Microembolic Signals Detection in Acute Ischemic Stroke
"Its Prevalence and Use for Evaluation of Treatment"

Hossam Mahmod1, Salma Hamed1, Naglaa Elkhayat1, Nevin El-Nahas1, Magd Fouad1, Hanaa Abd Elkader2

Departments of Neurology1, Radiology2, Ain Shams University; Egypt

ABSTRACT

Background: Embolization is the underlying pathogenic mechanism in many cases of stroke. Embolization is either cardioembolic or artery to artery occurring from extracranial carotid artery or from intracranial arteries. Asymptomatic microemboli can be detected by TCD which is known as microembolic signals (MES) detection. Objective: to study the prevalence of MES as detected by TCD in a sample of patients with acute ischemic stroke, to define its correlation with echocardiography and carotid duplex, and study the use of TCD monitoring in assessment of response to medical therapies. Methods: We did a prospective study on 50 patients with acute anterior circulation ischemic stroke. We divided patients according to clinical evaluation and investigations as carotid duplex and echocardiography into 3 groups (patients with potential cardioembolic source; patients with significant ipsilateral carotid artery pathology and patients with no relevant source). We performed TCD monitoring for MES detection in all patients and a second follow up recording was done for patients who had MES on first recording. Results: twenty percent had MES in our sample. MES detection was more common in cardiac patients (50%) compared to patients with ipsilateral carotid pathology (18%) (P value 0.000), MES was not detected in any of the patients with neither cardiac nor carotid source. On follow up, MES were less detected in patients receiving anticoagulation compared to patients receiving antplatelets. Conclusion: we think that MES detection in acute stroke patients could be helpful to identify patients at risk of further embolization and so warrants urgent use of effective anticoagulation. (Egypt J Neurol Psychiat Neurosurg. 2010; 47(1): 233-237)

Key Words: Microembolic signals, Stroke, TCD.

INTRODUCTION

Cerebral embolism is the underlying pathogenic mechanism in many cases of stroke. Emboli may arise from the heart; aortic, carotid, and vertebral artery plaques; intracranial atherosclerotic stenosis; or systemic venous thrombosis in the presence of a venous-to-arterial shunt1. Microemboli detection by TCD may allow identification of the pathophysiological cause of stroke and patients at high risk of further stroke. It may also allow the effectiveness of therapies to be tested2.

The aim of this study was to study the prevalence of MES as detected by TCD in a sample of patients with acute ischemic stroke, to define its correlation with echocardiology and carotid duplex, and to study the use of TCD monitoring in the assessment of the response to medical therapies.

SUBJECTS AND METHODS

This study is a prospective study performed on 50 patients received from Ain Shams university hospitals presented with acute ischemic stroke (first ever or recurrent). Patients were monitored by TCD to identify those in whom microembolic signals could be detected.

Inclusion criteria included anterior circulation acute ischemic stroke presenting within 48 hours from onset of symptoms. Patients positive for MES on initial TCD recording were enrolled for subsequent follow up reassessment of number of microembolic signals per hour.

Exclusion criteria included primary intracranial hemorrhage, posterior circulation stroke, onset of stroke more than 48 hours before TCD recording, acoustic window that did not allow TCD recordings and patients intolerant to monitoring.

All patients were subjected to clinical Evaluation, CT brain, MRI brain with DWI proving anterior circulation stroke (unless contraindicated as in cases of prosthetic heart valves, pacemaker, or patient
intolerance to examination), ECG for detection of AF, atrial flutter and recent myocardial infarction, transthoracic echocardiography, trans-esophageal echo in certain selected cases and carotid duplex ultrasonography with detailed estimation of the degree of stenosis and nature of plaque morphology.

According to clinical assessment and results of investigations, patients were classified into 3 groups:

A- **Patients with potential cardioembolic source:**
They were classified according to TOAST classification to high risk and medium risk cardioembolism.

B- **Patients with significant extracranial carotid artery disease:**
They included patients with ipsilateral carotid stenosis >50% or ipsilateral ulcerated or friable carotid plaque.

C- **Patients with neither cardiac nor carotid source:**
A one hour baseline TCD recording was performed on eligible patients from both middle cerebral arteries. If MES were identified, the patients were followed up 5 days by repeated TCD recording for 1 hour. Results of follow up were analysed as regards presence and number of MES aiming at comparing response to different medical therapies used, which are either antiplatelets alone, versus anticoagulants with or without antiplatelets.

