On the Auditory Transmission using Brainstem Evoked Response Audiometry in Indian Women with Iron Deficiency Anemia

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ABSTRACT

Iron deficiency anemia is a common nutritional disorder prevalent in many developing and underdeveloped countries. It affects various physiological aspects that have been vastly explored by researchers during developmental and non-developmental phases. The anemic status due to iron deficiency possibly leads to various neurodeficits and functional impairment. Brainstem evoked response audiometry (BERA) is an objective electrophysiological method used for assessing the transmission in the auditory pathways from the auditory nerve to the brainstem. Since iron deficiency anemia is widespread in women belonging to reproductive age, the present study aims to explore the impact of this type of anemia on hearing. The study included 30 anemic adult females belonging to the age group 18-30 years and 30 age matched controls. Hemoglobin and serum ferritin levels were investigated to evaluate the anemic status. BERA was performed on them to assess the auditory transmission. Results were compared between two groups by unpaired Student's t-test. A p value < 0.05 was considered significant. Mild increase in absolute latencies of wave I, III, V and mild increase inter-peak latencies of waves I – III, III – V and I-V in anemic group when compared to healthy controls, which was not statistically significant. Iron deficiency anemia may possibly effect the impulse transmission in auditory pathway, which may lead to sensorineural hearing loss in women.

KEY WORDS: ANAEMIA, NUTRITIONAL ANEMIA, ADULT FEMALES, EVOKED POTENTIALS, DEAFNESS.

INTRODUCTION

Anemia is a major health problem present globally affecting 1.6 billion people which is estimated to be 24.8% of the population, of which iron deficiency is a major contributing factor. The WHO estimates that Iron Deficiency Anemia (IDA) affects 30% of non-pregnant women of reproductive age and 42% of pregnant women. Women in developing countries are more susceptible to this deficiency due to low dietary intake, menstrual blood loss, and increased demand during pregnancy and lactation. National Family Health Survey (NFHS)-4 done in India during the year 2015-16 shows a prevalence of IDA in 53% of women belonging to the age group of 15-49 years (Alecia 2014).

According to WHO, IDA in non-pregnant adult females is blood hemoglobin <12 g/dl and serum ferritin <15 ng/ml. Iron is not only required during early developmental stages for normal brain growth but also plays an important role in later part of life for the maintenance of various metabolic activities and physiological functions. Besides iron having a key role in hemoglobin synthesis, it is required for non-hematological functions by nervous system during development (in-utero, infancy and childhood). Myelin synthesis, development of oligodendrocytes, neurogenesis, synthesis of neurotransmitters like dopamine, serotonin, catecholamines and GABA, all are iron dependent.

Researchers have found that iron is required during non-developmental phases of life as well. The uptake of iron by the brain lasts throughout the life and is utilized by the oligodendrocytes for formation and maintenance of myelin. Since myelin is involved in conduction in the nerve fibres, iron deficiency anemia which is a severe form of iron deficiency may be associated with alteration in brainstem auditory evoked potentials. BERA is used to assess the auditory transmission i.e generation and conduction of impulse in the auditory pathway. BERA represents the progressive activation of different levels of the auditory pathway consisting of I – V waves.

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Waves I & II arises from cochlear nerve, wave III from Cochlear Nucleus, wave IV from Superior Olivary Nucleus and wave V from Lateral Lemniscus. Latency of Wave I indicates peripheral transmission and wave III and V indicates brainstem transmission of auditory impulses. The inter peak latency between wave I-V depicts conduction time and is an index of central nervous system development. BERA can be used extensively to identify subclinical lesions associated with various demyelinating diseases and post hypoxic damage. Hence, we undertook the present study to explore whether iron deficiency anemia affects the brainstem auditory evoked potential and in turn on hearing in adult life.

MATERIAL AND METHODS

The study was conducted in the Central Neuro-Physiology lab of Acharya Vinoba Bhave Rural hospital and teaching institute, Jawaharlal Nehru Medical College, Wardha.

The cases (30) included females in the age group of 18-30 years whose blood hemoglobin level < 12g/dl and serum ferritin < 15 µg/L. The comparison group (30) (Normal females without IDA- non anemic) were age matched females with normal blood hemoglobin and Serum Ferritin levels. i.e hemoglobin levels > 12 g/dl and Serum ferritin levels > 15 µg/L (Algarin 2003).

The following was the exclusion criteria- Current pregnancy or pregnancy within the previous year, current lactation, hormonal contraceptive use, irregular menses, current blood donation, pre-existing ear diseases with clinical deafness, endocrine disorders (e.g: Diabetes Mellitus, Thyroid dysfunction), Neurological diseases and other types of anemia (Biacabe et al., 2001).

Table 1. Age & hematological parameters of anemic & non-anemic females.

Study Parameters	Cases (30 N) mean±SD	Controls (30 N) mean±SD
Age (years)	25.24±1.6	25.07±1.2
Hemoglobin (gm/dl)	10.90±2.14	12.56±0.80
Serum ferritin (µg/L)	12.75±0.62	24.27±1.12

Table 2. Absolute latencies of waves I, III & V of anemic & non-anemic females.

