

Original Research Article

Reversible alteration of brainstem auditory evoked potential in iron deficient anemic patients in response to treatment

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ABSTRACT

Background: Iron deficiency anemia is associated with central and peripheral nervous system disturbances. Iron is an essential component of brain growth, myelination, nerve impulse conduction, protein synthesis, hormone production, fundamental aspects of cellular energy metabolism and is involved in neurotransmitter synthesis including serotonin, norepinephrine and dopamine. Hence, its deficiency adversely affects motor performance, mental development as well as cognitive and behavioral functions. Since myelination is concerned with conduction in nerve fibers, iron deficiency potentially impairs neuronal transmission and leads to functional neurodeficit like hearing loss.

Methods: BAEP was recorded using RMS EMG EP MK2 machine in patients of iron deficiency anemia with haemoglobin less than 10.9 g/dl between 18-50 years of age who were followed up after 3 months of treatment and compared with 30 age and sex matched controls.

Results: BAEP absolute and interpeak latencies were prolonged in IDA patients as compared to the control groups which was reversible with iron replacement therapy.

Conclusions: Increased absolute and interpeak latencies of BAEP indicates impairment of auditory pathways in IDA patients. Thus, the electrophysiological study of BAEP provides an objective method for monitoring the function of CNS, especially the auditory function in iron deficiency anemia patients before and after iron replacement therapy. It is a non-invasive test for early diagnosis and therefore early treatment to prevent complications.

Keywords: Brainstem auditory evoked potential, Central Nervous system, Iron deficiency anemia

INTRODUCTION

Anemia is major public health problem affecting 1.6 billion people in both developing and developed countries with serious consequences like increased risk of maternal and childhood mortality.¹ According to the World Health Organization, iron deficiency anemia (IDA) resulted in 273,000 deaths in 2004, with 97% of the deaths occurring in low and middle-income countries.² Auditory dysfunction is an important consequence of iron deficiency anemia. Iron has a major role in myelin formation besides its involvement in the synthesis and

function of various neurotransmitters like serotonin, dopamine and catecholamines. For a rapid and maximum response, fast and correct conduction of impulses is required, which is achieved by formation of myelin sheath around neurons. In IDA, a subclinical involvement of auditory pathway in the brainstem occurs which is indicated by the increased absolute and interpeak latencies of the BAEP waves.³ Brainstem auditory evoked potentials (BAEPs) are the potentials recorded from the ear and the scalp in response to a brief auditory stimulation to assess the conduction through the auditory pathway up to midbrain. BAEPs comprise five or more

waves within 10 ms of the stimulus.⁴ It is described in terms of duration of onset of response.⁵

METHODS

The present, prospective randomized study was conducted in the Department of Physiology in collaboration with the Department of Medicine at Pt. B.D. Sharma PGIMS, Rohtak. Ethical clearance was taken from the ethical committee of Pt. B.D. Sharma PGIMS, Rohtak before the start of the research activity.

A written consent was taken from all the patients enrolled in the study after explaining the method of study in their own language. This study was planned to find out the response to iron replacement therapy and the correlation between hemoglobin and iron profile and BAEP parameters both pre and post treatment.

The subjects were divided into two groups:

Group 1

30 newly diagnosed cases of iron deficiency anemia of either sex of age group of 18-55 years before and after 3 months of iron therapy.

Group 2

30 age and sex matched controls.

BAEP recording

Subjects were put at ease and made to lie down, relaxed on a couch in a quiet room with low levels of electro-

acoustic interference. During monaural testing, it was important to mask contralateral ear to avoid recording a crossover response from inadvertent stimulation. Both ears were tested individually using shielded headphones. Two reference electrodes were attached to left and right mastoid designated as A1 and A2 respectively. One active electrode was attached on vertex labelled as Cz and one as ground electrode to forehead termed as Fz. All the electrodes were plugged to a junction-box and skin to electrode impedance had been monitored and kept below 5k Ohms. Absolute peak latencies of waves I, II, III, IV and V together with interpeak latencies of I-III, I-V and III-V were recorded.

BAEP settings

Click stimuli - 70 dB above patients hearing threshold for each ear, White noise at 30dB below intensity of stimulation click as a masking stimulus and a total of 2000 stimuli given by passing 0.1 ms pulses with Rate of stimulation - 10/sec.⁶

RESULTS

BAEP latencies of all absolute and interpeak waves of both ears decreased in response to iron replacement therapy after 3 months. Student's paired t-test was used for statistical analysis.

