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# Reversible alteration of Nerve Conduction Velocity in Iron Deficient Anemic Patients in Response to Treatment

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***Authors' contributions***

*This work was carried out in collaboration among all authors. Author GS designed the study, author PS performed the statistical analysis, author SG wrote the protocol, managed the literature searches, and wrote the first draft of the manuscript. Author SKA managed the analyses of the study. All authors read and approved the final manuscript.*

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## ABSTRACT

**Aim:** Evaluation of nerve conduction in adult patients of iron deficiency anemia and to study the response to treatment.
**Study Design:** Prospective randomized control study
**Place and Duration of Study:** Department of Medicine and Department of Physiology, PGIMS Rohtak
**Introduction:** 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

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like dysfunction in the peripheral nervous system such as paresthetic complaints.
**Method:** Nerve conduction was recorded using RMS EMG EP MK2 machine in 30 newly diagnosed patients of iron deficiency anemia with haemoglobin less than 10.9-4 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:** An increase in distal latencies and a decrease in amplitude and nerve conduction velocities of motor and sensory component of all the nerves was seen in IDA patients as compared to the control groups which was reversible with iron replacement therapy.
**Conclusion:** Altered values of nerve conduction parameters indicates peripheral neuropathy in IDA individuals with or without polyneuropathy. Thus, nerve conduction study provides an objective method for monitoring the function of PNS, especially the clinically silent peripheral nerve compromise in patients of iron deficiency anemia before and after iron replacement therapy. Thus NCS is a non-invasive test for early diagnosis and therefore early treatment to prevent complications.

*Keywords: Peripheral Nervous System (PNS); Iron Deficiency Anemia (IDA); Nerve Conduction Study (NCS).*

## 1. 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, due to defective myelination, a subclinical involvement of peripheral pathway in the brainstem occurs, which is indicated by an increase in distal latency and decrease in conduction velocity. The axon is also damaged as evidenced by decreased value of amplitude [3].

By giving electrical stimulation of adequate strength and recording the evoked potential in the nerves or muscles, sensory and motor nerve functioning can be examined by performing nerve conduction studies (NCS) [4,5]. Measurement of nerve conduction parameters is a frequently used non-invasive diagnostic method for identification of various neuropathies.

## 2. MATERIALS AND METHODS / EXPERIMENTAL DETAILS / METHODOLOGY

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. This study was planned to find out the response to iron replacement therapy (Enteral type of iron).

### 2.1 The Subjects were Divided Into Two Groups

#### 2.1.1 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.

#### 2.1.2 Group 2

30 age and sex matched controls.

### 2.2 Inclusion Criteria

The patients of moderate (Hb 8.0-10.9 g/dl) and severe anemia (Hb < 8.0 g/dl) of iron deficiency (confirmed by serum iron profile) for unknown duration were included in the study.

### 2.3 Exclusion Criteria

Patients with chronic disorders i.e. Hematological disorders, oncological disorders, diabetes mellitus, cerebrovascular diseases, motor neuron

diseases, Parkinsonism, multiple sclerosis, neuromuscular disorders, drug induced neuropathy, smoking, alcoholism, chronic hepatic and renal disorders, history of intake of drugs with known auditory neurotoxicity, deafness or any other ear disease were excluded from the study. Pregnant and lactating mothers were also excluded from the study.

### 2.4 NCS Recording

Equipment setup:
The recording was taken by using RMS EMG EPMK2 machine. One recording was taken pre treatment and one post treatment with iron.

Motor nerve conduction study was performed in:

A. Upper limb- Median nerve (left and right) and ulnar nerve (left and right).
B. Lower limb- Peroneal nerve (left and right) and tibial nerve (left and right).
Sensory nerve conduction study was performed in:
A. Upper limb- Median and ulnar nerve (left and right).
B. Lower limb- Sural nerve (left and right).

Two small button type silver electrodes were used as reference and recording electrode. Ground electrode was used for earthing.

Amplitude (mv), latency (ms), and conduction velocity (m/s) were recorded automatically by the machine and a printout was obtained.

### 2.5 Motor Nerve Conduction Study

Filter setting for motor nerve conduction study was 5Hz to 10 kHz and sweep speed was 2-5 ms/division. Patient was made to lie down comfortably in supine position and the procedure was explained to him/her.

### 2.6 Sensory Nerve Conduction Study

Filter setting for sensory nerve conduction study was 10Hz to 12 kHz and sweep speed 1-2 ms /division and gain 1-5 μv/division. Patient was made to lie down comfortably in supine position and the procedure had been explained to him/her [6].

## 3. RESULTS AND DISCUSSION

Equal number of men and women were involved in the study. Comparison of distal latency, amplitude and nerve conduction velocity in pre-treatment cases and controls in upper limb. (Motor: Median nerve and Ulnar nerve, Sensory: Median nerve and Ulnar nerve)

- There was an increase in distal latencies and a decrease in amplitude and nerve conduction velocities of motor and sensory component of bilateral median and ulnar nerves in iron deficient anemic patients as compared to control group.

