Electrophysiological study of peripheral nerves in hypertensive patients

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Abstract:
Twenty five normal subjects and seventy five hypertensive patients were included in this study. The electrophysiological tests done included three main divisions of the peripheral nerves: first: the sensory nerve function, the motor nerve function and the F – wave measurements. These tests were done for the patients and controls in parallel. In hypertensive patients the sensory nerve function, when compared with the control subjects, showed a significant deterioration. On contrary, assessing the motor nerve function showed completely normal nerve conduction parameters. Lastly, on assessing the F – wave parameters, only the latency of the slowest F – wave of the common peroneal nerve was prolonged which means that the smallest central fibers were also affected by hypertension. So, we see that the main effect of hypertension is on the axons of the smallest fibers. Lastly, it is possible to conclude that hypertensive disease could be associated with various types of peripheral neuropathy.

Introduction:
The nerve cells are excitable cells that are capable of self generation of electrochemical impulses at their membranes. As the primary function of the nervous system is to convey information from one part of the body to another part, which is achieved by nerve signals “impulses”. So, the nerves have
specialized functions that are integration and transmission of nerve impulses. Nerve signals are transmitted by action potentials, that arise at the junction of the axon hillock and the initial segment, because this segment has the lowest threshold for stimulation. These action potentials are rapid change in the membrane potential that spread along the nerve fiber membrane. To conduct a nerve signal, the action potential moves along the nerve fiber until it comes to the fiber end, so the axon and its branches are the main transmitting channels through which neurons affect other nerve cells and other tissues such as muscles or glands.

The electroneurography, also called nerve conduction study (NCS) is one of the constituent of electrophysiology and the electrophysiological tests provide reliable and reproducible approaches to the detection and characterization of nerve, muscle and neuromuscular junction disease.

Hypertension is an elevated blood pressure that is probably the most important public health problem in developed countries. It is so important because it is common, asymptomatic, easily detectable, and usually easily treated and if not it might lead to a lethal complication.

Subjects and methods:
Eighty four patients were referred by physicians to the unit of neurophysiology as having long term essential hypertension. Eight patients were excluded as they have diabetes mellitus and another patient because of the presence of renal failure. The age of the remaining seventy five patients, 36 females and 39 males, ranged from 38 to 61 years old. The duration of the disease diagnosis ranges from 6 to 10 years. Twenty five controls, 13 males and 12 females, were also included. Their ages ranged from 38 to 61 years old. All of them were free from any neurological problems, also, they were free from other diseases that may affect the nerve function, such as diabetes mellitus and renal failure.

All of the different measurements that subjects underwent were done in a quiet environment in the examining room with modulated temperature to be 25 to 28 C, and they were kept in this room for at least 15 minutes before being examined, and their body temperature ranged from 36.5 to 37.3 C, measured by a thermometer in the mouth, sublingually.

For the measurement of the blood pressure, the individual should be comfortably seated with the legs uncrossed, the back of the subject was supported by the chair and his/her arm was abducted, supinated and supported by a pillow placed on the near by couch. The height of the chair is arranged so that the middle of the cuff on the upper arm is at the level of the subject's right atrium, the mid-point of the sternum. The measurement of the blood pressure was repeated twice at about 1 minute apart and if the difference between the two readings is more than 5 mm Hg it was repeated again and the average of these readings was considered. From these, the mean blood pressure (MBP) is calculated for each one of the involved subjects, as follows: 

\[ \text{MBP} (\text{mmHg}) = \text{DBP} (\text{mmHg}) + \frac{1}{3} (\text{SBP} - \text{DBP}) \]

All subjects were investigated by a different electrophysiological studies of unilateral nerves, and such tests were done for the patients and controls in parallel using Micromed – EMG machine. All subjects were lying comfortably in supine position on an examination couch with the upper limb abducted 10 – 15° and flexed 10 – 15° at the elbow joint and the lower limb flexed 10 – 15° at the hip and knee joints. The tests done were sensory nerve fibers
measurements, the sites for stimulation and recording are shown in figure 1, including: latency, conduction velocity and amplitude (( for median, ulnar and sural nerves )), motor nerve fibers measurements, the sites for stimulation and recording are shown in figure 2, including: distal motor latency, motor nerve conduction velocity and amplitude (( for median, ulnar, posterior tibial and common peronial nerves )) and F – wave measurements including: minimum and maximum latencies, and the amplitude of the muscle potentials which is produced by the fastest fibers (( for Median, ulnar, posterior tibial and common peronial nerves )).

Using the Statistical Package for the Social Sciences (( SPSS )), the arithmetic mean and standard deviation of distribution of each of the parameters were calculated for all of the subjects.

Figure 1: The sites for stimulation and recording of the sensory nerve action potential of the a- Median, b- Ulnar and c- Sural nerves 18.
Figure 2: The sites for stimulation & recording of the motor nerve action potential of a- Median, b- Ulnar, c- com. peroneal & d- post. tibial nerves.
Results:
The characteristics of the seventy five hypertensive patients’ regarding their age, gender, temperature, mean blood pressure and the duration of the disease diagnosis were compared with that of their control group, twenty five subjects. These results and their level of significance were shown in table 1.

