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EFFECT OF IRON DEFICIENCY ANEMIA ON AUDIOVISUAL REACTION TIME IN ADOLESCENT GIRLS

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Abstract : Adolescent girls are at high risk of developing iron deficiency because of increased iron demands during puberty, menstrual losses, and limited dietary iron intake.

This study was carried out to demonstrate the effects of Iron Deficiency Anemia on Audiovisual reaction time in adolescent girls. Adolescent girls between 17-19 years of age with similar socioeconomic background were recruited from college of nursing for the study. They were all screened and categorized into two groups depending on their haemoglobin status. Students having Hb > 12 gm/dl formed the control group i.e. Group I (n=30). All students having Hb < 12 gm/dl and S.Ferritin < 12 µg/dl formed group II i.e. iron deficient anemic (IDA) group. The following haematological parameters were studied Hemoglobin (Hb), MCV, MCH, MCHC (using Sysmex kx-21 Autoanalyser), Serum.Iron, TIBC (Spectrophotometry), Serum.Ferritin (ELISA). Auditory and Visual reaction time were measured by reaction time instrument supplied by Medicaid system, chandigarh. The mean Hb levels in Group I was 12.93 $\pm$ 0.86 and Group II was 10.08±0.51 ($P<0.001$). The MCV, MCH, MCHC, S. Iron, S. Ferritin was also significantly less in group II as compared to group I ($P<0.001$). TIBC was significantly more in group II as compared to group I ($P<0.001$). Results showed that both ART and VRT were significantly increased ($P<0.001$) in iron deficient adolescents suggesting a deterioration in sensorimotor performance in anemics.

Key words : iron deficiency anemia reaction time auditory visual

INTRODUCTION

Iron deficiency (ID) is the single most common and highly preventable nutritional deficiency in the world. It is a major cause of anemia, affecting more than 2 billion people world-wide (1). Studies in India show that 65% infant and toddlers, 60% 1-6 yrs of age, 88% adolescent's girls and 85% pregnant women are anemic. The commonest form is iron deficiency anemia (2).

Adolescent girls are at highest risk of developing iron deficiency and iron deficiency

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anemia (IDA) because of their greater physiologic requirements, combined with increased menstrual losses and poor dietary intake.

Iron is necessary for many functions in the body like normal myelination (3), neuronal metabolic activity (4) and synthesis of neurotransmitters (dopamine, serotonin, GABA). Decreased attentiveness has been reported in the study on iron deficient children (5) and adolescents (6).

Researchers have documented altered transmission in auditory and visual systems in infants with ID (7, 8), similar measurements are lacking in adolescents suffering from iron deficiency anemia.

The present study was undertaken to study the effects of iron deficiency anemia on auditory and visual reaction time in adolescent girls. Reaction time means time taken by an individual to react to external stimulus. It provides an indirect index of processing capability of the central nervous system and also a simple means of determining sensorimotor performances (9).

MATERIALS AND METHODS

The present study was carried out in the Department of Physiology in association with Department of Pathology, Lady Hardinge Medical College and Associated Hospitals, New Delhi.

Apparently healthy adolescent girls (10) between the ages of 17-19 years- belonging to similar socioeconomic status were recruited for the study from the college of nursing. They were all screened and categorized into two groups depending on their haemoglobin status. Students having Hb > 12 gm/dl formed the control group i.e. Group I (n=30). Students with Hb < 12 gm/dl were further screened for S.Ferritin levels. All students having Hb < 12 gm/dl and S.Ferritin < 12 µg/dl (11) formed group II i.e. iron deficient anemic (IDA) group.

Each subject underwent detailed history taking and thorough clinical assessment. Girls with history of any acute/chronic disease/infection, physical/mental illness, genetic disease, hearing or visual disorder, haemolytic anemia, history of blood transfusion, receiving iron supplementation within 1 month were excluded from the study.

The subjects were briefed about the study protocol and informed consent was taken. The clearance from the ethical committee of the institution was taken for the study.

Age and anthropometric parameters were noted.

The study was done during the Post menstrual phase of the menstrual cycle to avoid any alteration in their values due to premenstrual phase (9). The recordings were conducted at the same time of the day in the morning, about 2 hrs after light breakfast.

Haematological Parameters :

The haematological parameters that were investigated were Haemoglobin content, MCV, MCH, MCHC, peripheral Blood smear,

S. Ferritin, S. Iron, and Total Iron Binding Capacity (TIBC). The Hb, MCV, MCH and MCHC were done by the coulter (Sysmex KX-21) Auto analyser. Serum Ferritin was determined by using direct immunoenzymatic colorimetric determination (Biomeda, REF DKO039), S. Iron (Bio Systems-Spain), COD 11509 and S. Total Iron Binding Capacity (Bio Systems-Spain), COD 11554) were measured by Spectrophotometry.