Statistically significant improvement was observed in wave I of left ear after 3 months of iron replacement therapy in anemic patients ($p < 0.01$). No statistically significant differences were observed for interpeak latencies of both ears in between pre-treatment cases and post-treatment cases ($p > 0.05$).

Table 1: Pre-treatment cases versus controls values on both sides.

		Controls					
		rt	left	Pre right	left	Post- right	left
Absolute Latency (ms)	I	1.47±0.4	1.51±0.38	1.65±0.33	1.80±0.38	1.58±0.36	1.54±0.33
	II	2.57±0.44	2.65±0.44	2.73±0.04	2.84±0.051	2.72±0.37	2.63±0.36
	III	3.63±0.45	3.52±0.63	3.66±0.67	3.84±0.73	3.65±0.41	3.64±0.43
	IV	4.58±0.55	4.67±0.69	4.68±0.55	4.9±0.88	4.56±0.63	4.73±0.58
	V	5.61±0.76	5.61±0.81	5.88±0.73	5.81±1.01	5.83±0.75	5.64±0.81
Interpeak Latency (ms)	I-III	1.98±0.66	2.00±0.57	2.15±0.55	2.14±0.85	2.10±0.55	2.09±0.46
	I-V	4.10±0.83	4.01±1.00	4.16±0.82	4.11±0.77	4.11±0.87	4.09±0.77
	III-V	2.01±0.63	1.97±0.53	2.09±0.55	2.12±0.53	2.05±0.58	2.05±0.47

Pre-treatment cases versus controls values on both sides: P-value was found to be more significant for wave I on left side in pre-treatment cases as compared to controls. Pre-treatment versus Post-treatment values on both sides: P-value was found to be significant for wave I on left side side in pre-treatment cases as compared to post-treatment cases.

DISCUSSION

In the current study there was a prolongation of all absolute and inter-peak latencies of both ears in iron deficient anemic patients. Our findings are consistent with those of Shankar et al and Cankaya et al. Kurekci et al, Algarin et al and Khalifa et al also observed similar

findings.⁷⁻¹¹ Cankaya et al showed significantly prolonged waves I, V and Interpeak latencies III-V in children between and 6 months of age.⁸ Kurekci et al showed there were slight decreases in latencies measured after the study, though not significant, when compared to the pre-treatment values.⁹ Algarin et al showed IDA children had

significantly longer latencies for all waves and all wave interpeak intervals except interval I–III.¹⁰

There were no differences in amplitude. In the present study, we have incorporated the effect of iron replacement therapy to study the changes in BAEP latencies in such patients. In the current study, statistically significant difference was observed in wave I of left ear in between cases and controls ($p < 0.01$). Statistically significant improvement was observed in wave I of left ear after 3 months of iron replacement therapy in anaemic patients ($p < 0.01$). The prolonged BAEP latencies in iron deficient anemic patients were reversible to a great extent with iron replacement therapy.

The findings in the present study of prolonged latencies and interpeak latencies in all waves in patients differed than in controls and denote the generalized affection of the ascending auditory pathways located in the brainstem (cochlear nuclei, superior olivary complex) and in the midbrain (lateral lemniscus and inferior colliculus).

These effects noted on ABR components could be attributed to the ischemic and thrombotic events associated with iron deficiency as iron deficiency causes thrombocytosis, hypercoagulable state and tissue hypoxia.⁹

Hearing abnormalities caused by iron deficiency anemia are best demonstrated by recording brainstem auditory evoked potentials (BAEPs). The severity of CNS dysfunction depends upon duration and degree of iron deficiency. Hence, electrophysiological and clinical improvement is seen in such patients after iron replacement therapy.^{12,13}

CONCLUSION

The electrophysiological study of BAEP provides an objective method for monitoring the function of CNS, especially the auditory function in iron deficiency anemia patients before and after iron replacement therapy. This neurophysiologic parameter permits quantization of the effects of iron deficiency anemia on the auditory pathway and the extent and rate of response to iron replacement therapy.

Thus, we can conclude that BAEP is a useful non-invasive tool for early detection of subclinical auditory dysfunction and in follow up of patients with appropriate dose and duration of iron replacement therapy.

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