

Transcranial doppler sonography diagnostic value for the cerebral flow velocity changes in the interictal phase of classic migraine

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Abstract

Background: An imbalance of the cerebrovascular response during functional activation of the brain has been postulated as a factor in the pathophysiology of migraine. The purpose of this study was to determine the transcranial doppler sonography (TDS) diagnostic value for the cerebral flow velocity changes in the interictal phase of classic migraine.

Methods: This study was carried out on 46 patients (23 cases and 23 controls). We used Doppler instrument via trans-temporal window and detected middle cerebral artery, anterior cerebral artery and posterior cerebral artery by 2 MHz probe. The flow velocity in the posterior cerebral artery before, during and immediately after stimulation was recorded. Stimulation was done using a flickering light in 100 seconds.

Results: At the baseline, the middle cerebral artery had more peak systolic velocity in migraineurs than the control group. Although peak systolic velocity changes in the mid-photic period is not statistically significant. On the other hand, post-photic peak systolic velocity increased significantly. The diagnostic accuracy of the peak systolic volume (PSV) changes in the posterior cerebral artery (PCA) for the migraine was 72.3%.

Conclusion: This stimulation we found altered cerebral vasomotor reactivity in the interictal phase in migraineurs with visual aura. This seemed to be an unavoidable hindrance for the wider implementation of functional TCD in diagnostic work up of migraine patients.

Key words: Transcranial Doppler sonography (TCD), Migraine with aura, Photo stimulation.

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Migraine is considered as a neurovascular coupling disorder where the cerebral vascular reactivity is malfunctioning and measuring hemodynamic changes during migraine without causing more disturbance has always been a challenge (1). The neuronal hypersensitivity to different intrinsic and extrinsic stimuli is the primary pathophysiological changes in the migraine. The migraineurs show a reduced adaptation to environmental stimuli due to no habituation in contrast to healthy controls. These features might also be transmitted to the cerebral vasoreactivity, but the results are conflicting so far. Some studies on the interictal migraineurs showed increased cerebral vasoreactivity to CO stimuli. In response to cardiovascular autonomic tests such as head-up tilt, cold pressure or Valsalva maneuver, the results were again conflicting (2-4).

In electrophysiological trials of migraine, patients showed absent habituation or even a potentiation of the response to repetitive stimuli. The habituation, as a reaction of adaptation to a stimulus that has proven innocuous, implies both attentive and cognitive aspects. This process is not confined to cortical areas involved in the processing of the specific like visual stimulus.

The absence of habituation has been interpreted as a dysfunction of the cortical information processing. It seems to be more pronounced in the interictal phase and tends to normalize just before and during the migraine attack. The significance of these electrophysiological findings for the cerebral perfusion and their relation to vasomotor reactivity is open, although close coupling has been observed during seizures (5). Changes in the CBFV are not only determined by the regional cerebral activation, but also by systemic factors. The autonomous reaction was more pronounced in migraineurs. Systemic factors such as blood pressure, heart rate, PCO intracranial pressure, etc. have caused a velocity increase in both arteries. On the other hand, the cerebral activation was higher in migraineurs, but it was not confined to areas supplied by the PCA.

The few studies using TCD which had addressed this question reported heterogeneous results. Probably it was due to different stimulations and recording procedures, small sample sizes, lack of control for medication and absence of matched control groups. In addition, the inclusion of both migraineurs with and without aura may have contributed to the heterogeneity of the results (5). There is still some controversy about alterations in velocity of blood flow and in cerebral vasomotor reactivity of intracranial arteries in migraineurs during the interictal phase (6). The purpose of this study was to determine the transcranial doppler sonography (TDS) diagnostic value for the cerebral flow velocity changes in the interictal phase of classic migraine.

Methods

Patients: In order to validate this study more, this was carried out on 46 subjects with equal number in control and case groups (23 cases and 23 controls). All subjects were randomly chosen and referred from the neurologist's private clinic to the TCD ward in Shafa Hospital, Kerman University of Medical Sciences. The patients were 20-40 years old and showed IHS criteria for migraine diagnosis. They were also asked about their family history and duration of their migraine disease. The controls were randomly

chosen from student participants and hospital staff that did not have history of chronic headache. Both groups were similar in age and sex. Two weeks ago, the samples in these groups did not show any of these problems: vascular disease, diabetes mellitus, smoking, addiction, drugs as calcium blockers or beta blockers and history of seizure. The patient group was evaluated in interictal phase and free from prophylactic drugs. In addition to exclusion criteria explained above, the control group did not have any history of vascular headache. The subjects were chosen by a neurologist and each subject had a specific number which was recognized and this number was referred to the TCD center (single blinded). The study procedure was approved by the Ethics Committee of Kerman University of Medical Sciences.

Before conducting the TCD test on the groups, they were all oriented about the test, procedure and the aim of study as well. The test was done after the patients willingly and fully cooperated in this research.

Experimental condition: After selecting the participants, they referred to TCD center. We used DWL X2 Doppler instrument via trans-temporal window and detected posterior cerebral artery (PCA) by 2 MHz probe. peak systolic (PSV), end diastolic (EDV) and pulsatility index (PI) in this artery was measured. The person was in supine position; we tried to make the auditory and sensory stimulus to minimal level. The Doppler probe was fixed over the patients head by frame to reduce the velocity changes by insonation angle.

