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SPINAL MOTONEURON EXCITABILITY IN IRON DEFICIENCY ANAEMIA

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Abstract : Decreased tissue oxygenation resulting from iron deficiency anaemia produces generalized weakness and fatigue. The precise physiological mechanism underlying this weakness is unknown and studies in this regard have been scarce. One possible underlying mechanism has been suggested to be reduction of spinal motoneuron excitability. F waves are low amplitude motor responses to nerve stimulation, produced by antidromic activation of the peripheral motor fibers, resulting in recurrent discharge of motoneurons. F waves have been established as an efficient tool to assess spinal motoneuron excitability. 15 patients of iron deficiency anaemia using inclusion criteria of hemoglobin level <9 g/dL and serum ferritin <15 µg/L were studied. 8 controls with hemoglobin levels >12 g/dL were also included. Bilateral median and common peroneal F wave studies were performed. F wave mean latency, chronodispersion, persistence and mean amplitude were studied. They were within the normal range and no significant differences between the patients and the controls were found. We conclude that spinal motoneuron excitability is not reduced in iron deficiency anaemia. A decreased tissue oxygenation leading to a change in the brain neurotransmitters may have a role to play.

Key words : anaemia, f-waves, motoneuron excitability, weakness

INTRODUCTION

Anaemia produces generalized weakness and fatigue. These symptoms along with tiredness, poor concentration, irritability, faintness and headache are generally regarded as non-specific. The precise physiologic mechanism producing such symptoms has received relatively little attention. A case report by Leis et al suggests that weakness and fatigue associated with severe anaemia may be due to relative depression of spinal motoneuron excitability (1).

F-waves have been used as a “probe” for changes in spinal cord excitability (2, 3). They are low amplitude, ubiquitous, inherently variable, delayed responses elicited by supramaximal shock to a motor

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nerve. They are seen after the M-response and are caused by antidromic reactivation of the motoneurons (4, 5, 6). F-waves have an established niche in clinical neurophysiology (7). F chronodispersion is a measure of the range of conduction in a series of F-waves. F-wave's amplitude and persistence reflect the antidromic excitability of a particular neuron pool (8).

Various F-wave parameters such as F wave latency are well established in the diagnostic evaluation of peripheral nerve disorders. They are particularly useful in assessing peripheral neuropathies. It has been shown that the use of other parameters such as persistence (percentage of trials in which F-waves occurred) or chronodispersion (difference between the maximum and minimum latency), further increases the diagnostic yield of F-wave studies (9).

The present study was undertaken to examine, using various F-wave parameters the effect of iron deficiency anaemia on the excitability of spinal motoneurons.

METHODS

Subjects: 15 patients, 11 females and 4 males, aged 24–44 years (mean 34.47, S.D. 5.96), with iron deficiency anaemia of varied etiology and severity were studied. The inclusion criteria were Hb < 9 g/dL (Sahli's method) and serum ferritin < 15 fig/L (Enzyme Immunoassay) (10). 8 healthy volunteers, 5 females and 3 males; ranging in age from 27 to 40 years (mean 33.38, S.D. 4.60), were also studied. All healthy volunteers had Hb > 12 g/dl. Informed consent was obtained from each subject. Patients with diabetic neuropathy, inflammatory demyelinating neuropathies or with any other nerve pathology or neurologic illness which could affect peripheral nerve conduction were excluded.

Electrodiagnostic techniques: Bilateral median and common peroneal F-wave studies were performed. The investigations were carried out at ambient room temperature of around 32°C and care was taken to ensure that the subject was relaxed. All studies were performed with surface electrodes using standardized technique (11). EB Neuro machine (MYTO software) was used for recording. The nerves were stimulated using supramaximal (25% above maximal) cathodal current pulses of 0.1 ms duration delivered at a frequency 1/sec. An amplifier gain of 500 μv/div and a sweep speed of 10 ms/div were used. Filter settings were 20 Hz to 5 kHz. A series of 20 stimuli were given and F-waves were recorded from abductor pollicis brevis and extensor digitorum brevis muscles. An F-wave was defined as an action potential atleast 20 μv in peak to peak amplitude. For each set of 20 stimuli the following F wave data were evaluated; mean latency, chronodispersion (CD), persistence and mean amplitude. Mean values for amplitude and latency were chosen because a previous study has shown that these parameters are normally distributed (12).

