THE INFLUENCE OF MYOCARDIAL INFARCTION ASSOCIATION IN ISCHEMIC CEREBRAL STROKE SUBJECTS ON THE 30 DAYS VITAL AND NEUROLOGICAL PROGNOSIS

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Abstract: The association of stroke and acute myocardial infarction may be considered either a consequence of the stroke, or a separate entity. Purpose: To appreciate the short term (30-days) evolution of the subjects that associate acute myocardial infarction to cerebral stroke within minimum one and maximum 7 days from the onset of the cerebral stroke using several parameters. Material and Methods: There were included 55 subjects divided in two groups: group A – association of myocardial infarction to stroke within 1 – 7 days from stroke's onset; group B – case control group having subjects with stroke and no myocardial infarction. Results: The burden of cardiovascular diseases did not differ significantly in the two groups, with the exception of hypertension and stroke history that were associated to group A, together with CRP presence, lower HDL cholesterol and higher CT/HDL cholesterol ratio when screened. In the intra-group analysis, persistent hypertension at 72 hours and hyperglycemia at 48 hours correlated to a severe neurological status (p<0.05, CI95%). The occurrence of myocardial infarction leads to a depreciation of the neurological status in group A subjects at 15 and 30 days when compared to group B subjects (p<0.05,CI95%). The mortality in the groups did not differ significantly. Conclusions: The association of a myocardial infarction to an ischemic stroke is an independent negative prognostic factor without influencing the mortality. When other risk factors are present they may be omitted in favor for the myocardial infarction on the respect to 30-days prognosis.

Cuvinte cheie: *accident vascular cerebral ischemic, infarct miocardic, prognostic*

Rezumat: *Asocierea dintre infarctul miocardic care survine în urma unui AVC ischemic poate fi considerată fie o consecinţă a evenimentului ischemic acut cerebral, fie o entitate sperată. Scop: de a aprecia evoluţia pe termen scurt (30 de zile) a subiecţilor care asociază la minim 24 de ore şi maxim 7 zile un infarct miocardic acut (IMA) la un AVC ischemic în funcţie de diverşi parametri. Material şi metodă: Au fost incluşi 55 de subiecţi divizaţi în două grupuri de studiu: grupul A – asociere de IMA la un AVC ischemic la 1 până la 7 zile de la debutul AVC; grupul B – grup case-control de subiecţi cu AVC ischemic, dar fară IMA. Rezultate: Încărcătura cardiovasculară nu a diferit semnificativ statistic între cele două grupe cu excepţia hipertensiunii arteriale şi a istoricului de AVC, care au fost specifice grupului A, împreună cu prezenţa valorilor ridicate ale PCR, nivel scăzut de HDL cholesterol şi raport ridicat CT/HDL-colesterol. La analiza intra-grup, HTA persistentă la 72 de ore şi hiperglicemia la 48 de ore s-au corelat cu un prognostic neurologic defavorabil (p<0.05, CI95%). Asocierea IMA conduce la o agravare semnificativ statistică a statusului neurologic la 15 şi 30 de zile la subiecţii grupului A vs. grupul B (p<0.05,CI95%). Mortalitatea nu diferă în cele două grupuri studiate. Concluzii: Asocierea unui infarct miocardic acut la un AVC ischemic este un factor de prognostic negativ independent, fără influenţă asupra mortalităţii. În cazul asocierii altor factori de risc vasculari, aceştia pot fi neglijaţi pentru prognosticul neurologic la 30 de zile.*

INTRODUCTION

The association of an acute myocardial infarction to an ischemic cerebral stroke may be considered a separate entity, but also a consequence of the first. The relation between the cerebral ischemic stroke and the myocardial infarction may be explained by the common phisiopathological background that both processes share. The Northern Manhattan Study (NOMAS) shows a 9.8% risk of stroke post acute myocardial infarction (AMI) at 5 years (1). The cerebral stroke represents an equivalent coronary risk factor with a cardiovascular cause risk mortality of 20% at 10 years.

The Registry of the Canadian Stroke Network data shows a 2.3% risk of stroke post AMI during hospitalization (2), but on the other hand the specialty literature does not make references the evolution of the subjects with AMI associated to stroke during the first 30 days from the stroke onset.

The purpose of the hereby study is to appreciate the neurological clinical evolution of the subjects that associate an acute myocardial infarction to an ischemic cerebral stroke at least 24 hours and maximum 7 days after the stroke onset in regard to several clinical and biological parameters that might play the role of a predictors in the neurological evolution on short term (30 days).

MATERIAL AND METHOD

The hereby-study design is an observation, longitudinal and case-control one, over a period of 2 and a half years, 2007 – 2009, with a studied population of 55 subjects, composed of two separate groups, selected from the Neurology Clinic of Arad.

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The inclusion criteria for group A are: subjects with ischemic stroke, or stroke in progression and AMI that occurred at minimum 24 hours and maximum 7 days from the stroke's onset. The subjects with concomitant stroke and AMI within 24 hours from stroke's onset were excluded in regard to the high mortality (83%) reported by the literature (3).

Group B is a case-control group. There were included subjects with certified ischemic cerebral stroke and no AMI randomly selected in respect to sex and age groups.

