Abnormalities in Trigeminal Nerve Conduction May be Predictor of Death in Chronic Hemodialysis Patients

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Abstract

Peripheral neuropathy is a well-known complication of chronic kidney disease (CKD).

Objective: The aim of this study was to analyse the abnormalities in trigeminal nerve conduction in patients treated with hemodialysis (HD) and to determine the relationship between this parameter and death.

Methodology: The cross-sectional study included 20 non-diabetic non-alcoholic patients with CKD stage 5 undergoing HD. Conduction of trigeminal nerve was performed using blink reflex.

Results: We found clinical evidence of trigeminal neuropathy in 20% of patients and blink reflex abnormalities in 60%. Blink reflex alterations were associated with dialysis time longer and death after one year of follow up (72 ± 19 months and 46 ± 17 months, p=0.03 and 75 vs. 37.5%, p=0.04, respectively).

Conclusion: The trigeminal nerve conduction study is useful to detect the abnormalities in peripheral nerves of the uremic patients under chronic HD and the late response may be associated with death.

Background

Peripheral neuropathy is a well-known complication of chronic kidney disease (CKD) and occurs in approximately 60-80% of patients suffering stage 5 CKD [1,2]. The frequency of peripheral neuropathy in patients with CKD has declined owing to improvements in the modalities, techniques and doses of dialysis [3,4]. Thus, uraemic neuropathy can be considered to be an indicator of inadequate treatment by dialysis [5]. It has been pointed out that uraemic neuropathy often remains mild or subclinical, and detectable only by electrophysiologic studies [6,7].

Patients with uraemic myopathy generally have a normal physical examination and normal laboratory findings, including electromyography studies and muscle enzyme activities; uraemic myopathy is thus diagnosed based on abnormal muscle biopsy findings [8]. There are few reports on nerve conduction studies in CKD patients and they were published more than 15 years ago [1-10]. There is only one study that described blink reflex in HD patients and none of them studied the prognostic value of abnormalities in peripheral nerves of the uremic patients undergoing chronic HD [11].

The aim of this study was to determine the frequency, type, and severity of electrophysiologic changes occurring in trigeminal nerve of CKD patients treated with HD using the blink reflex and to investigate the relationship between electrophysiologic parameters and death.

Methodology

Twenty adult non-diabetic non-alcoholic patients, aged between 40 and 75, were studied. They had controlled arterial pressure, CKD stage 5 (creatinine clearance below 2 ml/min/1.73 m² of corporal area), and were under HD from 12 to 180 months. For all patients, dialysis doses of at least 1.3 Kt/V were prescribed and polysulphona dialysers with at least 1.3 m² were employed. All subjects had a clinically normal mental status, with no clinical evidence of brainstem alterations. The inclusion criteria also was bilateral normal latency of the compound muscle action potential of the orbicularis oculi, obtained by percutaneous supramaximal stimuli applied to the facial nerve with the cathode placed just anterior to the mastoid process.

Clinical evaluation

The patients were questioned about their trigeminal neuropathy and examined carefully for these conditions. We asked them for the following symptoms: episodes of intense facial pain that affect lifestyle as it can be triggered by common activities such as eating, talking, shaving and brushing teeth. We also asked about autonomic (orthostatic hypotension, orthostatic dizziness, sweating, sphincter dysfunction, and impotence), positive sensory (pain and paresthesias), positive motor (fasciculations, restless leg syndrome, and cramps), and negative motor symptoms (atrophy and weakness).

Neurophysiologic investigation

Blink reflex was performed in subjects awake in dorsal decubitus, in a semi-darkened room with temperatures between 20 and 25°C. Surface 7 mm diameter platinum disc electrodes were positioned as
follows: Channel 1, exploratory electrode (G1) over the left orbicularis oculi muscle, 1 cm below the left lateral epicantal point; reference electrode (G2) 2 cm behind the left lateral epicantal point. Channel 2: symmetrical positioning in relation to Channel 1 electrodes, on the right side. Filter band-pass was set to 20-3000 Hz, sensitivity to 100 or 200 μV/cm, and analysis time to 10 ms/cm. Stimulation was by a cathode over the supraorbital foramen, with a single stimulus applied to each side, consisting of 0.2 ms square-wave pulses at 25 mA intensity. A ground electrode was positioned comfortably around the neck. Four recordings were obtained from each subject, two from each side, with a minimum of 2 min interstimuli intervals and without patient awareness of stimuli application time.

The criteria for abnormalities of the blink reflex were from a previous study of 20 adult normal volunteers performed in our laboratory. The superior limit of latency for R1 response is 12.8 (X=10.8, SD=0.66, X+3SD=12.78) and for R2 44.0 (X=36.0, SD=2.6, X+3SD=43.80). In this study we use the nomenclature: R1, early component of the blink reflex; R2i, ipsilateral late response; and R2c, contralateral late response.

