

Study of Hemodynamic Abnormalities by Transcranial Doppler Ultrasound in Patients of Migraine

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Abstract: Objective: 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 is to determine ictal and inter ictal hemodynamic abnormalities by Transcranial Doppler (TCD) Sonography and compare them in patients of Migraine with or without Aura with Controls.

Methods : This is Single Center, Prospective, Case Control study conducted on 100 patients (50 cases, 50 controls) during January 2013 to August 2014 in a Tertiary care hospital. Subjects were classified as ictal or interictal based on the presence or absence of headache at the time of examination respectively. Sonara Tek Transcranial Doppler machine was used to record flow velocities in middle cerebral artery, anterior and posterior cerebral arteries on both sides sequentially with 2 MHz transducer via transtemporal window.

Results: INTERICTAL STUDY: None of the examined vessels showed a significant change in the blood flow velocity in both migraine with aura and without aura patients. Neither were there significant differences found between the painful and non-painful side.

ICTAL STUDY GROUP: MCA Peak Velocities in the Migraine without Aura group showed significant reduction compared to controls (p value < 0.02). The MCA Mean Velocities were also lower than those of controls but did not reach statistical significance.

Conclusions: Current study shows that TCD Sonography can detect pathophysiological Hemodynamic abnormalities in Migraine patients during the Headache phase. Flow velocities of Middle Cerebral Artery were lower in the ictal group in migraine patients compared to controls.

Key words: MCA, TCD, MIGRAINE

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I. Introduction

Migraine is a common disabling brain disorder whose key manifestations are recurrent attacks of unilateral headache and interictal hypersensitivity to sensory stimuli. In the *Global Burden of Disease Survey 2010*, it was ranked as the third most prevalent disorder and seventh-highest specific cause of disability worldwide. (1) initial attack of migraine most commonly occurs during adolescence. It is more common in females after puberty, whereas in children there is a small male preponderance. Family history is present in upto 90% of patients. (2) Migraine attacks are separable into those with and without aura. The vascular changes in migraine headache is a well acknowledged fact and a large series on quantitative and qualitative intracranial vascular modifications during migraine have been reported. TCD has become useful as a non invasive modality in detecting changes in blood flow velocities in migraine thus contributing to its pathophysiology (3). Past TCD studies were undertaken to determine blood flow velocity as an indirect measurement of diameter of the large intracranial arteries. But these studies have come up with conflicting results, and have varied with regard to side of pain and delay in examination from last attack. (4)

The current study was done to look at the changes in flow velocities with the help of TCD and to determine diagnostic value of TCD for velocity changes and blood vessel caliber fluctuations in migraine patients.

II. Material And Methods

This Prospective Case Control Study was done in the Department of Neurology, King George Hospital, Visakhapatnam.

Study Design: Prospective Case Control Study.

Study Location: This was a tertiary care teaching hospital based study done in Department of Neurology, Andhra Medical College, Visakhapatnam.

Study Duration: January 2013 to August 2014.

Sample Size: 100 patients(50 CASES,50 CONTROLS)

Subjects & Selection Method:

50 patients who presented to the Neurology OPD with headache fulfilling the ICHD criteria for Migraine with or without Aura were recruited into the study after the Informed Consent. Ethics Committee Clearance was obtained prior to the initiation of the study.

Inclusion criteria for Cases:

- Age more than 15 years of age.
- History of headache fulfilling the ICHD criteria for migraine with and without aura.
- Normal neurological examination.

Exclusion criteria for Cases:

- Pregnancy
- Past history of transient ischemic attack
- Cardiovascular disease
- Hypertension
- On prophylactic medication in the last 72 hours.
- Smoking
- Metabolic and pulmonary diseases
- Alcohol abuse
- Chronic migraine

Controls: 50 healthy volunteers, matched for age were taken as controls.

Exclusion criteria for Controls :

- History of recurrent headache
- Hypertension
- Diabetes
- Pulmonary disease
- Cardiovascular disease
- Smoking
- Alcoholic abuse
- Pregnancy

III. Material And Methods

The subjects were diagnosed as migraine with or without aura based on the ICHD criteria.

Diagnostic criteria for Migraine without Aura:

A. At least five attacks fulfilling criteria B–D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)

C. Headache has at least two of the following four characteristics:

1. unilateral location
2. pulsating quality
3. moderate or severe pain intensity
4. aggravation by or causing avoidance of routine physical activity (e.g. walking or climbing stairs)

D. During headache at least one of the following:

1. nausea and/or vomiting
2. photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis.

