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RESEARCH ARTICLE

Motor nerve conduction parameters in patients with iron deficiency anemia

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ABSTRACT

Background: Worldwide, iron deficiency anemia (IDA) is the most common nutritional problem. Iron is very essential and has many important functions in brain energy metabolism, neurotransmitter function, and myelin formation. IDA may cause nerve dysfunctions. **Aims and Objectives:** The purpose of the present study was to investigate the effects of IDA on peripheral motor nerve function. **Materials and Methods:** A total of 40 individuals (25 females and 15 males) with IDA in the age range of 20-50 years from the Department of Medicine, SRM Medical College, as the study group and 30 participants (20 females and 10 males) without anemia as the control group were enrolled into this cross-sectional study. Patients with history of diabetes mellitus, neuromuscular, metabolic, vasculitic or rheumatologic diseases and those taking medications that may alter central or peripheral nerve function were excluded from the study. The motor nerve conduction parameters, *viz*., distal latency, amplitude of compound muscle action potential (CMAP), and motor nerve conduction velocity (MNCV) were recorded bilaterally in median, ulnar, and posterior tibial nerves using standard protocols and settings. Values from patients were compared with those of controls by unpaired student's t-test and one-way ANOVA. **Results:** The observations revealed significantly prolonged distal motor latencies, reduced CMAP amplitudes, and slowed MNCV in the peripheral nerves in IDA. **Conclusion:** The results indicated that the alteration in motor conduction parameters in IDA might be due to various functional and structural changes in peripheral nerves associated with iron deficiency.

KEY WORDS: Iron Deficiency Anemia; Motor Nerve Conduction; Peripheral Neuropathy

INTRODUCTION

Anemia is defined as reduction in the oxygen carrying capacity of blood as observed by reduced levels of hemoglobin concentration and red cell mass (hematocrit) leading to tissue hypoxia.[1] Anemia is one of the most common public health problems, especially in developing countries. Iron deficiency is reported to be the most prevalent nutritional problem in the world today with an estimated 2.5-5 billion people so affected.[2,3] Iron is essential for the health of many tissues. It is one of the micronutrients, most studied and is very essential for proper growth and functioning of the nervous system. Various studies had found the possibilities about the biological basis of the behavioral and cognitive developmental delays observed in iron-deficient infants. They were abnormalities in neurotransmitter metabolism,[4-6] decreased myelin formation,[7] and alterations in brain energy metabolism.[8] Furthermore, iron is involved in making many

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different proteins such as hemoglobin. Hemoglobin present in red blood cells helps them to transport oxygen. Low iron levels affect hemoglobin synthesis, making it harder for the body to make new red blood cells. The resulting low red blood cell level leads to chronic fatigue, pallor, and weakness.

Peripheral nerve function may be impaired in anemic patients with iron deficiency. However, there were very few studies and insufficient data about peripheral motor nerve functions in patients with iron deficiency anemia (IDA) which is the leading cause for anemia in the general population. The aim of the present study is to evaluate the possible adverse effects of IDA on peripheral motor nerve function.

MATERIALS AND METHODS

This cross-sectional study included 40 patients (25 females and 15 males) diagnosed with IDA attending the anemia clinic and the Department of Medicine at SRM Medical College Hospital, and 30 healthy participants (20 females and 10 males) without anemia, all in the age range of 20 - 50 years. The study was approval by the institutional ethical committee. The procedure was clearly explained to the patients recruited for the study, and written informed consent was obtained from the patients. Patients with history of cardiac, renal, hepatic, endocrine and mental illness, any acute illness, diabetes mellitus, alcohol addiction, leprosy, neuromuscular disorders, drug-induced neuropathy, family H/o neuropathy, malignancy, HIV, myopathy, those received blood transfusion, and those under treatment for anemia, etc., were excluded. A detailed history taking and clinical examination were performed.

As per the WHO guidelines, the patients with anemia were classified as mild when the hemoglobin level for men is 11-12.9, and the hemoglobin level for females is 11-11.9. The patients were considered to have moderate anemia when the hemoglobin level for both males and females is 8-10.9, and the patients were considered to have severe anemia when the hemoglobin level for both males and females is lower than 8. The participants were considered as non-anemic if the hemoglobin level for men is 13 or higher and the hemoglobin level for females is 12 or higher.[9]

Nerve conduction study was performed using the Neurostim machine, manufactured by Medicaid systems. Three disc surface electrodes were used with surface stimulators - Recording electrode, reference electrode, and ground electrode. The electrodes were placed after applying jelly to reduce resistance in air between electrode and skin surface. The ground electrode served as a zero voltage reference point. The temperature of the examination room was maintained at about 25-28°C. The patient was taken to the room, rested for a while so as to decrease the skin temperature to the recommended level of 32-34°C. Thereafter, the nerve conduction study procedure was carried out with the subject lying comfortably in supine position on the bed. For all the patients, we recorded parameters such as distal latency (DL), amplitude of compound muscle action potential (CMAP), and motor nerve conduction velocity (MNCV) after stimulation of the median, ulnar, and posterior tibial nerves on both sides.