Comparison of distal latency, amplitude and nerve conduction velocity in pre-treatment cases and post-treatment cases in upper limb

- There was a decrease in distal latencies and increase in amplitudes and nerve conduction velocities in iron deficient anemic patients with iron replacement therapy in all motor and sensory nerves of upper limb.

Comparison of distal latency, amplitude and nerve conduction velocity in pre-treatment cases and controls in lower limb. (Motor- Peroneal nerve and Tibial nerve, Sensory: Sural nerve)

- There was an increase in distal latencies and a decrease in amplitudes and nerve conduction velocities of sural nerve (sensory) and tibial and peroneal nerve (motor) of both sides in iron deficient anemic patients as compared to control group.

Comparison of distal latency, amplitude and nerve conduction velocity in pre-treatment cases and post-treatment cases in lower limb.

- There was a decrease in distal latencies and increase in amplitudes and nerve conduction velocities in iron deficient anemic patients with iron replacement therapy in tibial and peroneal nerves (motor) and sural nerves (sensory) of both sides.

### 3.1 Discussion

In the current study there was a prolongation of distal latencies and decrease in amplitudes and nerve conduction velocities of all the bilateral motor and sensory nerves in iron deficient anemic patients as compared to controls. Our findings are consistent with those of by Kabakus

et al. [7] and Swaminathan et al. [8]. Kumarasamy et al. [9] and Degirmenci et al. [10] also observed similar findings. Kabakus et al. discovered that in children with IDA, pretreatment values of the median/motor nerve conduction velocity (except amplitude), median/sensory nerve conduction velocity and tibial/motor nerve distal-amplitude were lower than for the control group ($p < 0.05$, $p < 0.01$ and $p < 0.001$, respectively) [7]. Degirmenci et al. found that Bilateral median nerve motor and sensory nerve conduction values, unilateral radial nerve conduction velocities, and peroneal nerve motor distal latency, tibial nerve motor conduction values (distal latency, amplitude, and nerve conduction velocity) with sural sensory nerve conductions, were statistically significant when compared with the control group ($P<0.05$). Prolonged peroneal nerve distal latencies were found and right median nerve and sural nerve sensory conduction velocities were slower than the reported normal reference values. After 3 months of oral iron treatment, a statistically significant recovery in the motor (median nerve distal latency and ulnar nerve CMAP amplitudes bilaterally, and tibial nerve conduction velocities) and sensory nerve conduction studies (median nerve SNAP amplitudes and nerve conduction velocities bilaterally, and radial nerve SNAP amplitudes and nerve conduction velocities) in the patients when compared with the pretreatment electrophysiological values ($P<0.05$) were found [10]. Swaminathan et al. showed a statistically significant increase in DL of the median and posterior tibial nerves in patients with IDA. In the ulnar, median, and posterior tibial nerves; MNCV and CMAP were significantly decreased, and DL was significantly prolonged as severity of anemia increases ($P < 0.05$) [8]. In the present study, we have incorporated the effect of iron replacement therapy to study the changes in nerve conduction parameters in IDA patients. The prolonged distal latencies and decreased amplitudes and nerve conduction velocities in iron deficient anemic patients were reversible to a great extent with iron replacement therapy. P value was found to be significant for motor components of amplitude of right median nerve ($p<0.05$), conduction velocity of right ulnar nerve ($p<0.05$) and distal latency ($p<0.001$), amplitude ($p<0.05$) and conduction velocity of left peroneal nerve ($p<0.05$) For the sensory part, p value was statistically significant for distal latency of right median nerve ($p<0.05$), conduction velocity of left median nerve ($p<0.005$), and conduction velocity of left sural nerve ($p<0.05$).

The findings of our study showed recovery in nerve conduction velocity values after iron therapy. This could be due to iron replacement of intracellular enzymes or recovery from anemia or both. Iron therapy in children with IDA has been shown to replace intra cellular iron-containing enzymes within 24 h. Peripheral neuropathy findings with iron therapy may be related to the restablishment of normal iron levels of enzymes, especially MAO [11,12].

## 4. CONCLUSION

Electrophysiological study of nerve conduction is useful for the evaluation and detection of clinically silent peripheral nerve compromise in patients of iron deficiency anemia. Thus, NCS is a useful non-invasive tool for early detection of peripheral neuropathy in iron deficient anemic individuals with or without polyneuropathy.

This study suggests that subclinical peripheral neuropathy develop in adults with iron deficiency anemia and that their symptoms are reversible by appropriate dose(100 mg elemental iron) and duration(at least 3 months) of iron therapy.

## CONSENT

All authors declare that 'written informed consent was obtained from the patient (or other approved parties) for publication of this article. A copy of the written consent is available for review by the Editorial office/Chief Editor/Editorial Board members of this journal.

## ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki."All participants signed consent form.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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