Diagnostic Criteria for Migraine with Aura :

A. At least two attacks fulfilling criteria B and C

B. One or more of the following fully reversible aura symptoms:

1. visual

2. sensory
 3. speech and/or language
 4. motor
 5. brainstem
 6. retinal
- C. At least two of the following four characteristics:
1. at least one aura symptom spreads gradually over ≥ 5 minutes, and/or two or more symptoms occur in succession.
 2. each individual aura symptom lasts 5-60 minutes
 3. at least one aura symptom is unilateral
 4. the aura is accompanied, or followed within 60 minutes, by headache
- D. Not better accounted for by another ICHD-3 diagnosis, and transient ischaemic attack has been excluded.

Procedure Methodology

50 cases were further classified as ictal and interictal based on the presence or absence of headache during the examination. 50 healthy volunteers, matched for age were taken as controls.

The patients in the ictal group were studied 6 hours after the onset of headache attack.

The SonaraTek Transcranial Doppler machine from Viasys Neurocare was used in the study.

2 MHz transducer was used to study the Middle Cerebral Artery, Anterior and Posterior cerebral arteries on both sides sequentially. The study was carried out in quiet room with the patient lying comfortably supine on a cot with the face forwards. Study was performed from the head end of the bed. Heart rate and blood pressure was measured at the beginning of each study. The transtemporal window was insonated to study the three arteries namely the MCA, ACA, PCA. The signal from the three arteries was obtained by changing the depth of the sample volume and the inclination of the probes. The flow velocities were recorded for all the three arteries on both hemispheres.

Statistical Analysis

The data was presented as mean \pm standard deviation or percentage of cohort affected. The significance between means of two parameters was compared using unpaired 't' test. The p value of less than 0.05 was considered statistically significant. For the statistical analysis Graphpad software was used

IV. Results

The study included 50 patients and 50 controls. The baseline characteristics regarding age were similar between Cases and Controls. The age range for cases and controls was 15 yrs to 45 yrs. Of the 50 subjects, 45 (90%) were Females and 5 (10%) were Males. Mean (\pm SD) duration of headache in cases was 5 yrs \pm 4 yrs. Headache lasted > 24 hrs in 16 (32%) subjects and < 24 hrs in 34 (68%) of subjects. Headache was holocranial in 19 (38%) and hemicranial in 31 (62%) of subjects. 17 (34%) had migraine with aura and 33 (66%) had migraine without aura. Number of patients who were studied at the time of headache, i.e., ictal period were 32 (64%). Those studied during the headache free period (72 hrs after the last headache), i.e., interictal were 18 (36%).

Comparing the mean of the Mean Velocities (MV) and Peak Velocities (PV) of MCA, ACA, PCA in subjects with migraine in the ICTAL PERIOD with those of controls :

This has been represented in figure 1

Figure 1: MCA MEAN MV AND PV COMPARISON

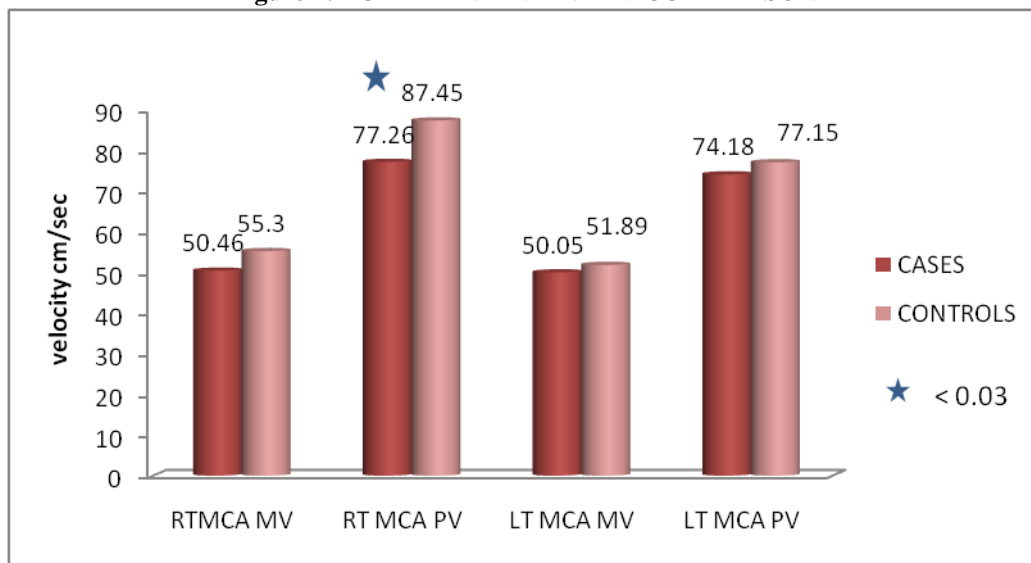


Fig 1 : Right MCA Mean Velocities and Peak Velocities among the ictal group were lower compared to controls. But only the MCA peak velocities were significantly lower compared to controls (p value < 0.03).

