ARAŞTIRMA YAZILARI ORIGINAL ARTICLE

LONG-TERM TRANSCRANIAL DOPPLER SONOGRAPHY AND MAGNETIC RESONANCE IMAGING FOR EVALUATION OF SILENT CEREBRAL EMBOLISM IN CEREBROVASCULAR ASYMPTOMATIC PROBANDS

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ABSTRACT

Background: Cerebral microembolism from the extracranial vascular system can be detected by transcranial Doppler sonography. The frequency of intracranial embolic signals correlates with the degree of extracranial atherosclerotic disease and presence of ischemic symptoms. Materials and Methods: In order to investigate the possible occurrence of embolic events in cerebrovascular asymptomatic persons with and without extracranial carotid artery disease we performed simultaneous bilateral transcranial Doppler sonography (TCD) monitoring of the middle cerebral arteries and magnetic resonance imaging (MRI) of the brain in 46 individuals (22 female, 24 male, mean age 61 ± 7 years). They were selected from a cohort of 500 randomly selected community dwelling volunteers without signs or symptoms of cerebrovascular disease. The investigated subjects consisted of all (6/500, 1.2%) persons with > 50% carotid stenosis and 40/500 randomly selected cases with either minimal to moderate carotid plaques (< 40% stenosis) or normal exams. TCD monitoring was repeated in 5/6 probands with severe atherosclerotic disease 26 - 41 weeks (mean 37 ± 5.5 weeks) after the first examination. TCD monitoring time was 45 - 60 minutes.

Results: MRI showed various lesions in 22/46 (47.8%) subjects. Microangiopathy-related cerebral damage (MARCD) was noted in 3/6 (50%) cases with high-grade carotid stenosis versus 5/15 (33.3%) of subjects with minimal to moderate carotid atherosclerosis and 3/25 (12%) with normal vessels. TCD failed to detect embolic events. This was even true for individuals with > 50% stenosis and those with ischemic brain abnormalities, including early confluent and confluent white matter changes as well as lacunes.

Conclusion: These findings underline the clinical relevance of cerebral embolism in symptomatic carotid artery disease.

Key words: Cerebral embolism, transcranial Doppler sonography, carotid artery disease, magnetic resonance imaging.

Introduction

Cerebral embolism from the heart or extracranial atherosclerotic carotid artery disease is an important mechanism to ischemic stroke. Embolus detection by means of transcranial Doppler sonography (TCD) has been shown to be a sensitive tool for the detection of spontaneous emboli in stroke patients [1-8]. Previous studies suggested a higher rate of embolic signals in stroke patients with high-grade carotid artery stenosis than in cerebrovascular asymptomatic patients with severe atherosclerotic disease [3,9]. The rate of embolic signals correlates with the appearance of plaque ulceration [4]. Also, in patients with large artery atherosclerosis a higher rate of embolism is described within affected than within unaffected cerebral hemispheres[8]. No embolic events were detected by several authors in small numbers of cerebrovascular asymptomatic probands without extracranial atherosclerotic disease [1-3, 10].

Silent brain infarction demonstrated by magnetic resonance imaging (MRI) is observed in cerebrovascular asymptomatic subjects and correlates with the grade of atherosclerotic disease and presence of ulcerated lesions [11]. Microangiopathy-related cerebral damage (MARCD) represents a common incidental MRI observation in the elderly [12]. However, the possible correlation of TCD-detected embolism to the presence or absence of brain lesions was not evaluated in these studies.

The aim of the present study was to evaluate the occurrence of embolic signals as a possible indicator for stroke risk by means of simultaneous bilateral TCD monitoring of the middle cerebral arteries (MCA) in a cohort of cerebrovascular asymptomatic probands with various degrees of carotid artery stenosis and presence of silent ischemic brain damage.

Subjects and Methods

In the setting of the Austrian Stroke Prevention Study [13] we studied 500 cerebrovascular asymptomatic probands by extracranial Doppler and Duplex sonography of the carotid and vertebral arteries (Vingmed CFM 750, Horton,

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Norway) and conventional TCD of the basal cerebral arteries (Transscan EME, Überlingen, Germany).

