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RESEARCH ARTICLE

CEREBROVASCULAR REACTIVITY IN INTERICTAL PHASE OF MIGRAINE

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ABSTRACT

Objective: To study the cerebrovascular reactivity in patients with migraine. **Background:** Migraine is an episodic disorder commonly encountered in daily practice. Multiple hypothesis have been proposed for the pathophysiology of migraine. It is a state of altered excitability capable of activating trigeminovascular system. It is a neurovascular coupling disorder where the cerebrovascular reactivity is malfunctioning. The neuronal hypersensitivity to different external and internal stimuli is the primary pathophysiological changes in these patients. The migraineurs show maladaptation to environmental stimuli owing to loss of adaptability compared to normal people. Several transcranial doppler studies have reflected the altered reactivity with varying outcomes in migraineurs. **Study design:** This study was conducted over a period of six months at tertiary hospital, RGGGH, chennai. We included 30 patients who satisfied criteria for migraine (with and without aura) as per IHS criteria and 30 age and sex matched controls. Transcranial doppler was performed on all patients. Cerebrovascular reactivity was assessed by repetitive photic stimulation. Average peak systolic velocity in middle cerebral artery and posterior cerebral artery was measured before and after photic stimulation. **Results:** The mean PSV in MCA in controls was 75.48±9.183 before and77.55±9.180 after stimulation PSV in patients before photic stimulation was 78.80±13.745 and 80.40±12.719 after stimulation. The change in PSV MCA was not significant($p<0.006$).The PSV PCA in patients before photic stimulation was 59.47±10.345 and 63.13±11.013 after photic stimulation the increase in PSV was statistically significant($p<.001$).The increase in PSV PCA in patients with aura was significant compared to those without aura($p<.002$). **Discussion:** The study demonstrated an increased PSV levels of PCA after photic stimulation and significantly higher in migraine with aura. We found an altered cerebrovascular reactivity in interictal phase of migraineurs, being more pronounced in migraine with aura. **Conclusion:** There was maladaptation of cerebrovascular reactivity in migrainuers, more so in patients with aura causing a disturbance in neurovascular homeostasis possibly inducing migraine attacks.

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INTRODUCTION

Migraine is common disorder we encounter in neurological practice. Its prevalence is about 12% in general population. Aura is subjective phenomena during which there is transient cortical spreading depression and it is seen in about 35% of patients with migraine (Weatherall, 2015). Several theories have been proposed for the pathophysiology of migraine, however it said to be multifactorial. It was found that there is activation of the trigeminovascular system and cortical spreading depression may be responsible for the aural symptoms. The threshold for excitability may be reduced in some of the individuals (Noseda, 2013). It was found that patients with migraine show increased sensitivity to changes in internal milieu and external stimuli like light sound smell etc.

There is maladaptation to various stimuli in patients with migraine and these changes may be reflected in cerebrovascular flow velocities. The vasodilation or vasoconstriction occurring in migraine may produce various changes in intracranial aretries and subsequent blood flow changes. The cerebral blood flow velocity changes to various stimuli in migraineurs and have been studied in various phases. These studies have shown varying outcomes (Dora, 2002; D'Andrea et al., 2016). Transcranial doppler is a safe non invasive tool to assess the cerebral blood flow velocities and vasomotor reactivity to various stimuli like CO, CO2, photic stimulation (Schwedt, 2015).

STUDY DESIGN AND METHODOLOGY

This study was conducted over period of six months at institute of neurology, madras medical college.30 patients who satisfied the criteria for migraine as per ICHD criteria were selected from headache outpatient clinic of our institute. 30 controls were selected who were age and sex matched with patients.
Inclusion criteria:

- Age 20-70 years
- Migraine as per IHS criteria
- Willing to participate

Exclusion criteria

- Arterial hypertension and brain disease
- Pregnancy
- Metabolic and pulmonary disease
- Alcohol abuse
- Migraine preventive drugs beta blockers, calcium channel blockers

All the included patients underwent a thorough history general and neurological examination. All the routine investigations were done and imaging was also done. All the patients were subjected to Transcranial doppler. Doppler study was done using 2MHz probe using a doppler machine in all patients during the interictal phase and also in controls. The doppler was performed on subjects in supine position. PSV of MCA and PCA were estimated using transtemporal window. After estimating the baseline values, photic stimulation using a flickering light was done binocularly for about 1minute from a distance of 1m and peak systolic velocities were estimated at the end of photic stimulation. Data were analyzed using statistical software sspsversion 18.0. Quantitative data were expressed as mean ±SD. Qualitative data were expressed a frequency and percentage. The following tests were done Independent-samples t-test of significance was used when comparing between two means χ2-test of significance was used to compare proportions between two qualitative parameters. Probability (P-value) P-value less than 0.05 was considered significant.

RESULTS

Demographic data: We included 30 patients, 25 female and 5male patients. The average duration of headache was 2.3 years in patients. Of 30 patients 12 had history of aura and all were visual aura and 18 were without any aura.30 controls were also included which were age and sex matched. No significant difference in demographic data was noted.

