Effect of hypochromic microcytic anaemia on hearing in the adolescent age group in India, as assessed by Brainstem Evoked Response Audiometry (BERA)

Ramit Dey, Piyali Das*, Subhradev Biswas, Goutam Banerjee, Sharmistha Ghoshal and Debasish Pramanik

Department of Physiology, Bankura Sammilani Medical College, Kenduadihi, Bankura, West Bengal 722101 India

*Correspondence Info:
Dr. Piyali Das
Associate Professor
Department of Physiology,
Bankura Sammilani Medical College,
Kenduadihi, Bankura, West Bengal 722101 India
E-mail: dr.piyali@yahoo.com

Abstract
Objectives: Anaemia mainly iron deficiency (hypochromic, microcytic) type is one of the major health problems in the developing countries like India. Because of the increased nutritional demand, anaemia is often prevalent in the adolescent age group which may further lead to various neurodeficits and functional impairment. But whether this type of anaemia in the said age group has any impact on the auditory impulse transmission has been inadequately explored, especially in India. Therefore, in the present study, attempt was made to verify whether hypochromic microcytic anaemia has any influence on functional integrity of auditory pathway as reflected by Brainstem Evoked Response Audiometry (BERA).

Methods: We included 40 adolescent subjects (12-16 years of age) with hypochromic microcytic anaemia from both sexes and 40 age sex matched non anaemic control and BERA recording was done in them. Findings were compared between two groups by unpaired Student’s t-test. Correlation was checked by Pearson’s co-efficient of correlation (r-value). P value< 0.05 was considered to be significant.

Results: We found increased absolute latencies of wave I, III, V as well as increased inter-peak latencies of waves I – III, III – V and I-V in anaemic group. Haemoglobin concentration showed significant negative correlation with I-III inter-peak latency as well as absolute latency of wave I.

Conclusion: Study concludes that hypochromic microcytic anaemia may have deleterious effect on impulse transmission in auditory pathway in the adolescent age group in India. Degree of affection may have direct association with severity of anaemia.

Keywords: Anaemia, deafness, iron deficiency.

1. Introduction
Anaemia mainly due to iron deficiency is the commonest nutritional disorder in developing countries like India. [1] As in other tissues, iron is an essential element and an important nutrient of the brain playing a major role in myelin formation [2]. It is also involved in the synthesis and function of various neurotransmitters namely dopamine, serotonin, catecholamine and possibly GABA [3,4]. There are data that indicate that iron uptake into the brain is maximal during the period of rapid brain growth [5] which coincides with the peak of myelination [6]. Since myelination is concerned with the conduction in nerve fibers, it is probable that, iron deficiency potentially impairs neuronal transmission and lead to functional neurodeficit like hearing loss. But whether the neurodeffict is actually due to iron deficiency or the effects of anaemia itself is grossly debated. Moreover, data pertaining to Indian population in this regard is quite insufficient. With this background, in the present study we tried to explore whether hypochromic microcytic anaemia which is the most prevalent anaemia in India, has any impact on auditory transmission, in the pubertal age group (12-16 years), as evidenced by recordings of BERA.

2. Material and Methods
It was a hospital based cross sectional study. Patients attending the General OPD of Bankura Sammilani Medical College, Bankura, with 12-16 years of age, from both sexes, were screened first by medical history and clinical examination for anaemia. Suitable candidates were subjected to haematological examination by PE-6800 Fully Auto Hematology Analyzer (Aspen Diagnostics Pvt Ltd). Those who were selected by haematological examination were undergone BERA recording on ALERON 401 RMS-ENG-
EP-MARK II machine. Controls were selected from healthy community volunteers on the basis of history, clinical examination and haematological assessment. Informed consent was taken from each subject as well as their legal guardians and the entire study was done with due permission from Institutional Ethics Committee following prescribed ethical standards [Institutional Ethics Committee permission letter No. PR-HC/6-119/87(53)].

While selecting cases and controls, following inclusion and exclusion criteria were taken into account:

2.1 Inclusion criteria

Children of 12-16 years of age, from both sexes, diagnosed to have hypochromic microcytic anaemia as per WHO criteria for anaemia diagnosis (Hb<12gm/dL, MCV<77fL, MCHC<32gm/dL) [7] and with no other mental or physical disorder were included as cases. Age sex matched, non anaemic, healthy volunteers with no history of mental or physical disorder were recruited as controls.