**TCD Methodology**
Detection of microembolic signals (MES) in the middle cerebral arteries (MCA’s) was done using a pulsed Doppler device (DWL Doppler box/DWL multi-dop X4, DWL Elektronische System GmbH, Germany) equipped with software for microemboli detection. Simultaneous bi-temporal non-invasive 1 hour TCD insonation and monitoring was performed continuously at two different insonation depths according to detectability of MCA signals (with 5mm difference) over both sides taking into consideration recording from relatively superficial site in cases with neither cardiac nor carotid source to detect probable intracranial embolization. Two 2 MHz TCD probes were fixed against the temporal bone window on both sides using a headset. The entire recording was witnessed and all events and potential sources of artifacts (such as probe slipping or patient blinking) were noted. Moreover, all monitoring sessions were recorded on hard disk for retrospective evaluation.

The identification of MES was done in agreement with international recommendations and performed both, on- and off-line. Signals accepted as microemboli were unidirectional from the baseline, lasting less than 0.3 second and having an intensity ≥7 dB higher than that of the background flow signal. In addition, they were associated with a characteristic chirping sound on the audible output. As recommended by the consensus on microembolus detection by TCD5, technical parameters affecting the detection of MES were maintained constant throughout and between recordings. MES were recorded as present/absent and the rate of occurrence was represented as MES/hour.

**Statistical Analysis**
The collected data were introduced to SPSS. Data was presented and suitable analysis was done according to the type of data obtained for each parameter.

**Descriptive statistics:** mean, standard deviation (±SD), minimum and maximum values (range) for numerical data, frequency and percentage of non-numerical data.

**Analytical statistics:** Chi-square test, Independent-Samples T Test, Paired-Samples T Test. P-value: level of significance: P>0.05: Non significant, <0.05: Significant, <0.01: Highly significant.

**RESULTS**

The final number of patients included in this study was 50 patients. Sixty seven patients were insonated for MES detection within 48 hours from onset of symptoms. Seven patients were excluded because of non detectable flow in MCA. Four patients did not tolerate completing the examination. Five patients had no temporal window for insonation. One patient died before doing his follow up (second) record. Thirty three patients were males and seventeen patients were females, with a mean age of 60.42 years.

Ten patients (20%) had MES. The total number of detected MES was 79. Mean value was 7.9 MES/patient. MES detection was more common in cardiac group of patients (50%) compared to patients with ipsilateral carotid pathology (18%). The difference was highly significant (P<0.001). Total number of detected MES in cardiac patients was74 (mean 4.6 per hour), while it was only 5 MES in carotid patients. MES was not detected in any of the patients with neither cardiac nor carotid disease.

Cardiac group included 16 patients (32%). Patients were classified into high and medium risk cardioembolic source as defined by TOAST classification. Twelve patients had high risk cardioembolic sources (8 patients with mitral valve disease, 2 with infective endocarditis (IEC), 1 with left atrial thrombus and 1 with dilated cardiomyopathy (DCM). Four patients had medium risk cardioembolic source due to AF alone. Eight patients out of 12 (66%) in the high risk group had MES on first record, while none of the medium risk group had MES on recording (P value=0.013).
In cardiac patients, 63% had bilateral emboli with total number of 75 MES on both records. Total number of MES decreased from 51 MES to 23 MES on second record. The decrease was 72% in anticoagulated patients compared to 13% in patients who received antiplatelets only (P value= 0.02).

There were 11 patients with significant carotid artery disease. MES were detected in 2 of them (18%). Both patients had soft ulcerated plaque. The 2 patients received antiplatelet therapy. One of them showed no decline of MES, while the other showed decline on the second recording.

Six patients out of 10 with positive MES on the first recording received anticoagulation before the follow up. The other 4 patients received antiplatelets only. Decline of MES was evident in the first group (63%) compared to the second group (33%).

Table 1. Frequency of MES in different subgroups.

<table>
<thead>
<tr>
<th>PATIENT GROUP</th>
<th>MES</th>
<th>Total</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+ve</td>
<td>-ve</td>
<td></td>
</tr>
<tr>
<td>Neither cardiac nor carotid</td>
<td>N.</td>
<td>0</td>
<td>23</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>0%</td>
<td>100%</td>
</tr>
<tr>
<td>Cardiac</td>
<td>N.</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>50%</td>
<td>50%</td>
</tr>
<tr>
<td>Carotid</td>
<td>N.</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>18%</td>
<td>82%</td>
</tr>
<tr>
<td>Total</td>
<td>N.</td>
<td>10</td>
<td>40</td>
</tr>
<tr>
<td></td>
<td>%</td>
<td>20%</td>
<td>80%</td>
</tr>
</tbody>
</table>

*Significant at P<0.001

DISCUSSION

We carried out TCD monitoring for MES detection in 50 patients with acute anterior circulation cerebral infarction. The aim of this work was to study the prevalence of microembolic signals in a sample of patients with acute ischemic stroke, to determine the different cerebroembolic sources, to determine the relationship between different cerebroembolic sources and the pattern of MES and to study the use of TCD monitoring in the assessment of the response to medical therapies.

