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The Secular Trend in the Incidence of Hemorrhagic Stroke in the Region of Osijek, Eastern Croatia in the Period 1988–2000 – A Hospital Based Study

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ABSTRACT

The purpose of the study was to establish the possible environmental influences in the observed peculiar rising and falling oscillations in the numbers of hemorrhagic stroke (HS) in Eastern Croatia (region of Osijek) during the last thirteen-years' period (1988–2000). In this period 1,222 HS were registered and treated. A constant increase in the incidence of HS was observed, from 60 (in 1988) to 139 (in 1998), with an average annual proportion of 16.5% of all stroke cases. A sharp increase in proportion of HS in total stroke incidence was recorded during the war in Croatia (1991–1995), with a peak incidence of 27.4% in 1993. Typical hypertensive intracerebral hemorrhage (ICH) was the most common (57.1%), atypical ICH occurred in 26.4%, subarachnoid hemorrhage (SAH) in 16.5%. Analysis of the annual number of hypertensive-ICH and SAH disclosed peculiar rising and falling oscillations. These variations were in correlation with heavy living conditions. During the war-period the SAH incidence sharply rose. Immediately after the war it suddenly decreased. The authors named this phenomenon a »pool depletion«, supposing the relatively stable proportion of the bearers of aneurysms in population. The observed variations seem to be the consequence of the war stress and other negative psychosocial and economic factors in post-war period, which increases the risk for SAH and typical hypertensive-ICH through complex pathophysiological mechanisms.

Introduction

Republic of Croatia is in region of Europe with high incidence of stroke¹. Data of secular mortality trends of cerebrovascular diseases (CVD) in Croatia in 30-year period (from 1958 to 1987) shows an increase of deaths from CVD by 264%, with highest rate in Osijek region, Eastern Croatia². Over the last decade a declining trend of stroke incidence in Europe has been shown, with the exception of Eastern European countries³. According to literature the incidence of hemorrhagic strokes (HS) varies with race and geographical factors. Intracerebral hemorrhages (ICH) accounts for about 10–15% of all strokes in North America and Europe, about 20–30% in Asia and about 12% in Australia and New Zealand. Subarachnoid hemorrhages (SAH) accounts for about 3–5% of all strokes, primary intraventricular hemorrhage 3.1%. A primary, nontraumatic SAH is regarded by definition to occur spontaneously, without specific trigger mechanisms, called often a »spontaneous subarachnoid hemorrhage«^{4,5}. It mostly results from rupture of an intracranial (saccular) aneurysm (IA), or, rarely, from other causes: blood dyscrasias, tumors or infections. Being associated with high rates of morbidity and mortality, it has been investigated by clinical and epidemiological methods regarding its incidence and course, trying to elucidate the risk factors in its etiology and the possible responsible pathophysiological mechanisms leading to the SAH manifestation. The great local and regional differences in the incidence of SAH in the general population have been established: from 8 per 100 000 in Norway⁶, 10 per 100,000 in North America⁷, to 29 per 100,000 in Japan⁸. More recently various triggering factors have been suspected to facilitate the SAH manifestation. Recent alcohol intake, cigarette smoking, diabetes mellitus, antico-

agulant treatment, contraceptives, have been found as possible facilitating factors for aneurysmal bleeding, – less than in patients with CH^{9–12}. Various combinations of environmental influences and vascular risk factors in some studies have been suspected to influence a significant circadian and circannual pattern of SAH occurrence^{13,14}. In a recent population-based study an increased occurrence of SAH and of ICH has been observed in the morning and early afternoon hours: no important role has been found for hypertension or climatic factors in their occurrence¹⁵.

The city of Osijek is industrial, trade and cultural center of the eastern Croatia with about 100,000 citizens. In our retrograde analysis of stroke patients treated at the Department of Neurology, University Hospital »Osijek«, we analyzed changes in the relations among the various subtypes of stroke incidence during the last decade. We paid attention to the peculiar rises and falls in the annual numbers of patients with HS during the years of the most intensive war activities in the city of Osijek and its surroundings (second half of the 1991 – 1994) and immediately after its ending. As in this period the local population went through the heavy war distresses, we compared this period with the years before and after the war: so we analyzed finally the whole thirteen years' period 1988 – 2000 in order to get a critical evaluation of the problem. Such an analysis was possible since practically all the citizens of Osijek and the inhabitants of its surroundings have been hospitalized for stroke in this hospital.

