Auditory Brainstem Evoked Responses In Migraine Patients
D Kaushal, S Sanjay Munjal, M Modi, N Panda

Citation

Abstract
INTRODUCTION:Migraine is a painful neurological condition and the pathogenesis of migraine is not completely understood. Some researchers are of opinion that cortex may be involved whereas others hold the brainstem responsible.AIM:The aim of the present study was to evaluate the brainstem auditory evoked potentials in patients with migraine.METHODOLOGY:25 patients in the age range of 10-45 years, diagnosed as having migraine (with or without aura) were taken as the study group. Out of these 25 subjects, 6 (4 males, 2 females) subjects reported headache during the testing period. Control group consisted of 25 healthy subjects in the age range of 10 to 45 years with no complaint of migraine. Brainstem auditory evoked potentials were recorded using insert ear phones.RESULTS:There was a significant difference between absolute latencies of study group and control group. Similarly, significant results were obtained for interpeak latencies between control and study group. It was observed that prolongation in interpeak latency was reported in those subjects who had an acute attack of migraine during ABR testing.CONCLUSION :It is concluded that there is an involvement of brainstem structures during migraine attack and this is supported by the prolongation of interpeak latencies of waves in ABER. Therefore, Auditory brainstem evoked responses can be used as an effective tool in making the neurophysiological evaluation of the auditory pathway which further plays an important role in the explanation of pathophysiology of migraine.

INTRODUCTION
Migraine is a painful neurological condition in which the most common symptom is an intense and disabling episodic headache. It is usually characterized by severe pain on one or both sides of head and accompanied by photophobia (hypersensitivity to light), phonophobia (hypersensitivity to sound) and nausea. Migraine is a frustrating chronic illness that is widespread in the population (10% diagnosed, 5% undiagnosed), with seriousness varying from a rare annoyance to a life-threatening daily experience. Three-fourths of adult migraine patients are female, although pre-pubertal migraine affects approximately equal numbers of boys and girls. There are four phases of migraine attack. These are:

1. The prodrome, which occurs hours or days before the headache.
2. The aura, which immediately precedes the headache.
3. The pain phase, or headache phase.
4. The postdrome.

* The diagnosis of migraine without aura, according to the International Headache Society, can be made according to the following criteria - 5 or more attacks, 4 hours to 3 days in duration, 2 or more of - unilateral location, pulsating quality, moderate to severe pain, aggravation by or avoidance of routine physical activity and 1 or more accompanying symptoms - nausea and/or vomiting, photophobia, phonophobia (“5, 4, 3, 2, 1 criteria”). For migraine with aura, only two attacks are required to justify the diagnosis.

Auditory brainstem evoked potentials (ABEPs) in non-invasive and reliable electrophysiological method to assess the function of brainstem structures travestied by auditory pathways. For detection of cerebral dysfunctions such as vertebrobasilar failure and transient ischemic attack which may involve the brainstem structures of the acoustic pathway, similar to migraine, the use ABEPs rather than VEPs has been preferred. Several studies have been
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conducted to explain the pathophysiology of migraine. Neurophysiological examination, especially auditory evoked potentials which enable us to make the neurophysiological evaluation of the auditory pathway play an important role in the explanation of pathophysiology of primary headaches, especially migraine. Studies shows that there was a significant prolongation of waves III and IV latencies of brainstem auditory evoked potentials in migraine patients [Zgorzalewicz M., 2005]. Moreover, there was a study in which sudden sensorineural hearing loss is reported in a patient during migraine attacks (A.F. Lipkins et al). Functional neuroimaging studies in patients with migraine during pain attacks had shown the activation of brainstem.

A study was conducted in which auditory brainstem responses were seen in pediatric population during the attack and asymptomatic period of migraine. It was found that ABR waves did not exceed clinical norms in migraine patients in headache-free period. But, important effects on ABR waveform latencies were detected during the attack. Peak latencies of wave V and interpeak latencies of I-V were prolonged during the attack in migraineurs on the left. The side of latency prolongation was not affected by the side of headache. When these parameters were separately compared for gender, they were prolonged in boys during the attack in migraineurs; however in girls, while there was statistically significant difference at interpeak latencies of I-V, no significant difference was noted at peak latencies of wave V. Results indicated a transient impairment of the auditory brainstem function during the headache in pediatric migraine patients (Firat Y. et al, 2006).

Another study also concluded that in migraine patients (including basilar migraine) peak latencies were pathologically delayed. Statistical analysis did not show any significant difference in regard to peak latencies and interpeak latencies between migraine patients and controls. However, side differences of all peaks (except peak IV, VI) were significantly increased in migraine patients as compared to controls. Results indicated a slight but permanent impairment of brainstem function in migraine (Schlake H.P. et al, 1990).