First TCD recording was done in first 48 hours from onset of symptoms because studies report decrease frequency of MES as time passes from onset5-7. Monitoring duration in our study was one hour in each record. This is in accordance with most of the studies on TCD monitoring for MES5. Some studies performed 30 min. recording8. Others recommended prolonged ambulatory monitoring for hours9.

Our results showed a 20% prevalence of MES in the whole group of patients. This is nearly in agreement with other studies which reported 16-28% prevalence1,12. Other studies showed less prevalence reported to be 5.7%.2 Some studies report higher prevalence like: 31-51%.3,13,14 This may be due to time of recording in relation to onset, duration of monitoring, treatment regimens received before recording, different pathophysiological factors related to stroke and technical factors.

Our results showed that the prevalence of MES was higher among the cardiac group (50%) compared to carotid group (18%). This is contrary other studies5,7,11,14 where MES were more prevalent in patients with carotid artery disease. This may be attributed to the fact that most of our cardiac cases are of the high risk group. Also our recording was done earlier before effective anticoagulation and for longer period of time.

Bilateral MES occurred in 63% of MES positive patients. This confirms the role of MES in identifying source of stroke by the suggestion that Ipsilateral MES are frequent in patients with carotid artery disease, whereas bilateral MES are suggestive of a cardioembolic origin5.

MES were detected in only 18% of the carotid patients. This number is similar to previous reports7,16. The two patients with positive MES in the carotid group had soft ulcerated plaque on their carotid duplex regardless of the degree of associated stenosis. This is similar to what was proposed that plaque ulceration and mobility were the main source of embolization and no association between degree of stenosis and embolization6. This may explain the lower frequency of MES in patients with carotid disease and clearly reflects racial difference in carotid pathology in Egyptians.

When coming to assessment of response to treatment, our results showed significant decline in anticoagulated patients compared to patients on antiplatelets. This is similar to what was reported previously5 that anticoagulation appears to decrease the prevalence of MES.
We failed to detect any MES in patients with neither cardiac nor carotid source. This agrees with previous reports. Other studies reported MES in patients with intracranial atherosclerosis. Other studies with evident MCA stenosis serious trial, especially this is common in Egypt.

In conclusion, we think that MES detection in acute stroke patients could be helpful to identify patients at risk of further embolization and so warrants urgent use of effective anticoagulation.

REFERENCES


الملخص العربي
دراسة انتشار كشف السذادات الشريانية في حالات الجلطة الدماغية الحادة وإمكانية استخدامها كوسيلة لتقييم العلاج من الأسباب الرئيسية للجلطات الدموية وجود سذادات شريانية سواء من القلب أو مرض السحايا، خاصة تلك المتباعدة من الشريان الشرياني للجلطات الدموية ويمكن كشف تلك السذادات الشريانية عن طريق فحص الدوبلر المطول عبر الدماغ.

الهدف من البحث:
- التعرف على انتشار كشف السذادات الشريانية في عينة من حالات الجلطة الدماغية الحادة.
- التعرف على مساهمة ذلك الفحص في المساعدة على تحديد مصدر السذادات الشريانية، و файла نتائجه بنتائج الموجات الصوتية على القلب والأشعة على الشريان السحايا.
- محاولة معرفة إمكانية استخدامها كوسيلة موضوعية لتقييم العلاج النادر لهذه الحالات.

طريقة البحث:
تمت دراسة خمسين مريضاً مصاباً بجلطة دماغية حادة وتم تقسيمهم إلى ثلاث مجموعات: مجموعة منها مصدر قولي للسذادات الشريانية وأخرى بضيق بالشريان السحايا وأخرى لم يكشف لها أي من السببين. تم عمل فحص المطول بالدوبلر عبر الدماغ لجميع المرضى، وعند اكتشاف وجود سذادات شريانية تم عمل متابعة لمهم فحص آخر بعد خمسة أيام.

النتائج:
- أظهرت النتائج انتشار السذادات الشريانية المكثفة بالدوبلر في (20%) من العينة وقد ظهرت نسبة أكبر (50%) ضمن المجموعة التي بها مصدر قولي للسذادات الشريانية مقارنةً بوجود مرض بالشريان السحايا (18%) في حين لم يتم اكتشاف أي منها ضمن المجموعة التي ليس بها مصدر قولي أو سحايا للسذادات.
- وعند القيام بالمتابعة يتبين أن السيداد شريانية بوجود الأول ظهر الخفاض أكثر بعددًا لدى المرضى الذين يتلقون مضادات للجلطات مقارنةً بالمرضى الذين يتلقون مضادات الصفائح.
- وقد استنتجنا أن هذا الاختبار قد يكون مفيداً في تحديد المرضى الذين ينبغي الاهتمام باستخدام مضادات للجلط فيهم بأسرع وقت عند حدوث الجلطة الدماغية.