Sensory and motor conduction studies in all four limbs characterizing axonal peripheral neuropathy also were performed [9].

Statistical methods

Data analysis was performed using SAS for Windows (version 9.2: SAS Institute, Cary, NC, USA). Variables with normal distribution are described using means ± standard deviation; variables with a non-normal distribution are described using medians and interquartile ranges. Categorical variables were expressed as proportions and compared with the chi-squared test. In all statistical tests, the level of significance was 5%.

Results

During the study period, a total of 20 patients treated by HD were studied. Table 1 shows the clinical, laboratory and dialysis characteristics of HD patients evaluated by blink reflex. The main etiology of CKD was hypertension (70%), 60% were male sex, mean age was 62 ± 11.7 years, and time on dialysis was 61 ± 16 months.

<table>
<thead>
<tr>
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<th>N=20</th>
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<tbody>
<tr>
<td>Male sex (%)</td>
<td>12 (60)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62 ± 11.7</td>
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<tr>
<td>Etiology of CKD (%)</td>
<td></td>
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<tr>
<td>Hypertension</td>
<td>14 (70)</td>
</tr>
<tr>
<td>Glomerulonephritis</td>
<td>5 (25)</td>
</tr>
<tr>
<td>Others</td>
<td>1 (5)</td>
</tr>
<tr>
<td>Time on dialysis (months)</td>
<td>61 ± 16</td>
</tr>
<tr>
<td>Delivered Kt/V</td>
<td>1.28 ± 0.11</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>10.9 ± 1.08</td>
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<tr>
<td>Peripheral neuropathy symptoms (%)</td>
<td>18 (90)</td>
</tr>
<tr>
<td>Trigeminal neuropathy symptoms (%)</td>
<td>4 (20)</td>
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<tr>
<td>Abnormal blink reflex (%)</td>
<td>12 (60)</td>
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<thead>
<tr>
<th></th>
<th>Abnormalities in blink reflex (n=12)</th>
<th>Non abnormalities in blink reflex (n=8)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex (%)</td>
<td>7 (58.3)</td>
<td>5 (62.5)</td>
<td>0.81</td>
</tr>
<tr>
<td>Age (years)</td>
<td>63 ± 12.7</td>
<td>61 ± 10.8</td>
<td>0.86</td>
</tr>
<tr>
<td>Etiology of CKD (%)</td>
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Eighteen of 20 patients exhibited at least one of peripheral neuropathy symptoms and only four patients presented clinical evidences of trigeminal neuropathy. Abnormal blink reflex was seen in 12 patients (60%); and all of them had electromyographical findings showing axonal peripheral neuropathy in motor and sensory conduction studies. Time on dialysis and death were higher in group with abnormalities of the blink reflex (72 ± 19 months vs. 46 ± 17 months, p=0.03 and 75 vs. 37.5%, p=0.04, respectively). Gender, age, etiology of CKD and delivered Kt/V were not significantly different between patients with and without abnormalities of the blink reflex (Table 2).
Discussion

The trigemino-facial or blink reflex is a very important response for eye protection. Since its original clinical description, it has been employed for different clinical purposes in neurology, including coma evaluation, facial paralysis, multiple sclerosis, migraine and encephalic vascular diseases [12-15]. Blink reflex studies in CKD are scanty and controversial and we only found 4 reports [11,16-18].

Correlation between blink reflex alterations and peripheral neuropathy was evident in one instance [16], possible in another [17], but in the third no peripheral nerve conduction studies were reported [18].

In our study 60% of patients undergoing HD had blink reflex abnormalities and they were associated with long term on dialysis and late death. From literature, the percentage of blink reflex abnormalities in patients treated with HD ranged from 28 to 87% [11,16-19].

It is well known that renal failure duration is an important factor linked to peripheral neuropathy [1,9]. From the 12 patients with abnormal blink reflex in this study, all of them showed abnormal sensory and motor conduction studies in all four limbs characterizing axonal peripheral neuropathy. In the previous studies with analysis of dialysis time, the results were controversial about correlation between blink reflex abnormalities and dialysis time [9,17]. We did not find association with dialysis dose, probably because delivered Kt/V was adequate in all patients (>1.2).

In conclusion, 60% of the patients undergoing chronic HD had neuropathy diagnosed by blink reflex abnormalities and axonal peripheral neuropathy was observed in 100% of the patients with blink reflex abnormalities. Blink reflex abnormalities were associated with time under HD and late death. The late response abnormalities in the blink reflex suggest subclinical brainstem dysfunction in CKD patients and may have prognostic value.

Consent

The patients provided full informed consent for gathering the data and publishing the cases.

References


Table 2: Clinical, laboratory and dialysis characteristics of patients undergoing hemodialysis according to the presence or not of abnormalities in trigeminal nerve conduction (blink reflex). CKD: chronic kidney disease