2.2 Exclusion criteria

Subjects with clinical evidence of any neurological deficit or those having concomitant systemic illness like diabetes mellitus, uremia, leprosy, malignancy, any type of peripheral neuropathy, history of intake of any neuro-toxic drug, or history of any traumatic lesion possibly affecting brainstem functions, pre-existing ear diseases with clinical deafness were excluded from the study. Known cases or subjects with family history of hereditary anaemia like thalassemia, sideroblastic anaemia which are other possible causes of hypochromic microcytic anaemia were also excluded. Diagnosed cases of lead poisoning were also excluded for similar reason.

2.3 Study parameters

Anthropometric parameters like height, weight, hematologic parameter like haemoglobin concentration, MCV, MCHC, electrophysiologic parameter like absolute latencies of wave I, III and V with inter-peak latencies of I-III and III-V, I-V and amplitude ratio of wave V and I were explored in the study.

2.4 procedure of BERA in brief:

We followed standard technique for recording of BERA [8].Recording was carried out in a quiet and dimly lit room with subject in supine position. Metallic surface electrodes were placed at the vertex (Cz), both ear lobes (AI and Ac) and forehead (ground). Monaural auditory stimulus consisting of rarefaction clicks of 100 μs square pulse were delivered through an electrically shielded earphone at a rate of 11.1/ second. Contralateral ear was masked with pure white noise 40 deci Bell (dB) below that of the BERA stimulus. A band pass of 10- 3000 Hz was used to filter out undesirable frequencies in the surrounding. Responses to 4000 click presentations were averaged for 10 milli second (msec). Wave forms obtained at 60 dB above the sensation threshold for that ear were recorded for analysis.

2.5 Statistical calculation

Significance of difference in the mean values of different parameters in two groups was assessed by Student’s “t” test and Correlation was checked by Pearson’s co-efficient of correlation (r-value). 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.

3. Result

Total 80 subjects were included in this study, among which, 40 were anemic cases and 40 were non-anemic control. Values of all the study parameters in anemic cases and non – anemic controls are given in the following table.

Table 1: Values of General Parameters in cases and controls

<table>
<thead>
<tr>
<th>Study Parameters</th>
<th>Cases (N=40)</th>
<th>Controls (N=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (Yrs.)</td>
<td>14.18 ± 1.6</td>
<td>13.46±1.93</td>
</tr>
<tr>
<td>Male:Female</td>
<td>28:12</td>
<td>30:10</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>42.59 ± 4.59</td>
<td>42.22 ± 3.95</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>153.71±5.77</td>
<td>151.31±4.08</td>
</tr>
<tr>
<td>Haemoglobin (gm/dl)</td>
<td>8.5±1.07</td>
<td>13.93±1.62*</td>
</tr>
<tr>
<td>MCV (fL)</td>
<td>75±1.22</td>
<td>86±1.2*</td>
</tr>
<tr>
<td>MCHC (gm/dL)</td>
<td>27.5±1.2</td>
<td>32.5 ±0.5*</td>
</tr>
</tbody>
</table>

*p<0.05, statistically significant

3.1 BERA findings:

Total 40 cases and 40 controls were subjected to the Brainstem Evoked Response Audiometry. We found increased absolute latencies of wave I, III, V as well as increased inter-peak latencies of I – III wave and III – V and I-V wave in anaemic group. The following tables (table 2 and 3) show the comparative analysis of BERA finding between cases and controls.

Table 2: Table showing absolute latencies of wave I, III and V in cases and controls

<table>
<thead>
<tr>
<th>Absolute Latencies</th>
<th>Wave forms</th>
<th>Cases</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wave I</td>
<td>1.88±0.27</td>
<td>1.68±0.3</td>
<td>p&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>Wave III</td>
<td>3.7±0.26</td>
<td>3.49±0.26</td>
<td>P&lt;0.03</td>
<td></td>
</tr>
<tr>
<td>Wave V</td>
<td>5.74±.56</td>
<td>5.14±0.42</td>
<td>P&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Table showing Interpeak latencies of waves I-III, III-V and I-V in cases and controls

<table>
<thead>
<tr>
<th>Interpeak Latencies</th>
<th>Wave forms</th>
<th>Cases</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-III</td>
<td>2.1±0.26</td>
<td>1.75±0.54</td>
<td>P&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>III-V</td>
<td>2.17±0.31</td>
<td>1.95±0.34</td>
<td>P&lt;0.05</td>
<td></td>
</tr>
<tr>
<td>I-V</td>
<td>4.21±0.29</td>
<td>3.96±0.51</td>
<td>P&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

