Relation of Trigeminal Nerve Conduction Abnormalities with Mortality 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 analysis 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). At logistic regression for death, time on dialysis and abnormal blink reflex were identified as factors associated with death (OR = 1.59, CI = 1.21-2.19, p=0.011; OR = 1.12, CI = 1.02-1.74, p = 0.006; respectively).

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

Keywords: Peripheral Neuropathy; Hemodialysis; Mortality

Introduction
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 abnor-
nal 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 from 2009 until 2010. They had controlled arterial pressure, CKD stage 5 (creatinine clearance between 40 and 75), 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.

After one year of initial evaluation, the analysis of patients death was performed.

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).

Neuropathologic 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 epicanthal point; reference electrode (G2) 2 cm behind the left lateral epicanthal point; Channel 2: symmetrical positioning in relation to Channel 1 electrodes, on the right side.

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. Categorical variables were expressed as proportions and compared with the chi-squared test. In all statistical tests, the level of significance was 5%. Multivariate analysis for death was performed using logistic regression model with calculations of Odds Ratio (OR) and the variable included were hypertension, age, sex, time on dialysis, delivered kt/V, haemoglobin, neuropathy symptoms, and abnormal reflex blink.

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.

Cite this article: Ponce D. Relation of Trigeminal Nerve Conduction Abnormalities with Mortality in Chronic Hemodialysis Patients. J J Nephro Urol. 2015, 2(4): 022.
Table 1. Clinical, laboratory and dialysis characteristics of patients undergoing hemodialysis and 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. 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.

<table>
<thead>
<tr>
<th></th>
<th>Abnormal blink reflex (n=12)</th>
<th>Normal 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>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>hypertension</td>
<td>9 (75)</td>
<td>5 (62.5)</td>
<td>0.43</td>
</tr>
<tr>
<td>glomerulonephritis</td>
<td>3 (25)</td>
<td>2 (25)</td>
<td>0.99</td>
</tr>
<tr>
<td>others</td>
<td>0 (0)</td>
<td>1 (12.5)</td>
<td>0.64</td>
</tr>
<tr>
<td>Time on dialysis (months)</td>
<td>72 ±19</td>
<td>46 ±17</td>
<td>0.03</td>
</tr>
<tr>
<td>Delivered Kt/V</td>
<td>1.31±0.10</td>
<td>1.25±0.13</td>
<td>0.61</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>10.6±1.04</td>
<td>11.2±1.11</td>
<td>0.34</td>
</tr>
<tr>
<td>peripheral neuropathy symptoms (%)</td>
<td>11 (91.6)</td>
<td>7 (87.5)</td>
<td>0.73</td>
</tr>
<tr>
<td>trigeminal neuropathy symptoms (%)</td>
<td>3 (25)</td>
<td>1 (12.5)</td>
<td>0.32</td>
</tr>
<tr>
<td>Death after one year (%)</td>
<td>9 (75)</td>
<td>3 (37.5)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

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).

<table>
<thead>
<tr>
<th></th>
<th>OR</th>
<th>IC</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>1.56</td>
<td>0.89-1.45</td>
<td>0.71</td>
</tr>
<tr>
<td>Age (years)</td>
<td>2.89</td>
<td>1.71-3.76</td>
<td>0.02</td>
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<tr>
<td>hypertension</td>
<td>1.45</td>
<td>0.78-1.89</td>
<td>0.43</td>
</tr>
<tr>
<td>Time on dialysis (per 1 year)</td>
<td>1.59</td>
<td>1.21-2.19</td>
<td>0.011</td>
</tr>
<tr>
<td>Delivered Kt/V (per 0.1)</td>
<td>1.31</td>
<td>0.91-2.25</td>
<td>0.62</td>
</tr>
<tr>
<td>Hemoglobin (per g/dl)</td>
<td>1.21</td>
<td>0.78-2.25</td>
<td>0.34</td>
</tr>
<tr>
<td>neuropathy symptoms</td>
<td>1.84</td>
<td>0.91-2.11</td>
<td>0.73</td>
</tr>
<tr>
<td>Abnormal blink reflex</td>
<td>1.12</td>
<td>1.02-1.74</td>
<td>0.006</td>
</tr>
</tbody>
</table>

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 abnormal blink reflex and they were associated with long term on dialysis and late death. From literature, the percentage of abnormal

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blink reflex abnormalities in patients treated with HD ranged from 28 to 87% [11,16-18].

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).

The limited number of subjects and no enough power to examine the relation between blink reflex and mortality are some limitations of this study.

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