During sonation of PCA, photo stimulation with the lamp of IP55 from Italy was done binocularly. Flickering light in 100 seconds from the distance about 1 meter was exposed to the subjects. The flow velocity was recorded before, 50 seconds after, and also at the end of stimulation. During the 'stimulus off' phase, the subjects were asked to close their eyes. The left side TCD on the subjects was done, but the patients with complaint of headache or aura in the right side, the data were measured in right side as well. We did not control any changes in the blood pressure, heart rate and end-tidal CO₂.

Statistical Methods: We used the independent t-test to compare the two groups. Then, for analyzing the confounding factors for migraine, we used the logistic regression model. We analyzed the diagnostic value of PCA differences by using the ROC curve.

Results

We studied 46 cases, 23 patients in each group. There were 19 women and 4 men in each of them. The mean age in the migraine group was 30.61 ± 6.8 and in the control group was 30.48 ± 6.25 years. The studied group did not have significant difference in the mean of age. The peak systolic flow velocity (PSV) of PCA in the beginning, middle and at the end of stimulation did not have significant difference between groups by independent t-test.

The change of PSV at the end of stimulation from the baseline was significantly greater in the migraine group as compared to the control group ($p = 0.013$). Analyzing by regression logistic model, showed that the age, sex and the baseline PSV were not significant factors for the studied groups. Table.1 shows the predictive value of the PSV changes for the migraine group by photic stimulation.

Table 1. Predictive values of different amounts of the Peak Systolic Velocity changes (PSV) of posterior cerebral artery at the end of photic stimulation from the baseline.

The PSV changes (millisecond)	Predictive values for migraine (percent)
8	81.6
7	77.3
6	72.4
5	66.8
4	60.8
3	54.4

Table 2. The cut off point for the sensitivity and specificity for diagnosis of migraine at the different Peak Systolic velocity (PSV) changes of Posterior cerebral artery.

PSV changes (millisecond)	Sensitivity (Percent)	Specificity (Percent)
7.5	4.3	100
6.5	17.4	100
5.5	36.1	100
4.5	47.8	82.6
3.5	47.8	73.9
2.5	56.5	69.8
1.5	82.6	52.2

In the end, we used the ROC curve to evaluate the diagnostic value of PSV changes in the migraine group. As the measured area of the curve was 0.723, the diagnostic accuracy of the PSV changes in the PCA for the migraine group was 72.3%. Table 2 shows the different cut points for PSV difference for the sensitivity and specificity of migraine diagnosis.

Discussion

A dysbalance of the cerebrovascular response during functional activation of the brain has been postulated as a factor in the pathophysiology of migraine (7). Habituation of cortical evoked responses to repetitive stimuli is reduced in migraine between attacks (8). It has been suggested that the pathogenesis of migraine is related to an imbalance in the activity between the brain stem nuclei regulating antinociception and the vascular control, rather than in primary vessel diameter changes (9,10). Other studies concluded that mild parasympathetic hypofunctioning with preserved sympathetic functioning was an established finding in migraine both with and without aura (11). It was assumed that a lack of habituation of the cerebrovascular response in migraineurs might contribute to a disturbance of the metabolic homeostasis of the brain that might induce migraine attacks (7). Data suggested an altered

neurovascular coupling in Occipital cortex of migraine patient's interictally. The published results of TCD studies of the main cerebral arteries, performed in patients with idiopathic headaches, especially with migraine, are controversial (9, 11, 12). Some authors could not find any changes, while the others observed increased blood flow (13). These results were, however, based on single examination, and the comparison on mean velocities calculated for the whole groups (12).

Bäcker et al. did the first TCD study to show habituation (7). They used the flickering photic stimulation on all the migraineurs, both classic and common. They observed the loss of habituation only in the middle cerebral artery, the fact that habituation in healthy subjects was confined to the MCA territory is surprising and in conflict with electrophysiological findings. As there were some critics to that study, in 2003, K Nedelchev et al. conducted a more accurate study. They used the check board display to stimulate visual pathway and simultaneously recorded the MCA and PCA arteries. The PCA showed the loss of habituation in the migraineurs (5).

In Backer's study, they used the flickering light. In our study, only the classic migraineurs participated. As we had evaluated the diagnostic value and measured the sensitivity and specificity of those hemodynamic changes, we focused on the PCA measurements. It is worth to mention again that the autonomous reaction was more pronounced in migraineurs. Systemic factors such as blood pressure, heart rate, PCO₂, intracranial pressure, etc. have caused a velocity increase in intracranial arteries. Also, the cerebral activation was higher in migraineurs, and was not confined to areas supplied by the PCA (4, 5, 14-16).

Transcranial Doppler testing of cerebrovascular changes is a reliable and interesting for the diagnostic evaluation and management of migraine patients. However, possible usefulness of this method in the diagnostics of migraine requires further investigation. Nevertheless, TCD ultrasonography offers the opportunity to noninvasively monitor cerebral blood flow parameters and, therefore, represents a valuable tool for vascular research in migraine.

We do not intend to imply a casual role of these preliminary findings in migraine pathogenesis, but we suggest that TCD be used in combination with other methods to study vascular changes in migrainous disorders. Our study showed the moderate diagnostic value for the PSV changes on the PCA. The value of TCD in the differential diagnosis of "vascular headache" and in the study of migraine pathophysiology will have to be determined in the future (17, 18). In summary, Using this stimulation, we found altered cerebral vasomotor reactivity in the interictal phase in migraineurs with visual aura. This seemed to be an unavoidable hindrance for the wider implementation of functional TCD in diagnostic work up of migraine patients.

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