Patients and Methods

In a retrospective analysis of the stroke registry data bank of patients admitted to Department of Neurology, University Hospital »Osijek«, we noted patients with

HS. We analyzed annual number of HS, proportion of HS in total stroke number, subtypes of disease (typical hypertensive-ICH, atypical nonhypertensive-ICH, SAH). Study protocol consisted of the case history and the specific diagnostic data (brain CT scan, cerebro-spinal liquid analysis, cerebral angiography) and autopsy reports. The SAH diagnosis was established in our cases by the following procedures: only by CT in 137 (85.62%) patients, only by lumbar puncture (LP) in 23 (14.38%), by CT and LP in 53 (33.12%) cases. Angiography was performed for possible surgical treatment in 145 (90.62%) patients. Autopsy was performed in 18 (11.25%) patients. During the main part of the Croatian Defense War (1991–1996), until the year 1995, especially at the end of 1991 and in 1992, the city and its narrow surroundings were under the heavy siege, experiencing the worst destruction, constant pressure and cruel attacks on civilian population from the bor-

dering occupied territories. In that period many citizens, especially children with their mothers and the aged, had been evacuated from the city. War devastation and suffering of a great number of people, demographic changes and different social and economic problems left consequences on the life of the inhabitants. Due to constant attacks the University Hospital was reorganized and located to the safer parts of the buildings, partly into the subterranean »atomic cover«. However, the great majority of personnel worked regularly even in the most dangerous conditions; also, the most of diagnostic facilities, surgical teams and others functioned normally during that period.

Results

The analyzed patients are presented in Table 1. In thirteen-years' period (1988–2000) 1,222 HS were registered and treated. A constant increase in the

TABLE 1
NUMBER OF PATIENTS WITH SAH, HS AND ALL PATIENTS WITH STROKE IN THE THIRTEEN YEARS PERIOD

Year	SAH	HS	All strokes	SAH in HS (%)	SAH in all strokes (%)
1988	9	60	522	15	1.72
1989	14	90	605	15.56	2.48
1990	15	76	583	19.74	2.31
1991	11	71	484	15.49	2.27
1992	16	81	360	19.53	4.44
1993	15	84	367	17.86	4.09
1994	17	84	483	20.22	3.52
1995	8	92	515	8.7	1.55
1996	11	100	645	11	1.71
1997	17	111	608	15.32	2.80
1998	27	139	709	19.42	3.81
1999	24	120	720	20	3.33
2000	21	114	787	18.42	2.67
Total	205	1,222	7,388	16.5	2.82

SAH = subarachnoid hemorrhage; HS = hemorrhagic stroke

incidence of HS was observed, from 60 (in 1988) to 139 (in 1998), with slight decline in 1999 and 2000 (Figure 1) and an average annual proportion of 16.5% of all stroke cases. A sharp increase in proportion of HS in total stroke incidence was recorded during the war in Croatia (1991–1995), with a peak incidence of 27.4% in 1993 (Figure 2). Typical hypertensive-ICH was the most common (in average 57.1%), atypical-ICH occurred in average 26.4%, SAH in average 16.5%.

Analysis of the annual number of hypertensive-ICH (Figure 3) and SAH (Figure 4) disclosed peculiar rising and falling oscillations. The number of SAH increased from 9 in 1988 to 21 in 2000. However, in prewar period (1988 to the first half of 1991) annual incidence of SAH varied between 9–15 per 100,000. In the worst war period (second half of 1991–1994) the incidence rose sharply, with a clear-cut decline in 1995 with 8 SAH cases. The absolute peak of SAH in all stroke cases was

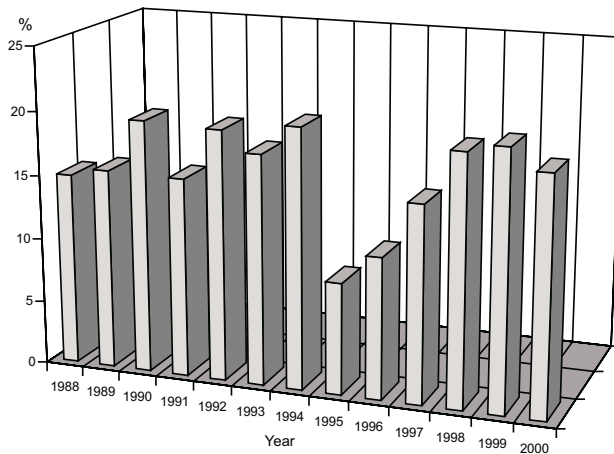


Fig. 1. HS incidence in the thirteen years' period (1988–2000).

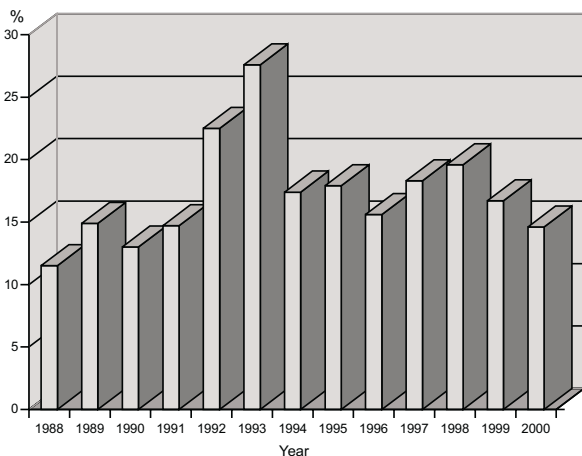


Fig. 2. Proportion of HS in the total number of strokes.