Statistical analysis: Levene's test was applied to test the homogeneity of variances.

For each parameter measured, statistical analysis was performed using a 2-tailed student's unpaired 't' test. Significance was set at 0.05 level.

RESULTS

All the 15 patients had Hb ranging between 6–9 g/dL. The controls had Hb ≥ 12 g/dL. Age and Hb level showed no correlation with F-wave mean latency, chronodispersion, mean amplitude and persistence.

There were no significant differences in the F-wave parameters studied between the right and left side and between the patients and controls. The data from each nerve and from both sides in summarized in Table I. Representative F responses are shown in Fig. 1.

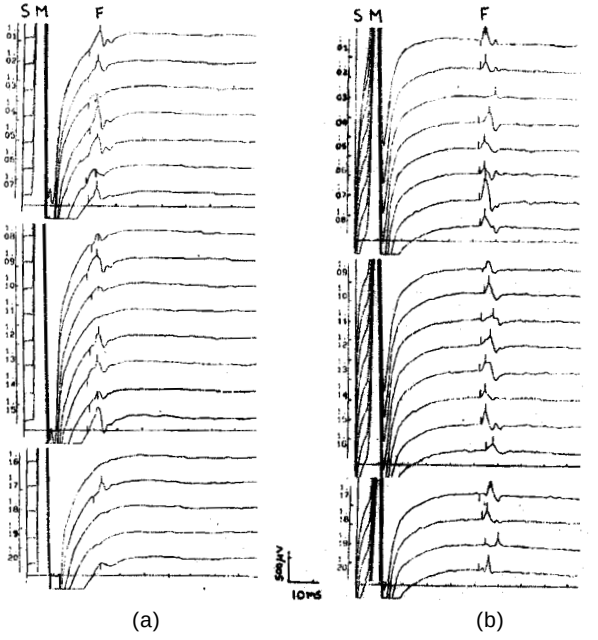

Fig. 1: Recording of F-responses from 20 successive stimuli in a 40 yr old female patient.
(a) From abductor pollicis brevis
(b) From extensor digitorum brevis
S = Stimulus
M = Direct M-response
F = F-response

TABLE I: Summary of F-response latency, amplitude, chronodispersion and persistence data.

F-response		*Abductor pollicis brevis*			*Extensor digitorum brevis*		
		Cases (n=15)	*Control (n=8)*	*P value*	*Cases (n=15)*	*Control (n=8)*	*P value*
Amplitude (μv)							
Mean±S.D.	R	287.27±100.3	257.38±53.73	0.443	135.47±32.48	155±36.20	0.201
	L	270.53±70.78	253.75±79.05	0.608	128.67±28.53	154.13±32.34	0.224
Latency (ms)							
Mean±S.D.	R	26.92±2.578	26.613±2.440	0.780	44.953±3.679	44.350±3.408	0.705
	L	25.540±1.981	27.263±3.399	0.137	44.820±3.595	43.78±2.973	0.496
Chronodispersion (ms)							
Mean±S.D.	R	3.213±0.955	3.250±0.583	0.922	2.620±0.890	2.475±0.886	0.713
	L	2.867±0.867	2.988±0.694	0.762	2.780±1.574	2.500±0.621	0.637
Persistence (%)							
Mean±S.D.	R	75.20±12.29	82.13±9.05	0.177	51.33±14.92	55.13±19.10	0.604
	L	74.93±9.16	77.50±4.99	0.473	54.60±17.07	54.40±11.29	0.988

DISCUSSION

Using WHO threshold values for Hb concentration, a meta-analysis of a large number of studies suggests that 30% of the world's population are anaemic (13). Studies in India show that 65% infant and toddlers, 60% 1–6 yrs of age, 88% adolescent girls and 85% pregnant women are anaemic. The commonest form is iron deficiency anaemia (14).

