

DURATION OF DELIRIUM IN THE ACUTE STAGE OF STROKE

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SUMMARY – The aim of the study was to determine duration of delirium in patients with acute stroke according to sex, age, type and localization of lesion. We assessed delirium prospectively in a sample of 233 consecutive patients with an acute (≤ 4 days) stroke using the Delirium Rating Scale (DRS-R-98) and Diagnostic and Statistical Manual of Mental Disorders (DSM IV). The average duration of delirium was 4 days in patients with ischemic stroke and 3 days in patients with hemorrhagic stroke. There was no statistically significant difference in delirium duration between these two patient groups. A longer duration of delirium was recorded in women and in patients older than 65. The period of delirium was longer in patients with right hemispheric lesions. Patients did not differ according to delirium duration, sex, age, type and localization of stroke. In two thirds of patients, the symptoms of delirium completely disappeared on medicamentous treatment, while in the remaining one third of patients certain symptoms of delirium persisted at discharge ($p=0.003$). Mortality rate was significantly higher in patients with delirium in the acute phase of stroke than in those without delirium ($p=0.009$). In conclusion, delirium is a temporary manifestation in two thirds of patients in the acute phase of stroke. Patient sex and age, and type and stroke localization have no influence on delirium duration.

Key words: *Cerebrovascular accident – complications; Cerebrovascular disorders – complications; Delirium – therapy; Delirium – etiology; Aged*

Introduction

Stroke is a known risk factor for the development of delirium¹. There have been only a small number of studies that assessed post-stroke delirium. These studies have yielded conflicting results and have screened for delirium using different measures at different time intervals. The main risk factors for delirium in stroke patients reported in the literature are aging^{2,3}, pre-existing cognitive disturbances⁴, presence of medical complications such as infections and electrolyte imbalance^{2,4}, presence of neglect², and severity of stroke³. The influ-

ence of stroke location is not clear as delirium has been described to occur more frequently in left-sided hemispheric lesions³ than in right-sided hemispheric lesions⁴. Delirium can be caused by different etiologic factors, e.g., metabolic disorders, infections, fever, cardiopulmonary disorders, epilepsy, ethanol, sedatives or illicit drugs, intoxication at stroke onset, or withdrawal during the next days, iatrogenic complication, pain, subdural hematoma or cerebral contusion, and pre-existing dementia. The estimated incidence of delirium in the early phase of stroke ranges from 13% to 48%, depending on the study population and delirium definition²⁻⁶. In patients with acute stroke, deliriant conditions are temporary and they fluctuate. The majority of patients recover within four weeks or less. If treatment is causal, the recovery is faster⁷.

The aim of the study was to determine the duration of delirium in patients with acute stroke according to sex, age, type and localization of lesion.

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Patients and Methods

In this prospective study conducted at University Department of Neurology, Tuzla University Clinical Center, in the period from November 2005 to April 2006, the prevalence of delirium after acute stroke and its influence on the acute stage outcome were analyzed. During the study period, 561 patients with first-ever stroke were hospitalized. The inclusion criteria were the diagnosis of cerebral infarct, intracerebral hemorrhage or subarachnoid hemorrhage (SAH) confirmed by computed tomography (CT); neuropsychiatric assessment performed within four days after the stroke onset, and Glasgow Coma Score (GCS) >5.

There were 59 stroke patients with delirium, 25 (42.4%) men and 34 (57.6%) women, mean age 70.0 ± 11.3 years. Patients with GCS ≤ 5 on the day of neuropsychiatric examination were excluded from the study, and so were patients with recurrent stroke, epileptic seizures onset of stroke, aphasia, early stage of dementia, and delirium caused by abuse of alcohol or other psychoactive substances. A neuropsychiatrist rated the presence and severity of the symptoms of delirium according to the Delirium Rating Scale R-98 (DRS-R-98)⁸ and Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition criteria for delirium⁹. DRS-R-98 is an observation scale of thirteen parts: Sleep-awake rhythm disorder (part 1), Perception and hallucination disorders (part 2), Imagination (part 3), Excitement tendencies (part 4), Language (part 5), Thinking process disorders (part 6), Anxiety (part 7), Motor breakage (part 8), Orientation (part 9), Concentration (part 10), Short-term memory (part 11), Long-term memory (part 12), and Space orientation capabilities (part 13). Besides these 13 items, another three facultative diagnostic items have been used as an aid in distinguishing delirium from other disorders for diagnostic and scientific purposes: chronological start of symptoms, variability of symptoms and physical disorders. Delirium was diagnosed in those patients that had >16 points on DRS-

R-98 and if they met the criteria for delirium according to the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition. Stroke, according to type, has been classified into (a) hemorrhagic (intracerebral hemorrhage and subarachnoid hemorrhage), and (b) ischemic stroke (according to the TOAST classification)¹⁰. According to localization, strokes were divided into strokes in the anterior or posterior cerebral circulation territory, and into right or left hemispheric strokes.