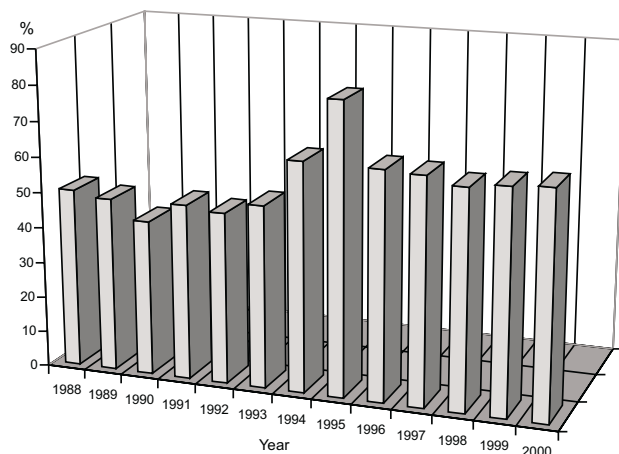


Fig. 3. Proportion of typical hypertensive-ICH in the total number of HS.

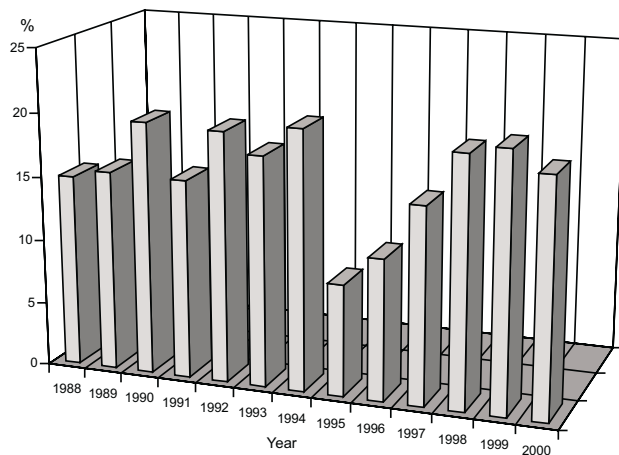


Fig. 4. Proportion of SAH in the total number of HS.

in 1992 (4.44%) (see Table 1). In the post-war years (1996–2000) the annual numbers of SAH patients gradually rose again, with the peak incidence in 1998. These variations were in correlation with heavy living conditions. During the war-period the SAH incidence sharply rose. Immediately after the war it suddenly decreased: The authors named this phenomenon a »pool depletion«, supposing the relatively stable proportion of the bearers of aneurysms in population.

Discussion

Ischemic stroke is far more common than HS, but consequences of HS are more severe. A high incidence of spontaneous intracranial hemorrhages in the region of Osijek, Eastern Croatia, during the war and the postwar period was reported earlier^{16–18}. The same observations were described during the Persian Gulf War in two hospitals in Jerusalem¹⁹, and during the war in Bosnia and Herze-

govina (1992–1996)²⁰. The higher proportion of HS in the total number of stroke cases, especially in 1991/92 could be partially explained by the Department bed shortage (some patients with »minor« stroke could not be hospitalized). Consistent increase in the next years should probably be considered as a consequence of the stress and other negative psychosocial conditions. Increased cigarette smoking and alcohol consumption which, according to some authors²¹, has a preferential impact on the occurrence of SAH could be one possible explanation for these changes, too. Abrupt decline in the incidence of SAH in 1995 could possibly be explained as a *pool-depletion* phenomenon: the individuals, bearers of the asymptomatic, *silent* saccular aneurysm, or other type of pre-existing vascular abnormalities, a precondition for manifestation of SAH, in the situations which facilitate the rupture of aneurysm, develop manifest form of the disease, SAH: in our patients it was the stress of war. The observed rise of the SAH incidence in the period 1992–1994 is so more considerable, while in this period, due to the above mentioned evacuation of some groups of Osijek citizens, the number of inhabitants fell to about 30,000. Exact figures are not known due to the fact that this number varied steadily due to the war operations in and around the city, which had all kinds of support from the rest of the non-occupied, central parts of the country. However, what can explain the observed changes, mostly the middle-aged citizens, men and women, capable to assure the normal functioning of the city under the siege, stayed in it. That is however, just the age group of inhabitants, bearers of IA, which tend to develop signs of the SAH. After the war operations started to decrease gradually, from 1994 on, the citizens started to return to the city, although this number has not equated that to the prewar times. Higher

frequency of HS, but not of SAH, was also described in the two hospitals in Jerusalem during the Persian Gulf War, ascribed by authors primarily to hypertension. However, in that situation there was an increased number of refugees, what could be one explanation for the described differences. A considerably higher rate of HS, particularly in the refugee groups, with overrepresentation in females and in the younger age groups, was found in the neighboring Bosnia and Herzegovina in the period after the Bosnian war 1992–1996^{20,22,23}.