Individuals with anaemia may complain of fatigue and are unable to tolerate significant exertion (15). Decreased physical activity has been reported in iron-deficient anaemic children (16). Toy et al in 2000 have reported that hemoglobin levels <7 g/dl presumably result in decreased tissue oxygenation, the precise mechanism by which altered tissue oxygenation produces weakness and fatigue remains to be elucidated (16). Whether the origin of fatigue is central (cerebral) or peripheral (neuromuscular) is unknown (16). Studies in this regard have been scarce. Kabakus et al in 2002 have used nerve conduction studies to suggest that peripheral neuropathy may develop in children with iron deficiency anaemia and the symptoms may improve by iron therapy (17). Few studies have supported these findings. Sobh et al in 1992 have shown that neurofatigue improves in patients of anaemia after treatment with erythropoietin (18).

A case report by Leis et al in 2003 suggests one possible mechanism for the underlying weakness in severe anaemia – a relative depression of the spinal motoneuron excitability, precipitated by spinal cord ischaemia (1). This depression is reflected physiologically by a reduction of F-wave and H-reflex activity. Their patient had an Hb concentration of 4.1 g/dl. Nerve conduction studies showed absent or decreased persistence of F-waves in all limbs. F-waves are low amplitude motor response to nerve stimulation, and are widely used for clinical purposes (7). The neurophysiological mechanism underlying the production of F-wave responses is antidromic activation of the peripheral motor fibres, resulting in recurrent discharge of motoneurons (19, 20). F-waves are usually inhibited in conditions causing a reduction of spinal excitability, such as flaccidity associated with acute upper motor neuron syndromes (21). Conversely, F-waves are found more readily and are usually of greater amplitude in conditions causing increased excitability of the spinal motoneuronal pools, such as voluntary contraction of the target muscle (22) and spasticity (23). Thus, as the generation of F-waves is influenced by the balance of excitatory and inhibitory post synaptic potentials on spinal motoneurons, study of the F-wave amplitude has been proposed as a method for measuring changes in motoneuron excitability (24, 8).

In the present study we have attempted to show the effect of iron deficiency anaemia on spinal motoneuron excitability. We have studied F-wave mean latency, chronodispersion, persistence and mean amplitude bilateral in median and common peroneal nerves. There were 15 patients of iron deficiency anaemia and 8 controls. All the 15 patients had Hb ranging from 6–9 g/dl and serum ferritin < 15 µg/L. The controls had Hb ≥ 12 g/dl. All the F-wave parameters were within the normal range

and there were no significant differences between the two sides and between the patients and the controls. Akyol et al in 2003 have conducted a study on patients of iron deficiency anaemia with restless leg syndrome and have reported similar results as that of our study (25). They have found no electrophysiological changes in the peripheral nerves, spinal cord and brainstem in the 34 cases they studied. We have used F-waves as an index of spinal motoneuron excitability as it has been shown to be a more sensitive test for motoneuron excitability assessment than the well known T and H-reflexes (26). Our data, using F-waves, suggests that motoneuron excitability is not depressed in iron deficiency anaemia when the Hb concentration ranges between 6-9 g/dl and serum ferritin is < 15 µg/L. The consequences of iron deficiency are numerous as iron plays a central part in the transport of oxygen in the body and is also essential in many enzyme systems. Iron deficiency anaemia is also known to affect neurotransmitter systems in the brain, which may produce its symptomatology (27).

Studies with larger number of subjects using more electrophysiological parameters like T, M and H reflexes may be done to further the present database.

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