Recording of Sensory Motor Functions:

Each subject was made familiar with the apparatus and the procedure to alleviate any fear or apprehension. ART and VRT were measured in a quiet room of Department of Physiology at LHMC, New Delhi. The ambient temperature maintained was 26±1°C. The tests were done with the subject sitting comfortably in a chair.

ART and VRT were measured by reaction time instrument supplied by Medicaid Systems (Chandigarh). This instrument is equipped with sensitive quartz clock which measures up to $1/10^{th}$ of a msec. Accuracy of this instrument is ± one digit. All the subjects were right handers and used their right hand to press the switch to stop the quartz clock of the apparatus. Before measuring VRT, each subject was asked to identify the flashing of yellow light. She was instructed to press the switch as soon as she saw the light. For VRT a soothing yellow light incorporated on the instrument was given. For measuring ART she was asked to concentrate on the sound signal produced and press the switch immediately. The sound signal was a continuous beep of 1 KHz on speaker. The intensity of the stimulus was same for both groups. To avoid the effect of lateralised stimulus, visual and auditory signals were given from the front of the subject. From the auto-display reaction time was noted. Three readings of each stimulus were noted after giving three practical trials and the lowest was taken as the reaction time (9).

Statistical analysis

Results were expressed as mean±S.D. Students't' test was used to compare the values between the two groups. Correlation between haematological parameters and reaction time was done using Pearson's Correlation. Adherence to 'P' values was followed.

RESULTS

There was no statistical difference between the age, height, weight and BMI of the two groups and hence they were comparable for the study (Table I).

Table II shows haematological values of the two groups. The mean haemoglobin level was 12.93±0.86 g/dL in control group and was 10.08±0.51 g/dL in group II. All the blood indices (MCV, MCH, and MCHC) were lower

TABLE I: Age, Anthropometric data & Body mass index (BMI) of the control and IDA group (mean±SD).

Parameters	*Group I (control) (n=30)*	*Group II (IDA) (n=30)*
Age (yrs)	18.07±0.58	18.07±0.52
Height (cm)	154.88±3.90	154.87±3.80
Weight (kg)	49.77±6.23	49.90±4.18
BMI (kg/m^2)	20.70±2.15	20.79±1.61

The differences between the two groups were not statistically significant.

TABLE II : Comparison of Haematological parameters and Iron status between the control and IDA group (mean±SD).

Parameters	*Group I (control) (n=30)*	*Group II (IDA) (n=30)*
Hematological		
Hb (gm/dl)	12.93±0.86	10.08±0.51**
MCV (fl)	86.98±4.09	76.89±3.07**
MCH (pg)	28.09±1.96	24.29±2.38**
MCHC (g/dl)	34.61±0.57	29.37±1.14**
Iron status		
S. Iron (µg/dl)	88.70±9.37	47.74±1.93**
S. Ferritin (ng/ml)	37.90±6.04	10.27±0.70**
TIBC (µg/dl)	256.30±2.49	478.20±48.57**

**P<0.001 - Highly significant.

in Group II thus confirming their anemic status. Table II also depicts iron status of both groups. Decreased S.Ferritin, S. Iron and increase in TIBC confirms that iron deficiency was the cause of the anemia in iron deficient anemic group.

In the present study, group II iron deficient anemic adolescents showed a significant increase in ART (225.97±20.26 msec) when compared to control iron replete group I (164.96±26.11 msec) – Table III. Similarly VRT was also more in Group II IDA (236.84±30.24 msec) as compared to the Group I control (209.08±12.00 msec) and the difference was highly significant P<0.001.

TABLE III : Showing comparison in the Auditory and Visual reaction time between Group I and Group II subjects (mean±SD).

Parameters	*Group I (control) (n=30)*	*Group II (IDA) (n=30)*
ART (msecs)	164.96±26.11	225.97±20.26**
VRT (msecs)	209.08±12.00	236.84±30.24**

**P<0.001 - Highly significant.

Further, a significant negative correlation (Table IV, V) of haemoglobin was observed with both auditory and visual reaction time. There was also a significant negative correlation of S.Ferritin with auditory reaction time (Table IV).

TABLE IV : Showing correlation of haemoglobin and serum ferritin with auditory reaction time between the two groups (n=30).

Parameters	*Group I (control)*		*Group II (IDA)*	
	r value	*p value*	*r value*	*p value*
Haemoglobin	–0.084	0.658	–0.841**	0.000
S. Ferritin	–0.126	0.505	–0.458*	0.011

**P<0.001 - Highly significant.
*P<0.05 - Significant.

TABLE V : Showing correlation of haemoglobin and S. Ferritin with visual reaction time between the two groups (n=30).

Parameters	*Group I (control)*		*Group II (IDA)*	
	r value	*p value*	*r value*	*p value*
Haemoglobin	–0.248	0.186	–0.543**	0.002
S. Ferritin	–0.050	0.794	–0.364	0.047

**P<0.001 - Highly significant.

DISCUSSION

Reaction time (RT) means time taken by an individual to react to external stimulus. The increase in RT indicates an impaired sensory-motor performance (9). RT measurement is a sensitive and reproducible test and it can be done with simple apparatus and set up. It is an inexpensive means for determination of sensory motor performance of an individual (9).

