Original article

DIAGNOSIS AND THERAPY IN TRANSITORY MYOCARDIAL ISCHEMIA IN SPONTANEOUS SUBARACHNOID HEMORRHAGE

Anica Pavlovic

Cardiac dysfunction occurring within subarachnoid hemorrhage named neurogenic stunned myocardium have great impact on intensive care of patients with subarachnoid hemorrhage (SAH). Timely diagnosis and treatment of such condition can provide better haemodynamics of damaged brain. The standard follow-up was performed in 30 patients with SAH during two years at the Clinic of Neurosurgery (2005, 2006). Serial electrocardiography, echocardiography, as well as laboratory findings of special biomarkers of left ventricular wall motion abnormalities were performed. All patients were treated with Urapidil, Metoprolol, $MgSO_4$ by scheme and ACE inhibitors. Ninety EKG were analyzed in the study, as well as 16 echocardiographies. The highest levels of CPK, CK-MB and TnI before and after the therapy were also recoded. EKGs showed the signs of ischemia in 9 of 30 patients at day 1 and 7 of 30 patients at day 3 of the therapy. The highest level of CK-MB was present during the 1st day with mean value of 67,80±1,83 IU/l that decreased at day 3 of the therapy with mean value of 66,8±1,83 IU/l, TnI was positive in 16 cases. It showed statistically significant decrease from 0,29 ng/ml till 0,187 ng/ml and $p<0,01$. Myocardial ischemia has been proven to be a very significant complication in SAH. Appropriate treatment of myocardial ischemia seems to improve systemic haemodynamics, as well as haemodynamics of the damaged brain. *Acta Medica Medianae 2008;47(1):19-21.*

Key words: *myocardial ischemia, treatment, spontaneous SAH*

Clinic of Neurosurgery, Clinical Center Nis

Contact: Anica Pavlovic
91 Narodnih heroja Street
18000 Nis, Serbia
Phone: 018/532-157
E-mail:beta.jo@sbb.co.yu

Introduction

Spontaneous subarachnoid hemorrhage (SAH) originating from aneurysm is a condition with extremely high mortality and morbidity rates. The prevalence for this condition is 1/10,000 in Europe and there are 28,000 people with this condition in the USA every year. Out of the total number of the patients with this condition, 10-15% die before reaching hospital and the mortality rate within the first month amounts to 35-47% (1,2).

The disruption of the myocardial function is a significant complication of this condition because it can additionally disrupt haemodynamics of the damaged brain (3). Experimental studies have shown that excessive release of noradrenaline on parasympathetic nerve fibers of the myocardium causes cardial dysfunction (4,5). The noradrenaline release represents a response to the hypothalamic dysfunction caused by blood rupture into the subarchnoid space (4,5,6,7).

The aim of this study was to prove the existence of myocardial ischemia in SAH as well as to examine the effects of cardio-specific therapy on such disorders.

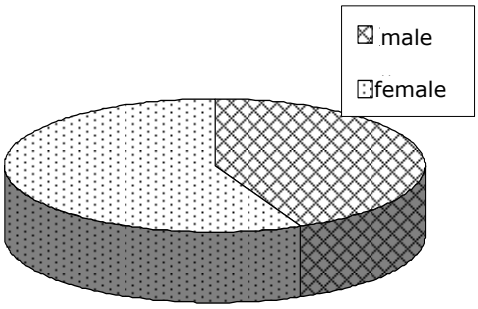
Material and methods

A prospective study was conducted on thirty patients during the period of two years (2005-2006). The basic criterion for including a patient into the study was: zero day of aneurism hemorrhage and negative anamnesis of coronary disorder. This study monitored the following parameters: 1) changes in EKG (rhythm, ST elevation, ST depression, negative T-waves, QRS complex width), 2) Biomarkers of myocardial ischemia (CPK, CK-MB and Tni test) and 3) Echocardiographic ischemia markers. On admission, patients were immediately clinically and neurologically tested, CT scanned (or the patients admitted had already been CT scanned). After the admission, biomarkers of ischemia i.e. myocardium necrosis were determined, and continuous two-lead EKG monitoring and continuous TA monitoring and pulse oximetry were performed. In addition to initial SAH therapy (anti-edematose therapy, sedoanalgesia, crystalloid and oxygenotherapy O2=2lit/min), the patients were also administered specific cardiologic therapy. It included administering Urapidil of

