to complications, mostly due to cardiovascular insufficiency and bronchopneumonia. Out of the 51 patients operated on extraordinarily in coma or sopor, 23 recovered (45%).

Causes of the death of the patients are given in Table 6.

Table 6

Cause of death

Cause of death	Number of patients
Brain oedema	8
Large (including intraventricular) hemorrhage	4
Recurrent intracerebral hemorrhage	2
Acute cardiovascular insufficiency	7
Bronchopneumonia	6
Purulent meningitis	1
Carcinomatosis	1
Thromboangiitis	1
Total	30

Discussion

According to the data available in the literature, it is still debatable when to operate on an intracerebral hemorrhage — whether to wait for the recovery of the patient's general state of health or to carry out an extraordinary operation.

From the recently published literature (1, 2, 3) it seems that computertomography is of immense diagnostic value in diagnosing the foci of intracerebral hemorrhages early, pointing out their exact size and location. Due to that circumstance neurosurgeons have become more active and carry out an operation on an intracerebral hemorrhage at once when it causes intracranial hypertension, and when the patient's consciousness is progressively deteriorating (3).

In our opinion (6, 7, 8) an extraordinary neurosurgical operation is necessary since the patients having large hemorrhages die mostly some hours or days after the formation of the hemorrhage. An early operation helps to avoid the development of a brain oedema and damage to the brain stem. It is obvious that the deeper the disturbances of consciousness, the greater the lethality. It is possible to save some patients who have been for a short time in deep coma by removing the hemorrhage early and by using intensive care after the operation.

According to the data of Yarnell and Earnest (4), 14% of the patients who needed an extraordinary operation recovered.

Conclusions

From this material we can conclude that in spite of high lethality neurosurgeons have to carry out an extraordinary operation on the patients having an intracerebral hemorrhage.

Only in case the hemorrhage is located deep in the brain hemisphere from which the blood has penetrated into the ventricles or the patients are in deep coma, surgical treatment is not indicated.

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ХИРУРГИЧЕСКОЕ ЛЕЧЕНИЕ СПОНТАННЫХ ВНУТРИМОЗГОВЫХ КРОВОИЗЛИЯНИЙ

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Резюме

В Тартуской нейрохирургической клинике занимаются хирургическим лечением спонтанных внутримозговых кровоизлияний с 1957 года. До 1978 г. оперировано 62 больных. Из них было мужчин 36, женщин — 26. В качестве этиологических факторов диагностировали гипертоническую болезнь вместе с атеросклерозом в 43 случаях, атеросклероз без повышения кровяного давления — в 6, артериовенозные аневризмы — в 2, хронический алкоголизм — в 5, тромбангит — в 1 случае. Этиология осталась невыясненной в 5 случаях.

Локализация очага внутримозгового кровоизлияния определялась по клинической картине и применению эхоэнцефалографических и ангиографических исследований.

Методом операции применяли или широкую краниотомию или трепанацию, всегда вместе с субтемпоральной декомпрессией. Твердую мозговую оболочку вскрывали, гематому пунктировали и аспирировали. Затем вскрывали полость гематомы и физиологическим раствором промывали-удаляли кровяные сгустки. В образовавшейся полости оставляли резиновую трубку на 24—48 часов.

Из оперированных в коматозном состоянии (31 больной) поправились 6 (19,4%), у 12 (38,7%) наблюдалось временное улучшение, они пришли в сознание, жили 6—117 дней после операции и умерли от компликаций — в основном от бронхопневмонии и сердечной недостаточности. Из оперированных в сопорозном состоянии (20 больных) — поправились 17, умерли 3, в сомнолентном состоянии (6 больных) — поправились 4, умерли 2 больных. 5 оперированных больных без расстройств сознания — поправились.

По мнению авторов, при внутримозговых гематомах показана экстренная операция. Глубокие внутриполушарные и интравентрикулярные кровоизлияния считаются неоперабельными.

IMMEDIATE AND LONG-TERM PROGNOSIS IN SAH DUE TO RUPTURED INTRACRANIAL ANEURYSMS

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Up to now considerable attention has been paid to the problems of prognosis and treatment of SAH caused by intracranial aneurysms. It has been estimated that about 35% of the patients with initial bleeding die within 2—3 days after the onset of symptoms (4, 5). But rebleeding has also been a major cause of death. Many neurosurgeons indicate high rebleeding rates with a high mortality during the first weeks after SAH (1, 2, 5, 6, 7). Although the frequency of rebleeding among non-operated patients then gradually diminishes, the figures for the following 2—3 years remain relatively high and are rather different in many neurosurgeons' reports — 30—69% (1, 3, 5).