The study protocol was approved by the Hospital Ethics Committee.

The statistical applicative software Med Calc v. 9.2.0.0 was used. The results obtained were analyzed by use of the standard statistical parameters, i.e. mean, Student's t-test, χ^2 -test, and Mann-Whitney test. A value of $P < 0.05$ was considered statistically significant. Kolmogorov-Smirnov test was employed for statistical parameters of data distribution.

Results

Out of 233 stroke patients that met the inclusion criteria, 59 (25.3%) were diagnosed with delirium. Intracerebral hemorrhage was present in nine and SAH in six of 15 patients with hemorrhagic stroke associated with delirium. The average duration of delirium in the acute stage of stroke was 4 days, range 1-18 days. The average duration of delirium was 4 days in patients with ischemic stroke and 3 days in patients with hemorrhagic stroke. There was no statistically significant difference in delirium duration between patients with hemorrhagic and ischemic stroke (Table 1).

A longer duration of delirium was recorded in women (5.5 ± 4.6 vs. 4.8 ± 4.5 days) and in patients older than 65 (5.6 ± 4.7 vs. 4.3 ± 4.0 days). The period of delirium was longer in patients with right hemispheric lesions (5.0 ± 5.0 vs. 4.6 ± 3.4 days). Patients in the acute stage of stroke did not differ according to delirium duration, sex, age, type and localization of stroke (Tables 2 and 3).

Table 1. Duration of delirium according to stroke types*

Type of stroke		Delirium duration	
		Mean (days)	Range (days)
Ischemic	(n = 44)	4	1-18**
Hemorrhage	(n = 9)	3	2 - 8
Average duration of delirium		4	1-18

*Patients with subarachnoid hemorrhage are not included; **Mann-Whitney test; $P=0.85$

Table 2. Duration of delirium in days according to age and sex

Sex and age	Patients with delirium n=59	Duration delirium(days) $\bar{x}\pm SD$
Male	25	4.8±4.5*
Female	34	5.5±4.6
≥65 yrs	44	5.6±4.7**
≤64 yrs	15	4.3±4.0

\bar{x} , mean; SD, standard deviation; *Student's t-test; P=0.59; **Student's t-test, P=0.29

Patients with delirium in the acute phase of stroke had a higher mortality rate during hospitalization (18.6% vs. 1.7%; χ^2 -test; P=0.009). Eleven of 59 patients with delirium died, including eight patients with ischemic stroke, two patients with intracerebral hemorrhage and one patient with SAH.

Discussion

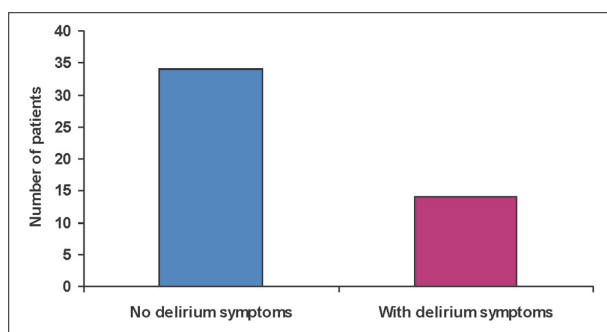
There is no consensus on the best screening tool for delirium post-stroke. Besides DSM-IV criteria, we used DRS as well, i.e. the reviewed version DRS-R-98, which is a more specified test for delirium compared to the

Table 3. Duration of delirium in days according to type and localization of stroke

Type and localization of stroke	Patients with delirium n=59	Duration delirium (days) $\bar{x}\pm SD$
Hemorrhage	9	4.1±2.4*
Ischemic	44	5.7±5.1
Subarachnoid hemorrhage	6	3.3±1.2
Left hemisphere	14	4.6±3.4**
Right hemisphere	24	5.0±5.0
Bihemispheric	21	5.9±4.9

\bar{x} , mean; SD, standard deviation; *ANOVA test; P=0.34; **ANOVA test; P=0.65

In two thirds of patients, the symptoms of delirium completely disappeared on medicamentous treatment, while the remaining one third of patients had certain symptoms of delirium at discharge (70.8% vs. 29.2%; P=0.003) (Fig. 1).



*Patients that died were not included; ** χ^2 -test

Fig. 1. Status of patients with delirium at discharge.

previous ones. DRS-R-98 is a valid and reliable symptom severity scale for delirium that has advantages over the original DRS for flexibility and breadth of symptom coverage. It is the only validated delirium rating instrument with sufficient breadth and detail for use in phenomenology and in longitudinal studies of delirium patients, including serial measurements in treatment research⁸.

