The usefulness of blink reflex in diabetic patients with or without polyneuropathy: A case-control study in central Indian subjects.

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Abstract

Cranial nerves are frequently affected in diabetic process. On routine nerve conduction studies, symptomatic peripheral and cranial neuropathy can be detected, however, subclinical involvement of cranial nerves may go unnoticed. Blink Reflex, which is a polysynaptic reflex, 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 blink reflex as a method for early diagnosis of subclinical involvement of cranial nerves in diabetic patients with or without polyneuropathy. A case control study was conducted on 150 subjects between ages of 40 and 60 years (50 age and sex matched controls, 100 cases diagnosed with Diabetes mellitus). A routine nerve conduction study and blink reflex evaluation was done in all the subjects. We found abnormal blink reflex response in 67% of diabetic patients studied. Both R1, R2 (ipsilateral and contralateral) latencies were found to be significantly prolonged in diabetic patients with or without polyneuropathy (P < 0.05 Vs control). All the latencies in diabetic patients with polyneuropathy were significantly prolonged relative to diabetic patients without polyneuropathy. In conclusion, study suggests that blink reflex is a useful non-invasive method for the detection of clinically silent cranial nerve compromise in diabetic patients.

Key words: Blink reflex, diabetes mellitus, polyneuropathy

Introduction

Diabetes mellitus (DM) affects the nervous system severely; however, peripheral nerves are more likely affected as compared to cranial nerves in this disease [1]. According to a statistics, incidence of cranial nerve involvement ranges between 3% to 14% [2]. Among the cranial nerves, 3rd, 4th, 6th and 7th cranial nerves are most frequently involved in diabetic process [3] whereas 5th, 9th and 10th cranial nerves are less often affected [4]. On routine nerve conduction studies, symptomatic peripheral and cranial neuropathy can be detected, however, subclinical involvement of cranial nerves may go unnoticed. Blink Reflex, which is essentially the electrical correlate of clinically evoked corneal reflex, has been shown to be an effective method for revealing subclinical involvement of cranial nerves in generalized neuropathies [4]. This reflex is a polysynaptic reflex that is most conveniently recorded from surface electrodes placed over the orbicularis oculi muscle after electrical stimulation of the supraorbital nerve. The afferent arc of the reflex is subserved by the trigeminal nerve, and the efferent arc by the facial nerve. The response is characterized by a short-latency ipsilateral response that is designated R1, followed by a more asynchronous, bilateral response, designated as R2 [5].

Therefore, the present study was undertaken to evaluate the efficacy of Blink Reflex as a method for early diagnosis of subclinical involvement of cranial nerves in diabetic patients with or without polyneuropathy in Central Indian rural population.

Materials and Methods

It was a case control study conducted on One hundred fifty subjects between ages of 40 and 60 years after getting their informed written consent to participate. (50 age and sex matched controls, 100 cases diagnosed with Diabetes mellitus according to W.H.O. criteria [6]) The diabetic patients were divided into two groups (n=50) according to having diabetic neuropathy or not on the basis of peripheral nerve conduction studies. All participants were examined to exclude history of systemic or neuromuscular disorders. 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 diabetic patients, 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.

**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 µV per division. Filter setting was at 2Hz to 10 KHz. Electrical pulse of 100 µs duration was used. Intensity at 15-25 mA

**Statistical Methods**

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). 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 between 40-60 years were included in the study. Age and sex wise distribution of all the study subjects is depicted in table 1. Age groups were not statistically different between male and females as well as between controls and cases (Table 1). Abnormal blink reflex response was observed in 67% of diabetic patients studied. On right as well as left sided stimulation, R1 latency was found to be significantly prolonged in diabetic patients with or without polyneuropathy as compared to healthy controls (P < 0.01). Ipsilateral and contralateral R2 latencies were also found to be significantly prolonged in diabetic patients with or without polyneuropathy (P < 0.01 Vs control). However, magnitude of prolongation of all the latencies was greater in diabetic patients with polyneuropathy as compared to diabetics without polyneuropathy (Table 2 and 3).