The discovery of a mutation in a brain calcium-channel gene in families with hemiplegic migraine and in families with episodic vertigo and ataxia suggests a possible mechanism for neurologic symptoms in patients with more common varieties of migraine. A defective calcium channel, primarily expressed in the brain and inner ear, could lead to reversible hair cell depolarization and auditory and vestibular symptoms. This hypothesis is currently being investigated in other families with migraine headaches and neurotologic symptoms (Robert W. Baloh MD, 1997).

Studies suggest that brainstem structures were also involved in migraine (Kuritzky A et al, 1981). Available evidence suggests that migraine pain is one symptom of several to many disorders of the serotoninergic control system, a dual hormone-neurotransmitter with numerous types of receptors. “Serotonin is known as one of the most important neurotransmitters.” This amine structured neurotransmitter level is influenced in migraine. Plasma serotonin level is essentially decreased during migraine attacks. It is known that reserpine has an amine-releasing effect. In one study, migraine-like episodes were constituted in thirty-three guinea pigs by intraperitoneal reserpine administration. Then, the auditory brainstem evoked potentials were recorded. All absolute and interpeak latency values were initially increased at the second hour of reserpine administration and reached to the maximum values at third hour, and then gradually decreased up to twelfth hour. This result mainly reflects the brainstem involvement in migraine-like attack induced by reserpine administration. Subsequent latency parameters which were close to baseline values may be attributed to the fact that those changes were temporary and follow the variations in the serotonin levels.

OBJECTIVES OF THE STUDY
Not much of research has been undertaken to find the site of lesion for migraine. Some researchers are of opinion that cortex may be involved whereas others hold the brainstem responsible. The present study was undertaken to find a possible clue to the involvement of brainstem structures in migraine patients.

AIM
The aim of the present study was to evaluate the brainstem auditory evoked potentials in patients with migraine.

METHODOLOGY
25 patients in the age range of 10-45 years, diagnosed as having migraine (with or without aura) according to criteria of International Headache Society (IHS) were taken as the study group. Out of these 25 subjects, 6 (4 males, 2 females) subjects reported headache during the testing period. Control group consisted of 25 healthy subjects in the age range of 10 to 45 years with no complaint of migraine. Those subjects were included in the study group who had no history of head trauma, stroke, tumor or any other neurological complaints,
no history of ear problems (otorrhoea, otalgia, aural fullness, tinnitus), no history of hearing loss and pure tone average less than or equal to 25dBHL.

**INSTRUMENTATION**

Pure tone audiometer (MADSEN ORBITER 922) was used for determining the hearing threshold. Brainstem auditory evoked potentials were recorded using insert ear phones. Impedance audiometer (SIEMENS SD30) was used to rule out any middle ear pathology.

In the ABR findings, absolute latencies of I, III, V peaks and interpeak latency difference between I -III, III –V, I-V peaks were evaluated. The click stimuli was presented at 90 dBnHL and 70 dBnHL intensity levels with the click rate of 19.3/sec. The total numbers of sweeps were 1024. The mode of stimulation was monaural. Sweeps were acquired at alternating polarity only. Electrode montage was +ve or non-inverting electrode placed at vertex, -ve or inverting electrode was placed at mastoid and ground electrode was placed at forehead.

**STATISTICAL ANALYSIS**

The results obtained were subjected to statistical analysis in which mean, S.D. values were compared and unpaired t-test was applied.

**RESULTS AND DISCUSSION**

**Figure 1**

Table 1: RIGHT EAR- COMPARISON OF STUDY Vs CONTROL GROUP

<table>
<thead>
<tr>
<th>LATENCY (msec)</th>
<th>STUDY GROUP</th>
<th>CONTROL GROUP</th>
<th>t Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1.59</td>
<td>1.50</td>
<td>1.68*</td>
</tr>
<tr>
<td>III</td>
<td>3.81</td>
<td>3.57</td>
<td>3.80***</td>
</tr>
<tr>
<td>V</td>
<td>5.68</td>
<td>5.25</td>
<td>3.86***</td>
</tr>
<tr>
<td>I-III</td>
<td>2.22</td>
<td>2.09</td>
<td>2.53</td>
</tr>
<tr>
<td>III-V</td>
<td>1.86</td>
<td>1.77</td>
<td>1.83</td>
</tr>
<tr>
<td>I-V</td>
<td>4.08</td>
<td>3.84</td>
<td>3.56**</td>
</tr>
</tbody>
</table>

Table 1 shows the comparison of absolute latency & interpeak latency difference between study and control group for right ear. From the table it can be inferred that there is a significant difference between absolute latencies of study group and control group (p< 0.05).