The main object of this study was to evaluate the rebleeding risk in connection with the aneurysm site, the neurological condition and the time interval elapsed from the initial bleeding, and also to examine the mortality due to recurrent SAH.

From 1966 through 1979, 168 patients with ruptured intracranial aneurysms were treated at the neurosurgical department of the Tallinn Republican Hospital.

The incidence of SAH caused by ruptured aneurysms was somewhat higher for women — 52% (96) than for men — 48% (72). No significant difference was apparent in their median ages — for women 45, for men 42 years.

Among our patients' 41% (67) had an aneurysm on the anterior cerebral-anterior communicating complex, 30% (53) on the intracranial portion of the internal carotid artery, 21% (39) on the middle cerebral distribution, 3% (5) on the posterior communicating and 2% (4) on the basilar artery.

In our series of 168 patients, 101 were treated surgically, 57 conservatively. The usual timing for surgery was 12—13 days from SAH or rebleeding. The reasons for conservative treatment wer mainly the refusal of the patients to accept an operation, or the type of aneurysms was considered technically difficult. In

some cases the patients were rather old or were suffering from other serious diseases. The patients in a poor neurological condition also belonged to this group.

Out of our 168 patients (those prior to an operation or those non-operated), 41% (69) had a recurrent bleeding, in 21% (35) of them it occurred twice.

The percentage of rebleeding was higher — 58% (39) for the anterior cerebral-anterior communicating complex, followed by 45% (24) for the internal carotid group and 15% (6) for the

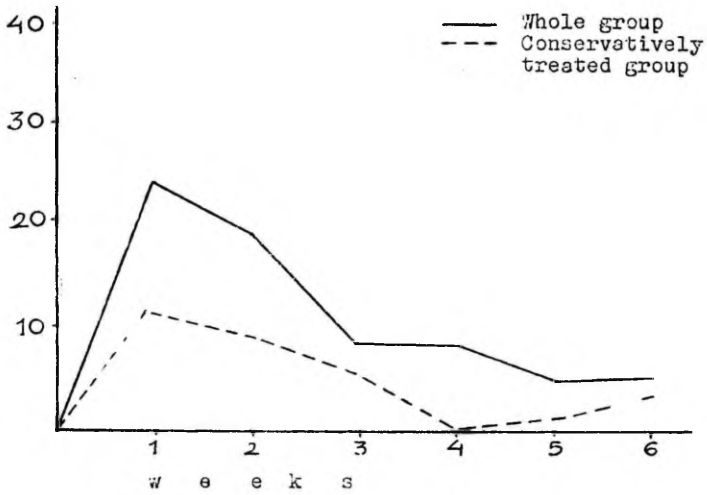

Fig. Graphic comparison of rebleeding rates at intervals following SAH for the whole group and the conservatively treated group

middle cerebral group. The corresponding figures for the second rebleeding were 30% (19), 25% (13) and 7% (3).

105 patients were admitted to our department in a relatively good, 63 in a poor condition (according to Botterell's classification). Recurrent SAH was observed in 42% (44 of patients in a good condition and 39% (25) in a poor condition.

The recurrence of SAH occurred within the first and the second week in 35% (24) and 28% (19) of the cases. The rebleeding rate was lower in the third and the fourth week — 12% (8) and 12% (8), respectively leaving 7% (5) and 7% (5) of cases for the following two weeks. Comparing the rebleeding rate of conservatively treated patients (which is nearest to the actual natural course following SAH) with the previous one, the corresponding numbers of cases for the weeks were — 11, 8, 5, —, 1, 3

respectively. In reveals that the rebleeding frequency distribution gradually diminished in the subsequent intervals (Figure 1).

3.5% (6) of the patients died because of a progressive deterioration of the clinical condition after SAH, 4% (7) following the rebleeding and 8% (14) after the second rebleeding. Of all 69 cases of recurrent SAH, death occurred in 30% (21) of the cases mostly following the second rebleeding — 20% (14). Mortality was directly related to the recurrence of SAH (Table 1).