There was no significant difference in the mean or peak velocities of other arteries on both sides.

Comparing the mean of the Mean Velocities (MV) and Peak Velocities (PV) of MCA, ACA, PCA in subjects with migraine in the INTERICTAL PERIOD with those of controls: No significant differences were observed in the mean and peak velocities of MCA, ACA, PCA of both sides between the inter ictal group and the control group.

To determine side to side differences of Mean and Peak Velocities during unilateral attacks of migraine with or without aura in the ICTAL STUDY:

Right Hemicranial Headache : Velocities of the right Hemicranial Headache group were compared with those of controls. This has been represented in figure 2

Figure 2 : MCA MEAN AND PEAK VELOCITIES

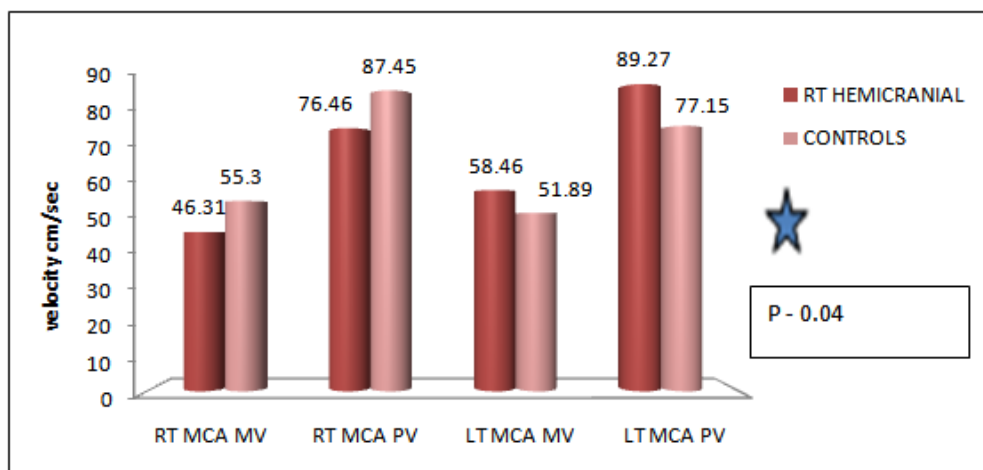


Fig 2 : The right MCA Mean and Peak Velocities were lower compared to controls. The MCA Mean Velocities were found to be significantly low on the right side compared to controls (p value < 0.04)

No significant difference was found in the velocities of the other arteries.

Left Hemicranial Headache : Velocities of the left Hemicranial Headache group were compared with those of controls. No significant difference in the velocities was observed between the flow velocities of the left Hemicranial group with that of controls. Also no significant differences were observed on side-to-side comparison of the velocities in the left Hemicranial group.

MIGRAINE WITHOUT AURA vs CONTROLS: Comparison of flow velocities between the two groups. This has been represented in figures 3 and 4