Similarly, significant results are obtained for interpeak latencies between control and study group (p<0.05). However, no significant difference is observed between study and control group for III-V interpeak latency (p>0.05).

To find out the occurrence of ABR abnormalities in migraine patients, the following criterion is taken:

Wave I-III interpeak latency delay >= 2.4 msec
Wave III-V interpeak latency delay >= 2.2 msec
Wave I-V interpeak latency delay >= 4.4 msec

Results obtained are as follows:

In right ear, out of 25 subjects, only 4 (16%) have prolonged I-III interpeak latency, 2 (8%) have prolonged III-V latency and 3 subjects (12%) have prolonged I-V latency latency. Moreover, it is observed that prolongation in interpeak latency is reported in those subjects who had an acute attack of migraine during ABR testing.

**Figure 2**

Table 2: LEFT EAR- COMPARISON OF STUDY Vs CONTROL GROUP

<table>
<thead>
<tr>
<th>LATENCY (msec)</th>
<th>STUDY GROUP</th>
<th>CONTROL GROUP</th>
<th>t Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
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<td>5.25</td>
<td>3.86***</td>
</tr>
<tr>
<td>I-III</td>
<td>2.22</td>
<td>2.09</td>
<td>2.53</td>
</tr>
<tr>
<td>III-V</td>
<td>1.86</td>
<td>1.77</td>
<td>1.83</td>
</tr>
<tr>
<td>I-V</td>
<td>4.08</td>
<td>3.84</td>
<td>3.56**</td>
</tr>
</tbody>
</table>

Table 2 shows the comparison of mean of absolute latencies and interpeak latencies difference between study and control group for left ear. From the table it can be inferred that there is a significant difference between absolute latencies of study group and control group (p<0.05).

Similarly, significant results are obtained for interpeak latencies between control and study group (p<0.05). However, no significant difference is observed between study and control group for III-V interpeak latency (p>0.05).

To find out the occurrence of ABR abnormalities in migraine patients, the following criterion is taken:

Wave I-III interpeak latency delay >= 2.4 msec
Wave III-V interpeak latency delay >= 2.2 msec
Wave I-V interpeak latency delay >= 4.4 msec

Results obtained are as follows:

In right ear, out of 25 subjects, only 4 (16%) have prolonged I-III interpeak latency, 2 (8%) have prolonged III-V latency and 3 subjects (12%) have prolonged I-V latency latency. Moreover, it is observed that prolongation in interpeak latency is reported in those subjects who had an acute attack of migraine during ABR testing.
Figure 3

Similarly, in left ear, out of 25 subjects, 3 (12%) has prolonged I-III interpeak latency, 1 (4%) has prolonged III-V and 1 (4%) subject has prolonged I-V latency.

It is also observed that prolongation of interpeak latencies in migraines is more in right ears than left ears.

Figure 4

In the present study, interpeak latencies of wave I-III & I-V is prolonged, but no prolongation is observed in interpeak latency of wave III-V. This result is supported by the results of previous studies in which interpeak latency of wave I-V was prolonged during the attack (Firat Y. et al, 2006). Similar results were obtained in another study in which prolongation of interpeak latencies I-III, III-V, I-V were reported in migraine patients (BayazitY, 2001).

The pathogenesis of migraine is not completely understood. Some researchers are of opinion that cortex may be involved whereas others hold the brainstem responsible. Functional neuroimaging studies in patients with migraine during pain attacks have shown the activation of brainstem. Present study also supports the involvement of brainstem structures during the migraine attack. Prolongation of interpeak latencies supports the brainstem activation theory of migraine. Moreover, it is suggested that the appearance of photophobia in patients with migraine may be related to the disturbances of brainstem functions (Zgorzalewicz M., 2005).

Recent discoveries have shed light on the neuronal events mediating both the aura and the headache phases of migraine, identifying a cerebral cortical origin of migraine aura, susceptibility to attacks based on cortical hyperexcitability, and headache originating in the trigeminovascular system and its central projections. Abnormal modulation of brain nociceptive systems, at first transient but becoming permanent with continuing illness and, predisposing to central sensitization, may explain the prolonged headache of the migraine attack and the shift of the migraine phenotype from episodic to chronic headache. Migraine attacks might also originate in abnormal nociceptive neuromodulator centers in the brainstem.

CONCLUSION

From the present study, it is concluded that there is an involvement of brainstem structures during migraine attack and this is supported by the prolongation of interpeak latencies of waves in ABER. Therefore, Auditory brainstem evoked responses (ABER) can be used as an effective tool in making the neurophysiological evaluation of the auditory pathway which further plays an important role in the explanation of pathophysiology of migraine.

References

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