Latency in milliseconds (ms) is the time from the onset of stimulus to the point of takeoff from baseline and is an index of speed of impulse travel.[10] Size of the response, called amplitude (in mV), is measured from the baseline to the top of the motor response. Conduction velocity (in M/s) reflects the fastest motor axons.[10]

$$CV\ (M/s) = \text{Distance (mm)} / (\text{Latency proximal} - \text{Latency distal (ms)})$$

Nerve conduction was performed bilaterally on all limbs and as left side data were similar to that of the right side; only right sided values were depicted. All the data were entered in MS Excel spreadsheet, and the statistical analysis was done using SPSS version 17.0. The data were expressed as mean ± standard deviation. Descriptive tables were generated, and Student *t*-test and one-way ANOVA were used to demonstrate the findings. $P < 0.05$ was considered to be statistically significant.

RESULTS

Table 1 compares the anthropometric parameters between patients with IDA ($n = 40$) and normal participants ($n = 30$) which show that there is no significant difference between the two groups. Table 2 compares the motor nerve conduction parameters such as DL, amplitude of CMAP, and MNCV between patients with IDA and normal participants and shows a statistically significant increase in DL of the median and posterior tibial nerves in patients with IDA. Table 3 compares the motor nerve conduction parameters between patients with mild, moderate, and severe anemia, which shows that in the ulnar, median, and posterior tibial nerves; MNCV and CMAP

Table 1: Comparison of anthropometric data between patients with IDA and normal participants

Parameters	Mean±SD		*P* value
	Group I-Patients with IDA (*n*=40)	Group II-Controls (*n*=30)	
Age	43.6±8.9	38.4±11.7	0.08
Height	158±11	161±8.8	0.228
Weight	60±10.9	63.7±11.6	0.576
BMI	23.06±4.03	24.01±4.24	0.144

P<0.05 is statistically significant. SD: Standard deviation, BMI: Body mass index

Table 2: Comparison of motor nerve conduction parameters between patients with IDA and normal participants

Nerve	Parameters	Mean±SD		*t* value	*P* value
		IDA (*n*=40)	Control (*n*=30)		
Median nerve	DL (msec)	3.72±0.91	3.03±0.35	3.175	0.002*
	CMAP amplitude (mV)	7.98±2.85	8.38±1.01	−5.98	0.55
	MNCV (m/sec)	51.41±4.93	58.55±2.48	−5.77	1.15
Ulnar nerve	DL (msec)	3.2±0.9	3.026±0.33	0.848	0.4
	CMAP amplitude (mV)	8.03±0.88	8.72±3.51	0.905	0.36
	MNCV (m/sec)	52.38±7.93	56.08±7.17	−1.659	0.11
Posterior tibial nerve	DL (msec)	3.66±0.74	3.24±0.135	2.12	0.04*
	CMAP amplitude (mV)	4.97±1.55	5.02±1.30	−0.11	0.91
	MNCV (m/sec)	44.99±6.0	46.1±6.44	−0.535	0.59

*Statistically significant, SD: Standard deviation, DL: Distal latency, CMAP: Compound muscle action potential, MNCV: Motor nerve conduction velocity

Table 3: Comparison of motor nerve conduction parameters between patients with mild, moderate, and severe anemia

Nerve	Parameters	Mean±SD			*F* value	*P* value
		Mild anemia	Moderate anemia	Severe anemia		
Median nerve	DL (msec)	3.24±0.5	3.76±0.39	4.63±0.33	15.07	0.00*
	CMAP amplitude (mV)	11.16±2.14	9.35±1.22	7.96±0.46	12.27	0.00*
	MNCV (m/sec)	57.6±4.2	52.47±3.43	52.12±4.54	3.46	0.05*
Ulnar nerve	DL (msec)	2.82±0.66	3.48±0.55	4.28±0.93	5.76	0.012*
	CMAP amplitude (mV)	11.56±1.82	8.9±2.48	6.49±1.17	7.19	0.05*
	MNCV (m/sec)	60.36±4.79	53.9±3.01	52.05±2.3	8.83	0.002*
Posterior tibial nerve	DL (msec)	3.02±0.408	3.67±0.44	4.08±0.77	5.14	0.017*
	CMAP amplitude (mV)	5.87±1.14	4.43±1.05	3.68±0.48	5.77	0.012*
	MNCV (m/sec)	50.58±2.04	45.8±3.69	44.97±1.85	5.35	0.015*