Table 1

Distribution of causes of death brought about by SAH for each aneurysm site

Aneurysm site	No. of SAH cases	No. of rebleedings	No. of second rebleedings	Cause of death			
				progressive decline	first rebleeding	second rebleeding	total
A.C.	67	39	19	1	4	8	13
I.C.	53	24	13	—	2	3	5
M.C.	39	6	3	1	1	3	5
P.C.	5	—	—	1	—	—	1
Basilar	4	—	—	3	—	—	3
Total	168	69	35	6	7	14	27

Death after surgery usually was caused by cerebral oedema or infarction, only in one case it was caused by rebleeding. The clip had slipped off from the neck of the aneurysm. The patient died before reoperation.

Data of follow-up results were obtained from 63 surgically and 29 conservatively treated patients (total 92). The patients were checked personally if possible, otherwise information was received from patients or district neurologists by mail.

During the mean follow-up interval of 3.5 years (from 6 months to 10 years), the mortality was 18% (17).

Recurrence of SAH was the cause of death for 10% (9) of the patients. In the conservatively treated group it was 21% (6), in

the surgically treated group — 5% (3). In 8 cases the remaining causes of death were 3 accidents, 4 cardiovascular and 1 pulmonary disease.

Among the conservatively treated patients fatal rebleeding occurred in two cases within 3 months, in the other cases within 1, 2, 4 and 10 years. In the surgically treated group these intervals were 3 months, 1 and 2 years. There were two non-fatal cases of rebleeding within 2 and 4 years — one proved and one suspected. Both patients were treated non-surgically.

Our results compared to those of some neurosurgeons (1, 5) indicate the relatively low fatal rebleeding rate in the follow-up study, especially after the lapse of two years from SAH.

According to our data, the aneurysm site and the time interval following the last bleeding were the important factors related to recurrent SAH. The time period in which rebleeding was most likely to occur was within 2—3 weeks, the rebleeding rate was higher for the patients having an aneurysm on the anterior cerebral-anterior communicating artery. Comparison of the rebleeding rate among patients in a good and a poor condition revealed no significant difference.

The mortality rate of the survivors of the first bleeding constantly increased after further rebleeding.

The risk of rebleeding with a subsequent mortality and the follow-up results give further support to the early surgical treatment to prevent the recurrence of SAH. The follow-up results may have been influenced by the small number of patients and therefore it needs further study. But a specific technical ability and experience of the surgeon are also important factors (postoperative mortality) in directing patients to surgery or in sending them to more specialised neurosurgical departments.

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НЕПОСРЕДСТВЕННЫЙ И ОТДАЛЕННЫЙ ПРОГНОЗ СУБАРАХНОИДАЛЬНЫХ КРОВОИЗЛИЯНИЙ, ОБУСЛОВЛЕННЫХ ИНТРАКРАНИАЛЬНЫМИ АНЕВРИЗМАМИ

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Резюме

В данном исследовании оценивался риск повторного кровоизлияния, связанный с локализацией аневризмы, тяжестью состояния больного после кровоизлияния при поступлении и сроком с момента заболевания.

Обследовано 168 больных, из них у 69 кровоизлияния повторились. Из госпитализированных больных после первого кровоизлияния умерло 3,5%, а после второго рецидива — 8% больных.

Наиболее часто наблюдались рецидивы кровоизлияний у больных с аневризмами передней или передней соединительной артерии — 58%, с аневризмами внутренней сонной артерии — 45%, реже у больных с аневризмами средней мозговой артерии — 15%.

Субарахнодиальные кровоизлияния повторились у 42% больных, поступивших в относительно хорошем и у 39% поступавших в более тяжёлом состоянии (классификация по Ботарелли).

Из случаев повторных кровоизлияний 35% наблюдалось в первую, 28% во вторую, 12% и 12% в третью и в четвёртую недели, а 7% и 7% в следующие две недели.

Катамнестически было обследовано 92 больных (средняя длительность катамнеза 3,5 года). От повторных кровоизлияний погибло 21% больных, получивших консервативное лечение, и 5% из оперированных.

По данным наших исследований, рецидивы субарахноидальных кровоизлияний наблюдались чаще у больных с аневризмами передней или передней соединительной артерий и внутренней сонной артерий. Кровоизлияния повторялись в большинстве случаев в первые две недели, и их частота не зависела от тяжести неврологического состояния после заболевания.

Следовательно, вопрос о предупреждении рецидивов субарахноидальных кровоизлияний при помощи хирургического вмешательства необходимо решить как можно раньше, в течение первых недель.

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