12.5 mg dosage every 15 min until the desired MAP is achieved, along with Metoprolol at maximum dosage of 15 mg IV/24 h and desired SF to 60/min. In addition, a maximum daily dosage of $MgSO_4$ at 30 mg/kg TT/24^h was administered. All results were statistically analyzed using standard descriptive methods (mean value). The trends of increase and decrease of myocardial ischemia signs were calculated using Kaplan-Meier analysis. The obtained results were analyzed using Student's t-test for unpaired and paired samples by univariate and multivariate regression analyses.

Results

The total number of examined patients was 30, 13 of which were male (43%) and 17 were female (57%).



Graph 1. The structure of examinees by gender

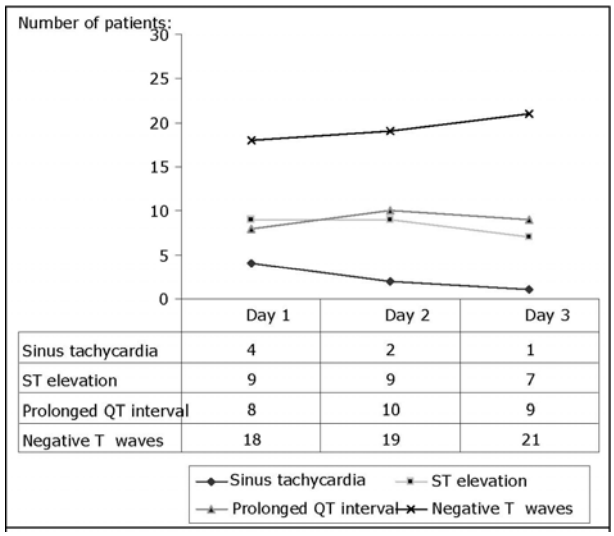
The average age of examinees was 58.33±9.01 years. The mean age of male patients was 57.77±9.48 years, whereas for female patients it was 58.76±8.91 years. Furthermore, there were no statistically significant differences among patients of the same gender in terms of age (t=0.29 and p>0.05). The structure of EKG changes over days is shown in a graph.

On admission, during the first day 93.3% of patients had CK-MB>10 IU/lit, whereas during the third day the percentage increased to 96.7% (χ^2=0,02 and p>0,05).

The values of the troponin test on admission were 0.29±0.77 ng/ml on average. On the first day, these values statistically significantly decreased to 0.24±0.63 ng/ml (p<0.01), whereas on the third day a significant plunge of values in comparison to the original value and in comparison to the TnI value from the first day (p<0.05) was noticeable (p<0.001) (See appendix 3).

On admission, ECHO heart test was performed in 8 patients and ischemia changes were diagnosed in 7 patients. The troponin test values were increased in 6 patients with ischemia changes (true positive values – SP), whereas in one patient with ischemia the troponin test value was lower than 0.04 ng/ml (false negative value – LN). Based on these data, diagnostic characteristics of the troponin test were calculated:

Test sensitivity (possibility to determine true positive value) was 85.7%; specificity (possibility to determine true negative value) was 100.0%, whereas total efficacy of the troponin test was 87.5%.



