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Original Article

Usefulness of blink reflex in hypothyroid patients with or without polyneuropathy : A case control study

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Abstract

Central nervous system (CNS) dysfunction is an important consequence of thyroid deficiency. Cranial nerves are frequently affected in hypothyroid process. On routine nerve conduction studies, symptomatic peripheral and cranial neuropathy can be detected, however, diagnosing subclinical cranial neuropathy pose the major problem. Blink reflex (BR), has been shown to be an effective method for revealing subclinical involvement of cranial nerves in generalized neuropathies. The present study was undertaken to evaluate the efficacy of BR as a method for early diagnosis of subclinical cranial neuropathy in hypothyroid patients with or without overt peripheral polyneuropathy. A case control study was conducted on 150 subjects aged 18 years and above (100 controls, 50 cases). A routine nerve conduction study and BR evaluation was done in all the subjects. We found abnormal BR response in 50% of hypothyroid patients studied. In hypothyroid patient without polyneuropathy R1 latency was significantly prolonged ($P<0.05$ Vs control).Ipsilateral and contralateral R2 latencies were significantly prolonged in hypothyroid cases with or without polyneuropathy on bilateral stimulation. Magnitude of prolongation was greater in with polyneuropathy group. In conclusion, study suggests that BR is a useful non-invasive method for the detection of clinically silent cranial nerve compromise in hypothyroid patients.

Introduction

More than 170 million people are affected by hypothyroidism in India (1). Central nervous system dysfunction is its important consequence. This disease process is known to cause peripheral as well as cranial neuropathy which can be diagnosed clinically when it is evident. However, diagnosing the subclinical neuropathy pose the major problem. Moreover, early diagnosis of damage to the peripheral nerve can be made with the help of existing advanced neurophysiologic tests, the same does not hold true for the subclinical diagnosis of damage to the cranial nerves. Electrophysiological study such as the blink reflex (BR) has been emerged as an effective method for revealing subclinical involvement of cranial nerves in generalized neuropathy especially in hypothyroid patients. The BR was first described in 1896 by

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Walker Overend, a british human physiologist, who described it as “a new cranial reflex” (2). This reflex has been the object of investigation in various pathological condition of posterior cranial fossa, brainstem and particularly in the lesion of some cranial nerves due to its anatomic and physiological characteristics. The electrically elicited BR is an exteroceptive-nociceptive reflex recorded on the orbicularis oculi muscle and comprised of three components: the two principal ones, R1 and R2 ipsilateral, third one R2 contralateral of well known characteristics (3).

Electrophysiological testing of cranial nerves is rarely performed in hypothyroid patients in neurophysiology practice. To our knowledge no such study has been previously conducted to test BR in rural central Indian hypothyroid individuals. This has led us to take up the present study to perform BR in patients of hypothyroidism with or without peripheral neuropathy confirmed with electrophysiological methods to determine the frequency of affection of cranial nerve conduction in hypothyroid individuals.

Materials and methods

It was a case control study conducted at Mahatma Gandhi Institute of Medical Sciences, Sevagram between October’ 11 and September’ 12. We recruited 150 subjects of more than 18 years of age. To make our study more robust, we recruited 2 controls for each case after getting their informed written consent to participate. (100 age and sex matched controls, 50 cases diagnosed with hypothyroidism). The consecutive patients diagnosed to have hypothyroidism or on thyroxin treatment, referred from department of Medicine were prospectively recruited for the study. The hypothyroid patients were divided into two groups according to having peripheral neuropathy (n=23) or not (n=27) on the basis of peripheral nerve conduction studies. All participants were examined to exclude history of systemic or neuromuscular disorders as well as neurological disorder like cognitive dysfunction or psychiatric disorder. All the subjects were enquired about their demographic and socio-economic variables as well as their personal history of exposure to vibrations, machines, or vehicles; habits like alcohol intake, smoking, any drug history and general symptom and sign related to hypothyroidism. Anthropometric and blood pressure measurements were recorded in all the subjects and serum total T3, total T4, and TSH concentrations were determined by chemiluminescence assay in cases. Relevant clinical history was taken and neurological examination was done. Subjects were excluded if reported a history of neuropathy, limb injury or ulcer, neuromuscular transmission disorder, myopathy and alcohol abuse. Patients with earlier cranial nerve involvement were also excluded. Institutional Ethics Committee’s approval was obtained and study was conducted at fixed room temperature of 30°C.