Earlier studies dealing with delirium occurrence after stroke did not observe delirium duration and its relation with sex, age, type and localization of lesion. In a study of rivastigmine in the treatment of delirium after stroke, Oldenbeuving *et al.* report that the mean duration of delirium was 6.7 (range 2-17) days. In total, 26 patients fulfilled these criteria, of which 17 were treated with orally administered rivastigmine in a total dose between 3 and 12 mg a day¹¹. In our study, patients were treated with orally administered haloperidol in a total dose between 2 and 4 mg a day and diazepam between

10 and 30 mg. The neuroleptic syndrome developed in one (1.7%) patient and haloperidol was discontinued.

Traditionally, delirium has been considered to have a good prognosis with complete recovery if the underlying cause can be reversed. In addition, delirium was felt to be a short-lived syndrome. Both these assumptions are being increasingly challenged. In studies of patients following hip replacement surgery, delirium is independently associated with poor functional outcome, death and institutionalization¹². In older patients, delirium is an independent risk factor of sustained poor cognitive and functional status during the year after a medical admission¹³. It is also an independent marker of increased mortality at discharge and at 12-month post-discharge period, with increased length of stay and institutionalization^{13,14}. In our study, the duration of delirium was shorter as compared with other studies because it was only measured in the group of patients whose symptoms of delirium were temporary manifestation during hospitalization. One third of our patients with delirium in the acute phase of stroke had some symptoms of delirium when they were discharged, and these patients were not taken into calculation of the duration of delirium.

There are few data on the outcome of post-stroke delirium, in particular the long-term sequels. Only one report shows 12-month follow-up data¹⁵. Hénon *et al.* report on the average length-of-stay of deliriant patients in stroke unit to be 12 days⁴. Mortality rates of patients with an acute stroke at the time of discharge and mortality rates six months later are not dependent on delirium occurrence. It is emphasized that the reason for this is that mortality in the acute stage of stroke is probably more influenced by the severity of stroke than by cognitive status. Post-stroke delirium is associated with an increased risk of institutionalization, increased need for geriatric rehabilitation, increased dependence at discharge and at 6 months, lower Mini Mental State Examination (MMSE) at 6 months and 12 months, and higher 6- and 12-month mortality rate^{4,5,15}.

The mortality rate of our patients with delirium in the acute stage of stroke was significantly higher than in those without delirium, while there was no statistically significant difference in the mortality rate according to the type of stroke. The occurrence of post-stroke delirium is often connected with other medical complications (respiratory and urinary infections), and these complications contribute to worse functional outcome¹⁶.

In conclusion, delirium is a temporary manifestation in two thirds of patients in the acute phase of stroke.

Patient sex and age, and type and localization of stroke have no influence on delirium duration. Stroke units should have protocols for screening, prevention and therapy of delirium in high risk stroke patients.

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Sažetak

TRAJANJE DELIRIJA U AKUTNOJ FAZI MOŽDANOG UDARA

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Cilj studije bio je utvrditi trajanje delirija u bolesnika s akutnim moždanim udarom u odnosu na spol, dob, vrstu i lokalizaciju oštećenja. Delirij smo procjenjivali prospektivno u uzorku od 233 uzastopna bolesnika s akutnim moždanim udarom (≤ 4 dana) pomoću Ljestvice za stupnjevanje delirija (DRS-R-98) i Dijagnostičkog statističkog priručnika za psihičke bolesti (DSM IV). Prosječno trajanje delirija bilo je 4 dana u bolesnika s ishemijskim moždanim udarom i 3 dana u onih s hemoragičnim moždanim udarom. Nije bilo statistički značajne razlike u trajanju delirija među ovim dvjema skupinama bolesnika. Duže trajanje delirija zabilježeno je kod žena te kod osoba starijih od 65 godina. Razdoblje delirija bilo je duže u bolesnika s oštećenjem u desnoj hemisferi. Među bolesnicima nije bilo razlike u odnosu na trajanje delirija, spol, dob, vrstu i lokalizaciju moždanog udara. U dvije trećine bolesnika simptomi delirija potpuno su se povukli uz medikamentno liječenje, dok je preostala jedna trećina bolesnika imala stanovite simptome delirija pri otpustu iz bolnice ($p=0,003$). Stopa smrtnosti bila je značajno viša u bolesnika s delirijem u akutnog fazi moždanog udara nego u onih bez delirija ($p=0,009$). U zaključku, delirij je prolazna pojava u dvije trećine bolesnika u akutnoj fazi moždanog udara. Spol, dob, te vrsta i lokalizacija moždanog udara nemaju utjecaja na trajanje delirija.

Ključne riječi: *Moždani udar – komplikacije; Cerebrovaskularne bolesti – komplikacije; Delirij – liječenje; Delirij – etiologija; Starije osobe*