Embolus detection by means of simultaneous bilateral monitoring of the MCA's (Multi Dop X2, DWL, Sipplingen) was performed in a subset of 46 individuals (22 female, 24 male, mean age 61 ± 7 years).

Carotid Duplex Scanning revealed > 50% stenosis of the internal carotid artery (ICA) in 6 (1.2%, 2 female, 4 male, mean age 69 ± 9 years) of the 500 subjects examined. These 6 cases were included into the TCD monitoring cohort as well as 40 consecutives (20 female, 20 male, mean age 60 ± 5 years) with either normal Doppler and Duplex sonography studies or atherosclerotic changes with < 40% lumen obstruction.

In persons with severe ICA stenosis, routine ultrasound examination revealed a 50-70% stenosis in 4 cases, in 2 subjects a > 90% stenosis was observed. No ulceration was found in the probands with < 50% stenosis. In the 40 subjects without severe ICA plaques, ultrasound examination was normal in 25 (62.5%). Minimal to moderate (< 40%) ICA plaques were shown in 15 (37.5%) subjects. Routine TCD of the anterior and posterior part of the circle of Willis did not reveal any occlusion or > 50% stenosis in all subjects.

In order to measure the possible occurrence of microemboli TCD monitoring was performed for at least 45 minutes in subjects with < 40% ICA stenosis and 1 hour in all cases with >50% ICA stenosis. The technique of TCD monitoring employed a 2-MHz pulsed-wave transducer with 2 ultrasound probes attached bilaterally to the patients' lateral temporal region and held in position by a special probe holder. The recorded Doppler signal was obtained by simultaneous insonation of the left and right MCA in a depth of 55-mm with a 15-mm width of axial sample volume. The Doppler signals (color-coded, fast-Fourier-transformed TCD spectra) were recorded on computer disc, video and audio tape and analyzed off-line. Determination of embolic events and differentiation from artifacts were based on the typical criteria of emboli which cause a signal occurring within the blood flow velocity spectrum with higher signal intensity than background intensity, short time duration and a typical acoustic signal.

Routine extracranial Doppler and Duplex sonography of the carotid arteries and TCD monitoring of the MCA's was repeated 26 - 41 weeks (mean 37 ± 5.5 weeks) after first examination in 5/6 probands with established > 50% ICA stenosis. TCD monitoring time was 60 minutes.

MRI was performed on 1.5T supraconducting magnets (Gyroscan S 15 and ACS, Philips, Eindhofen, The Netherlands) using T2-weighted (TR/TE 2000 to 2500/30 to 60 msec) sequences in the transverse orientation. All scans were read by an experienced investigator (R.S.). The scans were evaluated for white matter lesions (WML), lacunar lesions and infarctions. WML were graded according to a previously described scheme [12, 14, 15] as absent, punctuate, early confluent (grade 2) and confluent (grade 3). Lacunes were defined as focal lesions involving the basal ganglia, the internal capsule, the thalamus, or brain stem not exceeding a maximum diameter of 10 mm. MARCD was considered in individuals if they presented grade 2 or grade 3 WML or lacunes or infarction or any combination of these findings.

In order to evaluate a possible cardiac source of embolism all probands of the TCD monitoring group underwent electrocardiography (ECG) and transthoracal echocardiography.

Results

Transcranial Doppler monitoring did not reveal any embolic event. This was true for subjects with normal carotids and subjects with mild to severe atherosclerotic abnormalities. Also, individuals with MRI changes did not have transcranial Doppler signals indicative of emboli. Repetition of TCD monitoring 37 weeks after the first examination in the high risk group of subjects with high-grade stenosis was negative.

MRI was normal in 24/46 (52.2%) of the whole monitoring group (table 1). Punctuate WML were present in 11/46 (23.9%). A total of 11/46 (23.9%) individuals had MARCD. There was a higher number of individuals with MARCD in subjects with severe carotid stenosis (3/6, 50%) than in those with minimal to moderate carotid atherosclerosis (5/15, 33.3%) or normal vessels (3/25, 12%).