The follow-up has been scheduled at admission, 15 and 30 days of evolution. The methods used for evaluation were: neurological and cardiological clinical exam, CT-scan, or MRI, upon necessity, neurological standardized evaluation using the National Institute of Health Stroke Scale (NIHSS), pre-cerebral Doppler exam, enzymology study, ECG, qualitative test for CRP, glycemia control, blood pressure level, plasma lipids levels

RESULTS

The demographical data and the cardiovascular risk factors are illustrated in Table 1.

In group A (Table 2) the hyperglycemia at admission and at 48 h was predominant, but without influencing the compared neurological evolution in the two groups (p>0.05, CI95%). In the intra-group analysis, the persistent hyperglycemia at 48 h was a negative neurological prognostic factor.

Hypertension at admission and at 72 h was noticed more frequently in group A (Table 2). The neurological status of the subjects that did not present history of HBP and that did not receive blood pressure lowering medication during hospitalization, in fact those with transitory HBP, is with 3 point on the NIHSS scale more severe at 30 days for group A subjects (p=0.043, CI95%, 0.092 to 5.241).

8 subjects from the total of 55 did not follow a pre-cerebral Doppler exam for objective reasons. In the compared analysis, 47.8% of the group A subjects had an intima-media thickness (IMT) ranging in the interval 0.9 – 1.8 vs. 25% in group B. The carotid stenosis over 70% is predominant in group A (34.8% vs. 33.3%), without a statistical significant difference. The neurological status appreciated on the NIHSS in the subjects that presented carotid stenosis and associated an AMI to the cerebral stroke was with 3 points more severe (p<0.05, CI95%). In group A 33.78% of the subjects have an over 70% carotid stenosis homolateral to the cerebral lesion.

60% of the group A subjects were identified as positives for serum C reactive protein (CRP) vs. 23.3% in group B, with statistical significance for the two groups, the positivity for serum CRP being specific for group A (p=0.005, CI95%, -0.618 to -0.115).

As shown in Table 3 the absolute average values of plasma lipids were lower in group A, with a statistically significant difference for HDL-c (p=0.020, CI95%, -23.73 to -2.07, Mean Difference 12.90 mg/dL). The total cholesterol (TC) / HDL-c ratio was higher in group A subjects (p=0.031, CI95%, 0.11 to 2.21, Mean Difference 1.16). The TC/HDL-c ratio did not have statistically significant influence on the neurological evolution.

Table no. 1. The compared analysis of the demographical data, cardiovascular history and cardiovascular risk factors in the two studied groups

		Group A		Group B	
No. of subjects		25		30	
Male: female ratio		2.13:1		1.31:1	
Average age		63.60 ± 6.87		65.63 ± 7.84	
History of:					
		n	**%**	**n**	**%**
High blood pressure (HBP)*		16	64.0	11	36.7
Stroke*	Never	15	60.0	26	86.7
	Ischemic	3	12.0	2	6.7
	TIA	3	12.0	1	3.3
	Hemorrhagic	4	16.0	1	3.3
Dyslipidemia*		13	52.0	7	23.3
Diabetes mellitus*		12	48.0	6	20.0
Myocardial infarction		6	24.0	2	6.7
Peripheral arterial disease		7	28.0	3	10.0
Atrial fibrillation		7	28.0	6	20.0
Smoke	Yes	12	48.0	12	40.0
	No	7	28.0	14	46.7
	Ex-smoker	6	24.0	4	13.3
*p<0.05, CI95%, difference of statistical interest between the two groups					

Table no. 2. The incidence of hyperglycemia and high blood pressure in the studied groups

		Group A		Group B	
		n	**%**	**n**	**%**
Hyperglycemia	at admission	20	80.0%	18	60.0%
	at 48 h	16	64.0%	12	40.0%
Hypertension	at admission	23	92.0%	26	86.7%
	at 72 h	17	68.0%	25	83.3%

Table no. 3. The compared plasma lipids levels in the two groups

		Triglycerides mg/dL	TC mg/dL	HDL-c mg/dL	LDL-c mg/dL	TC/HDL-c
Group A	**Average**	252.40	241.28	46.36*	144.16	5.90*
	Median	206.00	254.00	38.00	150.00	5.75
	Standard deviation	92.416	57.699	20.692	56.577	2.30
	Minimum	110	122	26	30	2.21
	Maximum	400	324	104	225	10.83
Group B	**Average**	256.03	257.17	59.27*	146.20	4.74*
	Median	241.50	255.50	62.00	148.00	4.39
	Standard deviation	78.209	54.315	19.285	52.309	1.56
	Minimum	110	176	27	40	2.41
	Maximum	400	372	95	270	8.00
*p<0.05, CI95% when the two groups compared						

Table no. 4. The statistical analysis of the neurological evolution of the two groups at admission, 15 and 30 days appreciated on the NIHSS (group A. vs. group B)

	Mean Difference	95% Confidence Interval		p
		Minimum	Maximum	
NIHSS at admission	-1.727	-4.907	1.454	.281
NIHSS at 15 days	2.633	.088	5.178	.043
NIHSS at 30 days	3.290	1.407	5.173	.001