Electrophysiological methods

In all the subjects, nerve conduction study was done using RMS EMG EP Mark-II. For motor nerve study, duration was kept at 200 μs, filter was between 2 Hz to 10 KHz and sweep speed was 5 ms/D for lower limb and at 100 μs, 2Hz-5 KHz, 5ms/D respectively for upper limb. For sensory nerve study, duration was 100 μs, sweep speed 2 ms/D and filter was between 20 Hz to 3 KHz. Motor nerve tested were Median, Ulnar, Peroneal, Tibial and sensory study was done on Median,Ulnar and Sural nerve. Parameters studied for motor nerves were distal motor latency (DML), amplitude and conduction velocity (CV) whereas for sensory nerves were amplitude and conduction velocity. Belly tendon montage was used with cathode and anode 3 cm apart. For sensory nerves, antidromic study was done. Sensory nerve action potential amplitude was taken from peak to base. Ground electrode was placed between stimulating and recording electrodes. F-wave study which involved supramaximal stimulation was also performed on motor nerves. Minimum F-wave latency (F-min lat) was noted. The electrophysiological values are compared against the normative data (4, 5).

Blink reflex recording

Subjects were asked to lie in a supine position and relax in a quiet room with eyes closed. Recording was done simultaneously from both sides. Active electrode was placed at inferior orbicularis oculi muscle bilaterally and reference at just lateral to

lateral canthus bilaterally. Ground electrode was placed at forehead. Supraorbital nerve (branch of ophthalmic division of trigeminal nerve) was stimulated on both sides. Parameters recorded were i) R1 latency in milliseconds (ms) ii) R2 latency (ms) - Ipsilateral iii) R2 latency (ms) – contralateral. For blink reflex recording the sweep speed was set at 10 ms per division. Initial sensitivity was at 200 ìV per division. Filter setting was at 2Hz to 10 kHz. Electrical pulse of 100 ìs duration was used and intensity was at 15-25 mA.

Statistical analysis

Statistical analysis was done using Statistical Package for Social Sciences (SPSS) 10.0 version. Values obtained were expressed in the form of mean and standard deviation (SD). ANOVAs test was applied for comparison among three groups. Statistical significance in group means was assessed using a statistical test – Z test based on normal distribution. P value was taken as significant if found to be less than 0.05.

Results

One hundred fifty volunteers aged 18 years and above were included in the study. Age and sex wise distribution of all the study subjects is depicted in table I. Age groups were not statistically different between male and females as well as between controls and cases (Table I). Abnormal blink reflex response was observed in 50% of hypothyroid patients studied (72.22% abnormality in with polyneuropathy group and 37.5% abnormality in without polyneuropathy group). On Right as well as Left sided stimulation, R1 latency was not statistically different in hypothyroid with polyneuropathy patients and controls (P>0.05). However, in hypothyroid patient without polyneuropathy it was found to be significantly prolonged (P<0.05 Vs control). Ipsilateral and contralateral R2 latencies [R2 (i) and R2(c)] were found to be significantly prolonged in hypothyroid cases with or without polyneuropathy (P<0.05 Vs control) on bilateral stimulation. Magnitude of prolongation of R2 latencies was greater in hypothyroid patients with polyneuropathy as compared to hypothyroid without polyneuropathy bilaterally. With Right sided stimulation, on comparing hypothyroid patient with and without polyneuropathy, all the three latencies viz. R1, R2 (i), R2(c) were not statistically different (P>0.05). With Left sided stimulation R2 latencies were found to be significantly prolonged in hypothyroid with polyneuropathy group (P<0.05). However in R1 latency statistical difference was not observed between these two groups (Table II and III).

TABLE I: Gender and age wise distribution of total study subjects.

	Controls (n=100)		*Hypothyroid with PN (n=23)*		*Hypothyroid without PN (n=27)*		*P*
Sex	*Male*	*Female*	*Male*	*Female*	*Male*	*Female*	
Number (n)	20	80	7	16	2	25	NS
Age (years)	36.4±2.44	42.5±1.66	36.25±0.25	42.8±4.53	36.42±4.85	42.29±2.64	(P>0.05)

Data presented are mean±SD. NS - non-significant, PN - Polyneuropathy.

TABLE II: Blink reflex latencies in healthy and hypothyroid subjects with left sided stimulation.

Latencies (ms)	*Control*	*Hypothyroid with PN*	*Hypothyroid without PN*	*P*
R1 Latency	10.15±0.42	10.55±0.98	10.63±0.89*	0.005
R2 Latency(Ipsilateral)	26.49±4.14	43.02±4.03*	40.74±3.27*	0.000
R2 Latency(contra lateral)	31.02±28.62	43.52±4.50*	40.80±3.65*	0.001

Data presented are mean±SD. PN - Polyneuropathy, *P<0.05 vs Control group.