Among the blood parameters, Haemoglobin concentration showed significant negative correlation with absolute latency of wave I and inter-peak latency of I-III. Absolute latency of wave V and inter peak latencies of I-V, III-V were also found to have negative correlation with Haemoglobin concentration, though not statistically significant. Amplitude ratio of V:I did not show significant difference in cases and controls.
Figure 1 and 2 are showing BERA tracing of an anemic and an age sex matched non anaemic subject respectively at a specific decibel of acoustic stimulus where obvious prolongation of absolute latencies wave I, III and V and inter-peak latencies of wave I-III, III-V and I-V in anaemic subject is being seen.

**Figure 1: BERA tracing of an anaemic subject**

**Figure 2: BERA tracing of a non-anaemic subject**

4. **Discussion**

Anaemia mainly that due to iron deficiency is still a major health problem in country like India. Adolescence being a period of rapid growth, weight gain and blood volume expansion, overt anaemia is precipitated even by marginal iron deficiency during this period with adverse consequences. Not many studies are available on adolescent anaemia in India specially its consequences on various systems. In BERA, which is an objective electrophysiological recording, an evoked potential is created by the stimulating different structures of the auditory pathway and recorded using electrodes placed on the scalp. The resultant output is a series of waves that occur within 10 milliseconds of the stimulus presentation. The most consistent and clinically relevant wave forms of BERA include wave I, III and V which are generated from cochlea and distal portion of the auditory nerve, cochlear nucleus and lateral lemniscus and inferior colliculus respectively [9]. Absolute as well as interpeak latencies of the above wave forms are prolonged in a variety of disorders, including focal damage (demyelination, ischemia, tumors), or diffuse problems (degenerative disorders, posthypoxic damage, etc.) [10].

Our study revealed a significant prolongation of absolute latencies of wave I, III and V and interpeak latencies of I-III, III-V and I-V in hypochromic microcytic anaemia. Our finding is corroborative with that of Amin SB et al [11] who conducted a prospective study with latent iron deficiency in foetus in utero and auditory impairment in early infancy and found a significant latency defect in the said wave forms in iron deficiency. This may be due the fact that iron deficiency disrupts normal development of the auditory nerve and myelination process and thereby results in altered conduction velocity. [12] Amplitude ratios between wave V and I were not found to be significantly different in cases from controls. Finding is also supported by Algarin C et al. [13] who also found only differences in latency but not the amplitude in iron deficiency. Neurodeficit in iron deficiency may be due to lack of iron itself which is essentially needed by oligodendroglia for myelination and also as a co factor for various neuro transmitter in CNS like dopamine, serotonin etc. involved in hearing pathway also [14,13].

Anaemia is resulted only after long term or severe iron deficiency. Erythropenia with decreased mean cell volume and decreased haemoglobin synthesis are the consequences of progressive iron deficiency. Many of the previous studies addressed the problem of lower mental and motor scores in severe iron deficiency anaemia [15] we also found a negative correlation of haemoglobin concentration with absolute latency of wave I and interpeak latency of I-III which signifies that degree of affection may have direct association with severity of anaemia. Our finding is in agreement with Shankar et al [16]. In iron deficiency anaemia, apart from iron deficiency, effect of anaemia itself may hamper neuronal transmission. Lack of oxygen supply may have powerful consequences at the cellular, tissue and organ level. It can alter cellular transcription factor and thus affect protein synthesis. Long term oxygen deficiency may result in cell and tissue death [17]. All these mechanisms may ultimately lead to depression of neuronal activity specially in the brain in anaemia. All these facts may justify our study finding of increased absolute latencies of wave I, III and V and interpeak latencies of I-III, III-V and I-V in subjects with microcytic, hypochromic anaemia than their non-anaemic controls. This may suggest that anaemia specifically the
hypochromic microcytic type may affect hearing activity in adolescent age group. As this type of anaemia is mostly due to iron deficiency in this age group, supplementation with iron may be thought of to prevent the hearing impairment in suitable cases.

5. Conclusion

Our study concludes that hypochromic microcytic anaemia may affect the auditory transmission in adolescent age group as evidenced by recordings of BERA. Degree of affection may have direct association with severity of anaemia. Correction of anaemia may therefore have potential to reverse the situation and protect this valuable age group from future handicap.

References