Graph 2. EKG changes in patients with SAH

Table 1. Table of CK-MB values (IU/L)

Statistical parameter	On admission	Day 1	Day 3
Xsr	57,80	66,80	58,59
SD	10,062	12,054	9,152
Min	9,00	8,00	7,00

Table 2. Troponin test values (ng/ml)

Statistical parameter	On admission	Day 1	Day 3
Xsr	57,80	66,80	58,59
SD	10,062	12,054	9,152
Min	9,00	8,00	7,00

Discussion

The first aim of the study was to prove the existence of myocardial ischemia. Diagnostics of this problem may be included in considering further therapy of patients with SAH. EKG changes found in patients with SAH were not single markers of ischemia (8,9,10,11). They are significant in correlation with highly specific biomarkers (TnI and CK-MB for myocardium necrosis). In Naidech and Kathavale (9,10), EKG changes were not considered when estimating the degree of dysfunction of the left ventricle in SAH. Increased TnI values are highly specific for the existence of significant myocardial lesion and are connected with the dysfunction of the left ventricle in SAH (9). This was also shown by the Kathavale study (9). In our study, significantly increased TnI values are a justification for the application of a cardio-specific therapy for the treatment of myocardial ischemia. The decrease in the TnI level is statistically significant and proves that the selection of medicines for the study was justified. Considering the fact that no

prospective randomized study was conducted with the patients who had not received myocardium support therapy, it can be assumed that cardio-specific medicines have a positive effect on haemodynamics in SAH. As the sensitivity of the troponin test in comparison with echocardiographic monitoring of the patient is highly specific and amounts to 85.7%, the total efficacy of the troponin test enables a relevant estimate of myocardial condition, based on TnI analyses when there are no conditions for echocardiographic monitoring.

Conclusion

Timely and specific therapy of this significant complication of spontaneous subarachnoid hemorrhage may contribute to faster and easier recovery of systemic haemodynamics, and consequently, improve haemodynamics of cerebral circulation.

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DIJAGNOZA I TERAPIJA TRANZITORNE ISHEMIJE MIOKARDA U SPONTANOJ SUBARAHNOIDALNOJ HEMORAGIJI

Anica Pavlović

Miokardijalna disfunkcija nastala u okviru spontane subarahnoidalne hemoragije (SAH) ima veliki uticaj na intenzivno lečenje ovih bolesnika. Pravovremena dijagnostika i tretman ove komplikacije SAH-a može omogućiti bolju hemodinamiku oštećenom mozgu. Tokom 2005. i 2006. godine na Klinici za neurohirurgiju u Nišu praćeno je 30 bolesnika po tipu prospektivne studije. Praćeni su: promene u EKG-u, biomarkeri ishemije (nekroze miokarda) i ehokardiografske promene. Svim bolesnicima su ordinirani Urapidil, Metoprolol, MgSO4 po šemi kao i ACE inhibitori. Analizirano je 90 EKG-a, 16 EHO-a miokarda kao i najviše plazma koncentracije enzima CPK, CK-MB i TnI pre i posle uključivanja terapije u prva tri dana bolesti. Analizom EKG-a nađeno je da 9 od 30 bolesnika ima znake značajne ishemije prvog dana a 7 od 30 bolesnika trećeg dana bolesti. Najvišu plazma koncentraciju CK-MB nalazimo u prvom danu bolesti kod bolesnika sa srednjom vrednošću 67,8±1,83 IU/L sa padom plazma koncentracije u trećem danu i srednjom vrednošću od 66,8±1,80 IU/L. TnI je bio pozitivan (>0,04 ng/ml) kod 16 bolesnika gde TnI pokazuje statistički značajan pad vrednosti od 0,29 ng/ml prvog dana do 0,187 ng/ml i p<0,01. TnI test u poređenju sa EHO nalazima pokazuje visoku specifičnost 85,7% i ukupnu efikasnost od 87,5%.

Izbor ovakve kardiospecifične terapije kroz ovu studiju pokazuje se relevantnim zbog negativnog trenda kretanja plazma koncentracija svih biomarkera ishemije (nekroze) miokarda. *Acta Medica Medianae 2008;47(1):19-21.*

Ključne reči: *ishemija miokarda, tretman, spontana SAH*