Transcranial doppler results: The systolic velocities in MCA, in patient and control group was compared. There was no significant difference between PSV MCA between patient and the control group at baseline. After photic stimulation there was increase in peak velocities, however it was not statistically significant with p value (0.08). The systolic velocities in PCA were compared between the patient and the control group. The basline velocities in patients was comparatively higher in patient group. After photic stimulation the increase in PSV in patient group was higher and statistically significant (p-0.001) but the PSV changes in control group was not significant. The velocities were also compared in between two subgroups that is aura and without aura, the baseline PCA PSV in patients with aura was higher compared to those without aura. After photic stimulation the velocities in patient with aura was higher and statistically significant. The PSV in MCA however was not significant before and after photic stimulation in between the two subgroups.

DISCUSSION

In this study we used PSV of MCA and PCA using transcranial doppler to assess the cerebrovascular reactivity in migraineurs in their interictal phase. We used repetitive photic stimulation to assess the CVR.As we know in migraineurs it is the activation of trigeminovascular system and the associated secondary vascular changes ,the main pathophysiology.Here altered cerebrovascular response to functional stimulation has also been postulated as factor in pathophysiology in migraine. Several studies using transcranial doppler have been studied and have shown varying results (Bäcker et al., 2001). A review of several studies of doppler changes in migraine was analysed, both during spontaneous attacks and in interictal phase.

Table 1. Peak Systolic Velocity in MCA in control and patients

		Controls	Patients	N	Std. Deviation	Sig.(2-tailed)
Pair 1	MCA PSV – Before Photic timulation	75.48	78.80	30	13.745	0.12
	MCA PSV- After Photic stimulation	77.55	80.40	30	12.719	0.08

Table 2. Peak Systolic Velocity in PCA in control and patients

		Controls	Patients	N	Std. Deviation	Sig.(2-tailed)
Pair 2	PCA PSV – Before Phtoic stimulation	54.67	59.47	30	10.345	0.34
	PCA PSV- After photic stimulation	56.21	63.13	30	11.013	0.001

Table 3. Peak Systolic Velocities in Migraine with and without aura

	AURA	N	Mean	Std. Deviation	Std. Error Mean	Sig.(2-tailed)
PSV PCA– Before Photic stimulation	Yes	12	66.50	10.059	2.904	.002
	No	18	54.78	7.674	1.809	0.21
PSV PCA– After photic stimulation	Yes	12	70.67	10.316	2.978	.001
	No	18	56.11	8.443	1.990	0.09

The results of these studied were analysed and compared (Sheyestagul et al., 2017). In our study we noted slightly higher baseline flow velocities in both MCA and PCA in patients subgroup compared to control group however it was not significant, similarly other studies did not find significant differences in both subgroups, Kastrup et al found higher baseline velocities in patient group (Kastrup, 1998). During estimating PSV MCA, in our study we noted there was slight increase in flow velocity in patient group following photic stimulation as compared to control group, however it was not statistically significant. The results were similar to study done by Backer et al. (2001), where they used photic stimulation assess the blood flow velocities but they found an transient increasein flow velocity PSV MCAonly during the end of photic stimulation. PSV MCA was also studied in both the subgroups of migraine with aura and without aura, we did not find any significant changesin both the subgroups at end of photic stimulation. These results were similar to study done by Thei et al. (1990), who studied flow velocities MCA during motor tasks and found no significant differences in between the subgroups. However in study conducted by Thompsen et al(12),who studied cerebral reactivity to hypocapnia and found increased reactivityin patient with aura than without aura.

In our study we also assessed PSV PCA and found that the baseline values were higher in patients although not significant, and PSV PCA were higher after photic stimulation in migraine and was statistically significant. Similar results were observed in studies by Thacker et al. (Bäcker et al., 2001), and Seidghi et al. (2011), in this study they concluded that PSV PCA after photic stimulation was significantly higher from baseline. The PSV PCA as studied in both subgroups of with and without aura also showed significant increase in flow velocity after photic stimulation in patients with aura. Similar finding were noted in study by Wolf et al. (2009), where they found an increased PSV in PCA after photic stimulation in migraine with aura patients. However in study by Nedeltchev et al. (2004), found that increased flow velocities were noted in both MCA and PCA in migraine patients after visual stimulationcompared to control group. Similar findings were noted in study by manal et al. (2017). It was observed that the altered cerebral vasoreactivity by estimating the flow velocities was difficult to detect in MCA as compared to PCA as MCA had a larger area of supply and smaller branches (Reinhard et al., 2012). In our study we found an increased flow systolic velocities in patient subgroup in PCA after photic stimulation more so in migraine with aura subgroup of patients.

Conclusion

There was increased cerebrovascular reactivity in patients with migraine. There was further increase in Cerebrovascular reactivity in patients with aura. There was maladaptation of cerebrovascular reactivity in migraineurs, more so in patients with aura causing activation of the trigeminovascular system causing change in neurovascular homeostasis thereby inducing migraine attacks. Transcranial doppler can be useful tool to assess the cerebrovascular reactivity in migraineurs. This study demonstrates increased cerebrovascular reactivity in patients of migraine with aura using photic PSV. Photic PSV along with other indices can be valuable tool to assess CVR in patients with migraine

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