**Table 1. Gender and age wise distribution of total study subjects.**

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 50)</th>
<th>Diabetic with PN (n=50)</th>
<th>Diabetic without PN (n=50)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sex</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number (n)</td>
<td>26</td>
<td>27</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>51.19±5.46</td>
<td>50.88±7.68</td>
<td>52.66±6.36</td>
<td>NS</td>
</tr>
</tbody>
</table>

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

**Table 2. Blink reflex latencies in healthy and diabetic subjects with left sided stimulation.**

<table>
<thead>
<tr>
<th>Latencies (ms)</th>
<th>Control</th>
<th>Diabetic with PN</th>
<th>Diabetic without PN</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1 Latency</td>
<td>10.05±0.84</td>
<td>13.8±1.94*</td>
<td>12.07±1.42*</td>
</tr>
<tr>
<td>R2 Latency (Ipsilateral)</td>
<td>33.64±4.34</td>
<td>39.68±4.6*</td>
<td>36.8±4.5*</td>
</tr>
<tr>
<td>R2 Latency (contralateral)</td>
<td>33.81±4.29</td>
<td>39.66±4.35*</td>
<td>37.62±4.41*</td>
</tr>
</tbody>
</table>

Data are mean ± SD.  PN – Polyneuropathy  * P < 0.01 vs. Control group
Table 3. Blink reflex latencies in healthy and diabetic subjects with right sided stimulation.

<table>
<thead>
<tr>
<th>Latencies (ms)</th>
<th>Control</th>
<th>Diabetic with PN</th>
<th>Diabetic without PN</th>
</tr>
</thead>
<tbody>
<tr>
<td>R1 Latency</td>
<td>10.18±0.75</td>
<td>13.92±1.16*</td>
<td>12.34±1.01*</td>
</tr>
<tr>
<td>R2 Latency (Ipsilateral)</td>
<td>32.6±4.33</td>
<td>39.81±5.17*</td>
<td>36.12±7.23*</td>
</tr>
<tr>
<td>R2 Latency (contra lateral)</td>
<td>31.95±3.68</td>
<td>39.57±5.14*</td>
<td>37.25±6.21*</td>
</tr>
</tbody>
</table>

Data are mean ± SD. PN – Polyneuropathy * P < 0.01 vs. Control group

Discussion

Electrophysiologic study such as blink reflex is supposed to be an effective method for revealing subclinical involvement of cranial nerves in diabetes mellitus. The present study was aimed to assess the efficacy of blink reflex in early diagnosis of subclinical involvement of cranial nerves in diabetic patients with or without polyneuropathy. Abnormal blink reflex which is the marker of cranial nerve involvement in diabetic subjects was found in 67% of our cases. Our observation is co-existent with the findings recorded by Nazliel B et al [4] who recorded abnormal blink reflex in 55% of the diabetic patients they studied. Similarly, significant alteration in blink reflex was also reported by Trujillo Hernandez B et al [7]. However they observed the abnormality in lesser number of diabetic subjects (14.8-31.9%). Urban et al [8] recorded prolonged latency of facial nerve in 77.5% of diabetic subjects. Subclinical involvement of facial nerve in diabetes mellitus was also demonstrated by few other studies [1,9]. Findings in the present study are concordant with those of Kazem SS et al [10] who showed abnormality in blink reflex in 54.4% of diabetic subjects.

In present study, we documented prolonged R1,ipsilateral R2 and contralateral R2 latencies in diabetic individuals with or without polyneuropathy relative to controls and the differences were statistically significant (P < 0.01).

Similar findings are also recorded by Guney et al [11].Kazem SS et al [10] and Trujillo-Hernandez B et al [7].

Nazliel B et al [4] though showed significant prolongation in ipsilateral and contralateral R2 latencies, they did not observe significant difference in R1 value in diabetics relative to controls. This is not in agreement with our findings. Our observations also goes in contrast to findings noticed by Hausmanowa-Petrusewicz et al [12] who observed no change in facial nerve latency in diabetic subjects. However, the negative results they observed was attributed to mild nature of diabetes in their patients. In present study, we observed that magnitude of prolongation of all the latencies was greater in diabetic patients with polyneuropathy as compared to diabetics without polyneuropathy. These findings coincides with the observations by Kazem SS et al[10].Guney F et al [11] reported that R1 latencies in diabetic patients with polyneuropathy were prolonged relative to diabetics without polyneuropathy and the differences were statistically significant. These observations go hand in hand with our findings. These findings presumably reflect that cranial nerves especially facial and trigeminal are severely affected in diabetic process though the disease process remains clinically silent. Xu T et al [13] also stressed upon the importance of blink reflex in locating lesion of trigeminal or facial nerve or lesion of brain stem even of subclinical degree at the early time.

Therefore, based upon above observations and discussion, we are of opinion that blink reflex is a useful non-invasive method for the detection of clinically silent cranial nerve compromise in diabetic patients.

References

7. Trujillo-Hernández B, Huerta M, Pérez-Vargas D, Trujillo X, Vásquez C.Blink reflex alterations in...


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