Both Auditory and Visual reaction time were found to be prolonged in the present

study in iron deficient adolescents as compared to iron replete adolescents. Similar results have been derived in many of the earlier studies.

Web and Oski (12) found that ID anemic children had a longer latency period than non-anemic subjects on visualization of an after image. In one of the studies, the authors suggested that it was specifically visual attention that was affected in IDA (13).

Kabakus et al (14) have used nerve conduction studies to suggest that peripheral neuropathy may develop in children having iron deficiency anemia and the symptoms may improve by iron therapy. In a study done on infants (13) it was seen that those infants who did not receive iron had less efficient information processing. Information processing tasks involve a number of processes including speed and discrimination. Many significant findings have suggested that more specific cognitive process such as attention which can influence speed of mental processing, response times and learning under certain conditions, are affected by IDA (13). Based on data in a study (13), a hypothesis is that the ability to discriminate may be sensitive to iron deficiency anemia.

Significant improvement in IQ, concentration, speed of information processing and memory was noticed after partial correction of anemia in patients treated with recombinant human erythropoietin (15). Yehuda et al (16) found that people who received iron for IDA reported improved memory, attention, mood and energy before any improvement in Hb indices.

Shivani et al (17) concluded that spinal motoneuron excitability is not reduced in iron deficiency anaemia as depicted by bilateral median and common peroneal F wave studies where F wave mean latency, chronodispersion, persistence and mean amplitude were within the normal range between anemics and control group.

Leis et al (18) in a case report suggest one possible mechanism for the underlying weakness in severe anaemia- a relative depression of the spinal motoneuron excitability, precipitated by spinal cord ischaemia.

Murray et al (19) found that administration of iron resulted in an improvement in both performance and the time taken to complete the reaction time task, in a recent study done on young women. Whether the impact of anaemia on reaction time is peripheral or central is still unknown. Studies in this regard have been scarce.

Studies conducted in infants have led us to assume that ID disrupts brain functioning only during development. However, newer evidence from animal models and in humans with restless leg syndrome (RLS) suggests that brain ID at any time in life is likely to disrupt metabolic processes and to be followed by changes in cognitive and behavioural functioning (19).

The chief cells involved in myelination are oligodendrocytes which depend on iron availability for normal function. The formation of fully mature myelin is a process that takes months or even years (7), and it is thus plausible that the effects of a

developmental insult might be observed later on i.e. during adolescence, even if the apparent cause were treated.

In animal models, there is evidence that early IDA effects on myelination are not reversed with iron therapy (7). Lasting behavioural effects in rats, with a history of IDA in infancy, were observed in both motor and sensory functions in adulthood (20). Neuro functional studies have shown that even after iron therapy in IDA infants slower transmission was seen in both the auditory and visual systems at preschool age (21). In a follow up study (22) done on adolescents who had iron deficiency anemia in infancy, it was seen that they performed worse on tests of overall mental, motor and in specific Neuro cognitive tests at adolescence age also when compared to their peers who had good iron status in infancy.

Strong evidence also exists for iron deficiency impact upon cell metabolism and morphology, in particular, for the hippocampal formation. There is a decrease in neuronal metabolism, dendritic growth and arborization and synapse formation which is not recovered by iron repletion (21, 22).

Studies document the alteration of dopaminergic functioning in iron deficiency (7). Dopaminergic neurotransmission has specific roles in circuits involved in transmitting visual and auditory information (7). It is well established that dopamine is implicated in memory, learning and attention as well as in motor control, hormonal regulation, stress responsivity, addiction and emotional affect (23).

Serotonin also seems to play a role in neurotransmission in auditory pathway and it has been seen that substances which deplete serotonin increase the amplitude of some BAEP components (24). In our study, a significant negative correlation of haemoglobin was observed with both auditory and visual reaction time. S.Ferritin showed a significant negative correlation with auditory reaction time. In a recent study (8), haemoglobin level and iron parameters showed a correlation with the latencies of VEP waves. The authors suggested that anemic hypoxia and/or iron deficiency per se could possibly cause the latencies to be increased.

Decreased tissue oxygenation resulting from IDA produces generalized weakness and fatigue. These symptoms along with other symptoms of anemia viz tiredness, poor concentration, poor attention and irritability could be the reason for prolongation of ART and VRT. Ballin and colleagues found that iron treated adolescent group reported decreased lassitude, improved mood and ability to concentrate (6).

Conclusion

Hypomyelination of auditory and visual sensory pathways, alteration of neurotransmission systems, delayed and/or asynchronous maturation of neural interactions among different sensory modalities, and decreased neuronal metabolic activity might be responsible for prolongation in ART and VRT in IDA. Moreover, these mechanisms are not mutually exclusive and might act synergistically to induce altered function.

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