Stress is a process involving interaction between the person and the environment. The nature of this interaction depends upon both the person's psychological characteristics and the environmental situation. Determined by the psychological and environmental characteristics the person – environment interaction is transmitted by some efferent messages from the brain to the body in the service of adaptation and coping. The resulting changes at the level of specific tissues and organs, or, in some cases also behavioral, at the level of the brain executive mechanisms, contribute over time and during the aging process to the development of some diseases²⁶. One simple explanation of the increased rate of SAH manifestation during the chronic stress are the threats of war and the connected fear, factors implicated in the increased occurrence of hypertension^{24–26} and so, possibly, facilitating the increased occurrence of SAH and typical hypertensive-ICH. Various metabolic and hormonal mechanisms probably play a role here, analogous to the hypothesis of Nyquist et al.¹⁵.

The investigated rates of aneurysms rupturing during the pregnancy could be instructive for the problem of »pool depletion« phenomenon. Ruptured aneurysms are responsible for 6% of maternal deaths. Out of these, 8% rupture in the first 3 months, 22% in the next 3.59% between

the 7th and the 9th month, only 3% during the labor and 8% in the puerperium²⁷. A higher percentage of deaths during labor could be expected because of the extreme exertion and the accompanying hypertension. The occurrence of SAH, different from so expected, could be explained either by the »pool depletion« or may have quite different pathomechanisms which interfere with more basic mechanisms regulating the cerebral circulation and the status of blood vessels, or by the combination of both.

Conclusion

The number of HS in Eastern Croatia oscillated in last thirteen-years' period in a peculiar way, rising and falling manner,

correlated and probably connected with the heavy living conditions in the city under the siege during the recent war. During the war period the SAH incidence sharply rose. The observed changes are probably not a mere coincidence, being the consequence of the war stress causing heavy social and economic situation. Stress increases the risk for HS through mechanisms for the time being not fully understood, probably mediated by complex pathophysiological mechanisms, like in the observed circadian or circannual variations or during the pregnancy. Immediately after the war another period followed when the SAH incidence suddenly decreased: this phenomenon the authors hypothesized as a »pool depletion«.

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SEKULARNO KRETANJE INCIDENCIJE HEMORAGIČKOG MOŽDANOG UDARA U OSJEČKOJ REGIJI, ISTOČNA HRVATSKA, U RAZDOBLJU 1988–2000: STUDIJA TEMELJENA NA BOLNIČKIM PODACIMA

S A Ž E T A K

Cilj istraživanja bio je utvrditi mogući utjecaj okolišnih čimbenika na zamijećene oscilacije u broju hemoragičkih moždanih udara (HMU) u istočnoj Hrvatskoj, (osječka regija), tijekom trinaestogodišnjeg razdoblja (1988–2000). U tom razdoblju dijagnosticirano je i liječeno 1222 HMU-a. Zabilježen je konstantan rast incidencije bolesti od 60 (tijekom 1988) do 139 slučajeva (tijekom 2000), uz prosječni udjel od 16,5% svih moždanih udara. Nagli porast udjela HMU-a među inzultima zabilježen je tijekom Domo-vinskog rata (1991–1995), a najviši udjel od 27,4% je zabilježen 1993 godine. Tipične hipertenzivne intracerebralne hemoragije (ICH) bile su najčešće (57,1%), atipične ICH u 26,4%, a subarahnoidalne hemoragije (SAH) su se javljale u 16,5% slučajeva HMU-a. Analiza kretanja hipertenzivnih ICH-a i SAH-a po godinama pokazala je velike oscilacije koje su koincidirale s teškim uvjetima življenja. Tijekom ratnog razdoblja incidencija SAH-a je naglo porasla. Ubrzo nakon rata dolazi do naglog pada incidencije. Autori su ovu pojavu nazvali »pool depletion« fenomen, imajući u vidu relativno stalnu proporciju aneurizmi u populaciji. Čini se da su uočene varijacije posljedica ratnog stresa i drugih negativnih socioekonomskih čimbenika u poslijeratnom razdoblju, te da u ovim okolnostima putem složenih patofizioloških mehanizama raste rizik za SAH-e i tipične hipertenzivne ICH-e.