*Statistically significant, SD: Standard deviation, DL: Distal latency, CMAP: Compound muscle action potential, MNCV: Motor nerve conduction velocity

were significantly decreased, and DL was significantly prolonged as severity of anemia increases ($P < 0.05$).

DISCUSSION

In the present study, we compared the motor nerve conduction parameters of 40 patients with IDA with that of 30 controls. The comparison of age, height, and body mass index of controls and patients with IDA did not reveal any significant difference. This suggests that the groups were matched as shown in Table 1.

Patients with IDA showed significantly prolonged distal motor latencies, for median and posterior tibial nerves as shown in Table 2. The CMAP amplitudes were reduced, and MNCV were slowed for median, ulnar, and posterior tibial nerves in patients with IDA but not statistically significant. These findings for motor conduction parameters in IDA were consistent with that reported by Kabakus et al.[11]

Despite strong evidence that iron deficiency in utero or early postnatal life can affect cerebral development, very few studies have related the effect of IDA to peripheral neuropathies. Kabakus et al.[11] assessed nerve conduction in the median and posterior tibial nerves in 18 children with IDA and 12 healthy children and found that in IDA children, nerves conduction velocity and distal amplitude values were lower compared with controls. They showed that IDA patients had peripheral neuropathy and also that could be improved with 3 months of iron therapy. However, these results were not confirmed in another study, in which 34 patients affected by IDA were subjected to electrophysiological examination, including motor and sensory nerve conduction, F-responses, H-reflex, blink-reflex, and mixed nerve silent periods. The authors concluded that IDA does not cause significant electrophysiological changes in peripheral nerves.[12]

In our study, in the ulnar, median, and posterior tibial nerves, the amplitude of CMAP and MNCV was significantly decreased, and DL was significantly prolonged as the severity of anemia increases ($P < 0.05$) which shows the development of peripheral neuropathy in IDA (Table 3).

The mechanisms involved in the development of neuropathy in IDA were not yet fully established. As iron has an important role in various metabolic and enzymatic processes, iron deficiency may have various effects on neurological functions such as decreased motor activity and intellectual functions such as decreased social interaction and attention to tasks, etc.[13]

According to Youdim[14] and Cook,[15] iron deficiency causes alterations in many metabolic processes including mitochondrial electron transport, synthesis and degradation of neurotransmitters, and the synthesis of proteins that have an impact on the functioning of the nervous system.

Moreover, IDA has well-known and reported effects on the nervous system including depression, decreased mental alertness, and disorders of sleep rhythm.[16] The iron-containing enzymes such as monoamine oxidase (MAO), catalase, and cytochromes of the central and peripheral nervous system, could be affected adversely by iron deficiency. El-Sebae et al.[17] found decreased MAO levels in delayed neuropathy in study performed on sheep. According to Brett et al., nerves could also be affected by the IDA chronic ischemia process.[18] As the neurons are highly sensitive to iron toxicity and as the iron is essential for myelin formation and maintenance of nervous system, both iron overload and iron deficiency may induce peripheral neuropathy.[19,20] Myelin is a dielectric material that forms a sheath that forms an insulating and protective coating around nerve fibers. Studies in rats showed that iron deficiency leads to reduced levels of myelination and a shortage of myelin proteins and lipids.[16,21] According to Ortiz et al.,[19] these effects seem to be long-lasting.

According to Beard and Connor,[22] iron deficiency causes disruption in myelination, neurotransmitter neurochemistry, and neuronal energetics in neural functioning. In future, more studies could be done to gain a better understanding of iron transport across the blood-nerve barrier, on the role of Schwann cells in regulating axon iron uptake, and on how iron participates in myelin synthesis.

CONCLUSION

Our study confirms the involvement of peripheral nerves in IDA. In adults, as the iron deficiency has insidious onset, diagnosis can be delayed by months or years and the neuropathic manifestations can go unrecognized for a longer period. Therefore, performing electrophysiological studies in IDA patients are suggested, early in the course of the disease to detect nervous system involvement. Further research is needed to see whether the neurological dysfunction in IDA is reversible with the appropriate iron replacement therapy.

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