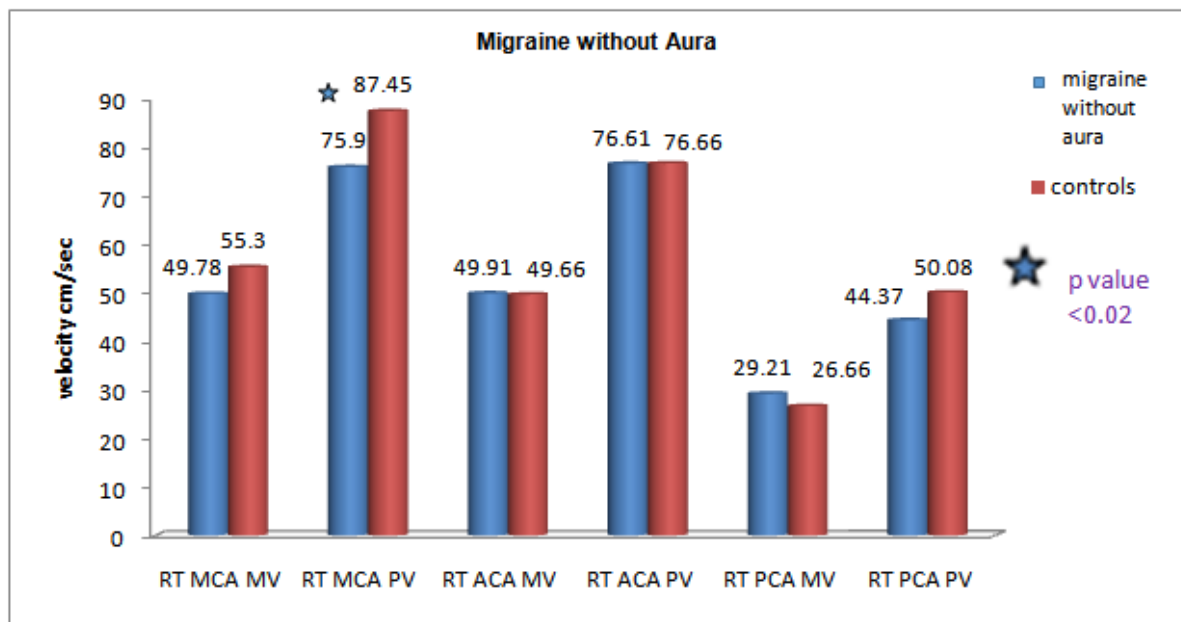


Figure 3: Right Hemispheric velocities in Migraine without Aura group and controls

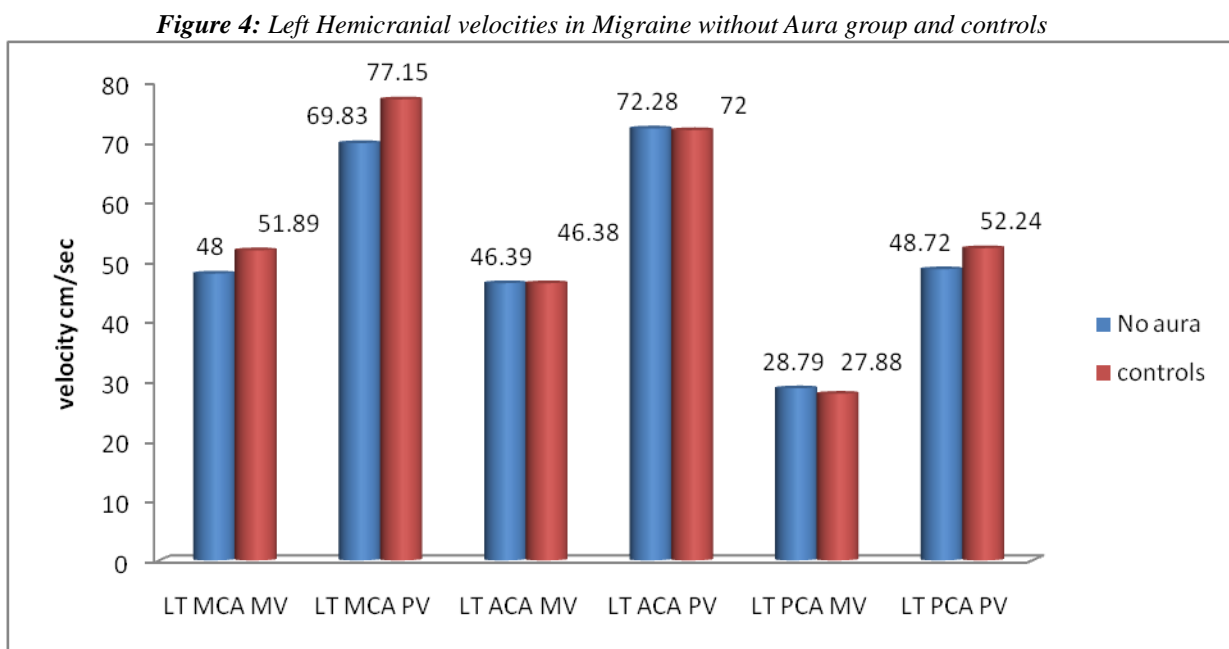


Figure 4: Left Hemispheric velocities in Migraine without Aura group and controls

Fig 3,4 : The right MCA Peak Velocity were found to be significantly lower compared to the controls (p value < 0.02). The right MCA mean velocity was also lower compared to controls but did not reach statistical significance.

There was no significant difference found in the velocities of all the other vessels.