Table no. 5. The compared neurological evolution in the two studied groups appreciated on the NIHSS

		n	Min.	Max.	Average	Standard deviation
Group A	NIHSS at admission	25	7	32	16.24	5.739
	NIHSS after AMI	25	11	32	19.76	5.532
	NIHSS at 15 days	22	8	24	15.36	4.054
	NIHSS at 30 days	20	4	17	10.65	3.200
Group B	NIHSS at admission	30	6	32	17.97	5.951
	NIHSS after AMI**	**	**	**	**	**
	NIHSS at 15 days	26	4	24	12.73	4.609
	NIHSS at 30 days e	25	2	13	7.36	3.040
	**not applicable					

The data from the present study demonstrated that the group A subjects have a more severe neurological status when compared to group B, aspect well illustrated in Table 4.

The different pattern of evolution was noticed only after the occurrence of the myocardial infarction, event that determined a worsening neurological status for group A subjects of 2.63 and 3.29 on the NIHSS at 15, respectively 30 days of evolution (p<0.05, CI95%).

The NIHSS score in group A shows a significant deterioration after the association of the AMI to the cerebral stroke. The mean NIHSS disadvantage for these subjects was 3.52 point, difference with statistical significance when compared to the admission NIHSS score. (p=0.001, CI95%, 4.459 to 2.581) (Table 5).

Most of the group A subjects associated an AMI during the first 5 days from the stroke onset (day 3.68).

The mortality was 20.00% (n=5) in group A vs. 16.70% (n=5) in group B without statistical significance, or being influenced by any of the parameters discussed above.

DISCUSSIONS

The association of an acute myocardial infarction to an ischemic cerebral stroke is an independently negative neurological prognostic factor, without being influenced by other associated vascular risk factors.

High glycemia in the acute phase of a stroke is associated to a poor survival and rehabilitation prognostic, an approximately 3 times higher mortality (4) probably as a consequence of the limitation of the ischemic penumbra area and the gradual extension of the necrosis area (5). In the hereby study this aspect has not been observed maybe due to the severity of the association of an AMI and stroke. On the other hand, the hyperglycemia in acute stroke phase may play a protective role, aspect known as “the glucose paradox” (6).

A recent study shows that 52% of the stroke subjects have HBP values when admitted in the emergency department (7). Frequently, even without a pertinent therapeutical intervention there is noticed a spontaneous lowering in the blood pressure during a time span of 10 days, with normalization of the values that begins day 3 from stroke onset (8), thus underling the limited and transitory character of HBP in the subjects with stroke but no hypertension history; however HBP presents a 1.5 to 5 times higher risk of mortality, or a more sever neurological status with a significant handicap (7). In the hereby study the BP values correlated to a more severe neurological status of about 3 points on the NIHSS in both studied groups.

The North American Symptomatic Carotid Endarterectomy Trial (NASCET) and European Carotid Surgery Trial (ECST) underline that a significantly hemodynamic carotid stenosis begins from a luminal obstruction of over 70% (9) and literature data show a 30% incidence for a stroke ipsilateral to a carotid stenosis higher than 70%. The incidence for a stroke ipsilateral to a carotid stenosis of over 70% in the hereby study was 37.78% in group A.

High CRP levels represent a non-specific reaction to cellular death, tissular lesions, or inflammation. The cerebral necrosis during ischemia and the myocardial necrosis are powerful stimuli for the CRP synthesis (10). It is unclear whether to consider the CRP a predictive test, or a therapeutical target in the subjects with atheromatosis (11). The results of the study presented above show that the subjects with AMI and stroke association have more frequently high CRP levels vs. group B, phenomenon eventually explained due to a more extensive atheromatosis, or a more ample response to the myocardial and cerebral necrosis.

In the International Stroke Trial the risk of death by coronary disease in stroke, or TIA subjects is 1.5% at 14 days (14); The European Cooperative Acute Stroke Study I (ECASS I) and the Trial of Org 10172 in Acute Stroke Treatment (TOAST) show a 2%, respectively 0.5% risk of death, but at much longer intervals (15). The NOMAS study presents an incidence of AMI mortality in cerebral stroke subjects of 19% at 30 days (1), values that are close to the ones presented in the results of the present study. In the studied groups the mortality rate as high as 20% and may be explained by the highly dangerous morbid association stroke - AMI, but without a significantly difference in the two groups.

There is a lack of pertinent literature data in order to compare the neurological evolution of the subjects that associate stroke and AMI during hospitalization. It is generally accepted that 20% to 40% of the stroke subjects have positive tests for silent coronaropathy. The incidence of AMI post stroke varies from 7.7% to 20% and presumably it was supposed that their association is a severe clinical situation (15).

CONCLUSIONS

The obtained data in our study shows that the association of an myocardial infarction to an acute stroke in the first week from the onset of the cerebro-vascular disease is a factor of negative prognosis independently of the subject's neurological evolution not influencing the mortality rate of the subject. Associating other vascular risk factors bring a severe neurological prognosis but they may be omitted from the prognosis of such a subject when they present first a stroke and after a myocardial infarction.

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