Lacunar lesions were noted in 6/11 (54.5%) subjects of the whole MARCD group and in all 3 cases with high-grade carotid stenosis and pathological MRI findings. Brain infarction was present in only one subject of the MARCD group

(1/11, 2.2%), involving the thalamus region, however, with no correlation to an extracranial vessel pathology (table 2).

Table 1: Magnetic resonance imaging in 46 cerebrovascular asymptomatic subjects with and without extracranial carotid artery stenosis.

	whole study group	no stenosis	stenosis < 40%	stenosis > 50%
	n=46	n=25	n=15	n=6
normal	24 (52.2%)	12 (48%)	9 (60%)	3 (50%)
WML punctuate only	11 (23.9%)	10 (40%)	1 (6.6%)	0 (0%)
MARCD	11 (23.9%)	3 (12%)	5 (33.3%)	3 (50%)

White matter lesions (WML), Microangiopathy-related cerebral damage (MARCD).

Table 2: Magnetic resonance imaging in 11 cerebrovascular asymptomatic subjects with MARCD, with and without extracranial carotid artery stenosis.

	whole study group	no stenosis	Stenosis < 40%	Stenosis > 50%
	n=11	n=3	n=5	n=3
only WML grade 2 and/or 3	4	2	2	0
only lacunes or with WML	6	0	3	3
infarction	1	1	0	0

ECG and echocardiography revealed no potential source of embolism in 43 (93.5%) subjects, atrial fibrillation was present in one case and there was a history of myocardial infarction and presence of prolapsed of the mitral valve in two other cases.

Discussion

This is a prospective long-term investigation in cerebrovascular asymptomatic individuals examining the occurrence of cerebral emboli in various risk groups defined by the severity of atherosclerosis and MRI-detected ischemic brain lesions.

As suspected, embolic signals did not occur in probands with normal extracranial arteries. This is in accordance to previous studies demonstrating the absence of sonographic detectable emboli in controls without history of ischemic events and no evidence of carotid atherosclerotic lesions [1-3, 10]. However, it was surprising that individuals with minimal to moderate carotid artery plaques and even cases with severe ICA stenosis did not show embolic signals. This contrasts studies in cerebrovascular asymptomatic subjects which describe emboli generating from carotid artery stenosis. The occurrence of embolic events in a cohort of cerebrovascular asymptomatic cases with severe ICA stenosis is reported by Siebler et al [3] but with a lower rate of embolic events when compared to neurologically symptomatic patients with high-grade carotid stenosis. Asymptomatic embolic signals in subjects with carotid stenosis were detected by Markus et al [10] usually unilateral and ipsilateral to the stenosis. One explanation for the absence of embolic events might be the lack of plaque ulceration in our study participants which is known to be a leading factor of embolization. Valton et al [4] revealed a trend towards more severe stenosis in cases with embolic signals, but without statistical significance. A strong correlation was found between occurrence of emboli and an image of ulceration on carotid angiography.

The relationship between asymptomatic carotid lesions and silent brain infarcts confirmed on MRI was investigated by Hougaku et al [11]. These authors reported a higher incidence of brain lesions in cases with high-grade stenosis or ulcerated lesions. In line with this study, showing a significant correlation of presence of asymptomatic carotid lesions and silent brain infarcts, 50% of our subjects with severe carotid artery stenosis showed MARCD, while this was seen in only 33.3% of those with mild to moderate ICA stenosis and in 12% with normal carotids. In line with a recent study [8] revealing no embolic signals in patients with lacunar stroke, the absence of embolic events is probably due to the fact that all brain lesions seen in our study participants with high-grade stenosis were related to lacunar lesions.

The absence of embolic signals in normal subjects and the frequent occurrence of such findings in stroke patients as has been reported in previous studies suggest that the presence of such signals in any individual is a strong risk indicator for subsequent strokes.

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