Absolute Latencies (ms)	Cases mean±SD	Controls mean±SD
Wave I	1.84±0.23	1.62±0.31
Wave III	3.74±0.26	3.46±0.24
Wave V	5.70±.56	5.53±0.30

*p <0.05

After undergoing complete medical history and clinical examination, the suitable cases and controls were subjected to hematological evaluation and BERA recording. Blood Hemoglobin concentration was estimated using automatic Coulter method and Serum Ferritin estimation was done by ELISA (VITROS 5600 (ICSH)). BERA was recorded using Neuron Spectrum-5, Neurosoft Chroma (Russia). BERA is an evoked potential generated by a brief click transmitted from an acoustic transducer in the form of an insert earphone or headphone. The elicited waveform response is measured by surface electrodes typically placed at the vertex of the scalp and mastoid. The waveform peaks are labeled I-V. These waveforms normally occur within a 10-millisecond time period after a click stimulus presented at high intensities (70 dB normal hearing level [nHL]). The following parameters were recorded - absolute latencies of wave I, II, III, IV and V with inter-peak latencies of I-III and III-V, I-V (Beard et al., 1993).

Statistical Analysis: Significance of difference in the mean values of different parameters in two groups was assessed by Student's "t" test and p-value < 0.05 was considered to be significant. All the values were expressed as mean and 1 standard deviation. Calculations were done using SPSS (version 18) and Microsoft Excel software (Chung et al., 2014).

RESULTS AND DISCUSSION

Total 60 subjects were included in this study, among which, 30 were anemic cases and 30 were non-anemic controls. Values of all the study parameters of the anemic cases and non - anemic controls are given in the Table 1 (Falkingham et al., 2010).

Table 3. Inter-peak latencies of anemic & non-anemic females.

Inter-peak latencies (ms)	Cases mean±SD	Controls mean±SD
I-III	2.38 ±0.23	2.12 ±2.43
III-V	2.40± 0.49	2.32± 0.31
I-V	3.56± 0.48	3.11 ± 0.12

*p <0.05

The absolute latencies (Table 2) and inter-peak latencies (Table 3) of the anemic females were prolonged when compared to non-anemic females but were not statistically significant (p >0.05) (Ferraro & Durrant 1994).

Anemia, particularly iron deficiency anemia is a prevalent disorder either due reduced intake or increased loss. 53% of Indian women belonging to reproductive age group suffer from Iron deficiency anemia. The major cause of anemia in women is due to nutritional deficiency, increased requirement during pregnancy

and lactation, loss during menstruation and parturition, intake of phytates. Iron deficiency anemia is a grave form of iron deficiency and this deficiency has an impact on various physiological functions. BERA is a noninvasive electrophysiological tool to assess the auditory transmission. The different structures of the auditory pathway are stimulated and recorded from the scalp and mastoid using electrodes. The wave I is generated from cochlea, wave III is generated from cochlear nucleus and wave V is generated from lateral lemniscus and inferior colliculus (Hill 1989) (Lozano et al., 2019; Lozoff 2007; McLean et al., 2019; Shankar et al., 2000; Ortiz et al., 2004; Ramit & Das 2016).

Alteration in the process of impulse transmission leads to prolonging of absolute latencies (I,III,V) and inter-peak latencies (I-III, III-V, I-V), found in disorders like demyelination, ischemia & degeneration leading to hearing impairment. In our study the absolute and inter-peak latencies were prolonged in anemic women when compared to non-anemic women, however the difference was not statistically significant. Similar evidences were demonstrated N. Shankar et al. where the absolute & inter-peak latencies were increased in anemic children. Ramit Dey studied 40 subjects with IDA in the age group of 12-16 years and found increased absolute latencies in the waves I, III & V and also increased inter-peak latencies indicating delayed transmission in auditory pathway when compared to non-anemic subjects (Schieffer et al., 2017; Starr 1994; Stockard et al., 1993).

Algerin C et al. reported significantly prolonged absolute and inter-peak latencies in children. In a cohort study done in children the prevalence of hearing loss was 3.0% in children with IDA and 1.7% in those without IDA. Similar studies in the U.S.A and Taiwan in adult population has suggested IDA may be a significant causal factor for sensorineural hearing loss. The possible mechanisms explained for neuro-deficits in IDA are that since iron is an important cofactor required for DNA synthesis and neurotransmitter metabolism, its low levels may hamper normal physiological functioning; dependence of oligodendrocytes on iron for myelination hampers impulse transmission and low hemoglobin in anemia leads to reduced oxygen delivery leading to increased ischemia in these tissues (Wang et al., 2020).

Since there is data mounting regarding the effects of IDA during developmental stages like infancy, childhood and adolescence; the present study focuses on non-developmental effects of IDA in adult females. Because of high prevalence of IDA in developing countries these females are vulnerable to deleterious effects of IDA particularly auditory response. Further research studies involving larger population, correlating the different waves of BERA with different grades of anemia and prospective studies to demonstrate the effect of iron supplementation on BERA are required for confirmatory conclusions.

CONCLUSION

The findings in our are indicative of a neurological impairment consequent to IDA though, perhaps, the significance could not be revealed as women showed only mild anemia and may be greater numbers need to be studied. Correction of anemia is extremely important as persistence of anemia may lead to sensorineural hearing loss in women.

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