TABLE III: Blink reflex latencies in healthy and hypothyroid subjects with right sided stimulation.

Latencies (ms)	*Control*	*Hypothyroidwith PN*	*Hypothyroid without PN*	*P*
R1 Latency	10.29±0.48	10.61±0.74	10.65±0.64*	0.006
R2 Latency(Ipsilateral)	26.87±3.63	43.74±2.95*	42.42±3.65*	0.000
R2 Latency(contra lateral)	28.09±2.82	43.99±2.96*	42.08±3.87*	0.000

Data presented are mean±SD. PN - Polyneuropathy, *P<0.05 vs. Control group.

Discussion

Central nervous system dysfunction is an important consequence of thyroid hormone deficiency (6). Localization of a lesion to brainstem has mostly been dependent upon clinical findings especially when the lesion cannot be visualized radiographically (7). Electrophysiological studies of blink reflex, however, may be useful in revealing subclinical abnormality of cranial nerves in metabolic disease (7, 8). Hence, it is reasonable to find out subclinical neuropathy involving cranial nerves in hypothyroid patients using electrophysiological tool like blink reflex.

In present study, we documented abnormal blink reflex in 50% of hypothyroid individuals and latencies were significantly prolonged in them (P<0.05). Our finding coincides with the observation by Nazliel B et al who reported significantly prolonged ipsilateral and contralateral R2 latency in hypothyroid subjects as compared to control (3). The observation held true in both - hypothyroid subjects with and without polyneuropathy. They found no statistically significant difference between control and hypothyroid individuals as far as R1 latency was concerned (P>0.05). This observation is in agreement with our finding. Similar observation was also reported by Oflazoglu B et al who found significantly prolonged R1, R2 (i), R2(c) latencies in hypothyroid individuals (9). However, their observation regarding R1 latency goes in contrast to our finding.

Yuksel G et al found blink reflex alteration in 50% hypothyroid subjects they studied. Our observation co-existent with this finding (10). They also observed significant prolongation in R2 latencies in hypothyroid subjects. We too, have reported comparable observation. Our finding are supported by observation of Nazliel B et al who found no significant latency difference for R1, ipsilateral and contralateral R2 latencies in hypothyroid subjects with or without polyneuropathy i.e. clinical or subclinical hypothyroid neuropathy (3). We observed significant abnormality in blink reflex in hypothyroid individuals even without polyneuropathy. This finding presumably reflects that cranial nerves are affected in hypothyroidism though this neuropathy clinically remains silent.

Thyroid hormones are involved in many functions of the central and peripheral nervous system (11). This is the reason why do we get neurological dysfunction in patients with hypothyroidism. The metabolic and hormonal changes in hypothyroidism cause central nervous system (CNS) dysfunction in up to 78% of the patients (11, 12). The severity of CNS dysfunction depends upon duration and degree of hormonal deficiency. Hence electrophysiological and clinical improvement is seen in such patients after hormone replacement therapy (13). The peripheral nerve abnormality associated with hypothyroidism may be of entrapment type or polyneuropathy (13, 14).

Neurological dysfunction associated with disorder of the thyroid gland may be a result of hormonal imbalance or may be related to the immune mechanism associated with thyroid diseases (15-17). The thyroid hormone affects the central and peripheral nervous system via its role in gene expression, myelin production, its effects on the neurotransmitter system and axonal transportation (6, 13). In hypothyroidism the metabolic alteration caused by hormonal imbalance affects the Schwann cell, inducing a segmental demyelination. Primary axonal degeneration has also been shown electrophysiologically in hypothyroidism. Initially only functional loss is seen in nerve, but later structural alteration may occurs as the disease progresses (18, 19).

Thyroid hormone is known to influence the synthesis of protein and the production of enzyme and myelin (3). Myelin synthesis is an important factor in determining the speed of impulse transmission along complex polysynaptic pathway such as those mediating the evoked potential and blink reflex (3, 6). Low body temperature, diminished myelin production and alteration in cerebral metabolism during acute hypothyroidism may be the cause for blink reflex alteration in hypothyroid patients. Hormonal and metabolic changes are responsible for the electrophysiological changes in hypothyroidism in the form of abnormal blink reflex which occurs early in the disease course. The determination of this abnormality suggests that blink reflex might be useful for the evaluation and detection of clinically silent cranial nerve compromise in hypothyroid patients. Therefore, based upon above observations and discussion, we are of opinion that blink reflex is a useful non-invasive tool for early detection of cranial neuropathy in hypothyroid individuals with or without polyneuropathy.

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