No significant differences were observed between the velocities of Migraine with Aura group and the controls.

V. Discussion

The role of vasodilatation in migraine has been vividly debated in the past. Some researchers view vasodilatation of meningeal or cerebral blood vessels as a primary trigger for migraine headaches, and consider vasoconstriction necessary for acute anti-migraine efficacy (5). Others feel that vasodilatation is a secondary phenomenon, due to activation of the trigeminovascular system and release of vasoactive neuropeptides.

Vasodilation would primarily be involved in sustaining and worsening of the headache during migraine attacks(6). Past TCD studies were undertaken to determine blood flow velocity as an indirect measurement of diameter of the large intracranial arteries.

The present study was aimed to assess any differences in the flow velocities of MCA, ACA, PCA between interictal study and controls; ictal study and controls; and also if the velocities differed between painful and painless sides among those with lateralized headache.

Study included 50 patients of whom 32 were examined during the headache and 18 were examined in the interictal period i.e., 72 hours after the last headache episode.

INTERICTAL STUDY :In the interictal study, none of the examined vessels showed a significant change in the blood flow velocity in both migraine with aura and without aura patients. Neither were there significant differences found between the painful and non-painful sides. This is in accordance with the results of *De Benedittis G et al (7)* and *Zwetsloot CP et al (8)* who also failed to show significant blood flow velocity changes in the intracranial arteries in the interictal period in migraine without aura patients compared to controls. SPECT study done by *De Benedittis et al* also did not show rCBF asymmetries.

ICTAL STUDY :Parameters were analyzed to identify any significant differences between the ictal group and the controls. The Peak Flow Velocities in the right MCA were significantly reduced compared to controls (p value < 0.03) and *might represent an increase in the MCA luminal diameter (cross sectional area) suggesting vasodilatation of large vessel.*

The right MCA Mean Velocities also were reduced but did not reach statistical significance. No difference was found in the velocities of the remaining vessels. The reduction in flow velocities in the middle cerebral artery in the ictal group is consistent with the results of the studies done by *Thei et al (9)*, *Thomsen et al(10)*, *Benedittis et al (7)*. *Reduction of flow velocities was seen only on the right side and no changes were observed on the left side. This discrepancy could be explained by several factors including the various technical limitations of TCD. TCD measures only a short span of cardiac cycle. Also it insonates only a small segment of the vessel at any given time. Finally, TCD is a blind procedure and the angle of insonation may not always be optimal*

The MCA Peak Velocities in the migraine without aura group showed significant reduction compared to controls (p value < 0.02). The MCA mean velocities were also lower than those of controls but did not reach statistical significance. This is in accordance with the studies done by *Thei et al(9)* demonstrated a CBV reduction during spontaneous attacks of migraine without aura. *This might suggest an increase in the luminal cross sectional area in this group during the headache period suggestive of dilatation of the MCA arteries.*

Contrary to the migraine without aura group, migraine with aura group did not show any difference in the flow velocities compared to the control group. Results on flow velocities during migraine with aura have varied results among different studies. *Zwetsloot et al (8)* in their study on blood flow velocities in migraine attacks showed no significant difference compared to the attack free state.

This study shows a discrepancy between the observations of the two groups of migraine with aura and without aura. This could be explained by several factors such as the delay in examination time from headache onset being 6 hours in the present study. Most of the studies in migraine with aura patients had been conducted within 6 hours of headache onset. Also the sample size was small. As TCD insonates only a small segment of the blood vessel at any given time and only a short span of cardiac cycles, hence certain changes could have been missed.

To study asymmetries of the blood flow velocity in patients with Lateralized Headache :Right Hemicranial Headache group, the Mean Velocities of the right MCA were significantly low compared to controls (p value < 0.04).The reduction in flow velocity might suggest a dilatation of MCA on the headache side.This is in accordance with the study by *Thomsen et al (10)*

VI. Conclusion

Flow velocities of Middle Cerebral Artery were lower in the ictal group in migraine patients compared to controls. The reduction of MCA flow velocities was observed in the Migraine without Aura group and on the right side in the right Hemicranial Headache group, a finding that supports the **arterial vasodilatation theory of migraine**

This study highlights ability of TCD Sonography in detecting pathophysiological hemodynamic abnormalities in migraine patients during the headache phase. TCD ultrasonography offers the opportunity to noninvasively monitor cerebral blood flow parameters and, therefore, represents a valuable tool for vascular research in Migraine.

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No Conflicts of Interest in the study.

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