Table 1: The characteristics of patients with HRT and their control group

<table>
<thead>
<tr>
<th>Character</th>
<th>Control group</th>
<th>HRT Patients</th>
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<tbody>
<tr>
<td>Age (Year ± SD)</td>
<td>47.32 ± 7.41</td>
<td>49.88 ± 6.73 NS</td>
</tr>
<tr>
<td>Gender (Number &amp; Percent)</td>
<td>13 (52%)</td>
<td>39 (52%) NS</td>
</tr>
<tr>
<td></td>
<td>12 (48%)</td>
<td>36 (48%) NS</td>
</tr>
<tr>
<td>Temperature (°C ± SD)</td>
<td>36.85 ± 0.26</td>
<td>36.92 ± 0.23 NS</td>
</tr>
<tr>
<td>Mean Blood Pressure (mmHg ± SD)</td>
<td>100.21 ± 4.54</td>
<td>117.87 ± 6.50 HS</td>
</tr>
<tr>
<td>Duration of the diagnosis (year ± SD)</td>
<td></td>
<td>7.62 ± 1.12</td>
</tr>
</tbody>
</table>

NS=Non significance=p-value>0.05, HS=Highly significant = p - value < 0.001
All of the sensory latency, sensory conduction velocity and sensory amplitude were measured, and the results together with level of significance are shown in figures 3,4&5.
Figure 3: Effect of HRT on sensory latency of median, ulnar and sural nerves.

* = Statistically significant difference between control and patient groups (p-value < 0.05)
Figure 4: Effect of HRT on sensory conduction velocity of the median, ulnar, posterior tibial and common peroneal nerves.

* = Statistically significant difference between control and patient groups (p-value < 0.05)

Figure 5: Effect of HRT on sensory amplitude of median, ulnar & sural nerves.

All of the DML, motor CV and motor Amp. were measured in the HRT patients and in their control group. The results together with the level of significance are shown figures 6, 7 & 8.

Figure 6: Effect of HRT on DML of median, ulnar, post. tib. & com. per. Ns.
Figure 7: Effect of HRT on MCV of median, ulnar, post. tib. & com. per. Ns.

Figure 8: Effect of HRT on M amp. of median, ulnar, post. tib. and com. per. Ns.
All of the minimum F – wave latency ($F_{\text{min}}$), maximum F – wave latency ($F_{\text{max}}$) and amplitude of the minimum F – wave ($F_{\text{min}}$ Amp.) were measured, and the results together with their level of significance are shown in figures 9, 10 & 11.

**Figure 9**: Effect of HRT on $F_{\text{min}}$ of median, ulnar, post. tib. & com. per. Ns.

**Figure 10**: Effect of HRT on $F_{\text{max}}$ of median, ulnar, post. tib. & com. per. Ns.

* = Statistically significant difference between control and patient groups (p-value < 0.05)
Discussion:
The readings of the mean blood pressure of the twenty five control subjects were consistent with other researches and studies 3,6&29.
As mentioned above, the control group were chosen to be of about similar age and sex of the HRT patient group to eliminate any possible effect of these to parameters on the results of the study 34&45. This is proved by the absence of any significant difference when comparing these variants between the patients' and control groups.
On the other hand there was a high increase in the patients' MBP readings when compared with that of the control group. This together with a valuable history of long lasting hypertension categorize these subjects to be a HRT patients 5&12.
The overall neurological involvement in patients with HRT is peripheral sensory neuropathy mainly of axonal type, a finding strongly proved by Edwards et al., (2007) 11 with an early secondary demyelination observed only in the sural nerve. Further more a demyelinative changes are also seen in the smallest nerve fibers (( central segment )) of the common peroneal nerve.
These finding are generally consistent with that of Creager and Herman (2000) 7 and Tesfaye et al., (2005) 36 who stated that the incidence of neuropathy is associated with a potentially modifiable cardiovascular risk factors, as HRT. Also, Teunissen et al., (2002) 37 found that patients with chronic idiopathic axonal polyneuropathy more often had manifest HRT than controls. Furthermore, Sibal et al., (2006) 34 reported that people who developed neuropathy usually have higher systolic and diastolic blood pressure than those remain free from neuropathy. At the same time, some scientists proved that aggressive treatment of HRT is the standard clinical practice in the management of nephropathy 7. During their work on diabetic neuropathy, a lot of researchers suggested a strong relationship between HRT and diabetic symmetrical polyneuropathy and that HRT has the greatest impact on the development of this polyneuropathy 2,10,13,16&32. On the other hand, our findings are inconsistent with
that of Cho et al., (2006) who reported an unexplained negative association between hypertension and peripheral neuropathy, and furthermore different from the findings of Mold et al., (2004) who stated that a history of HRT is protective against the development of the neuropathy. Lastly, arterial HRT may be considered as an independent risk factor for the development of polyneuropathy especially in the elderly.

The affection of the lower limbs’ nerve fibers are worse than that of the upper limbs, a finding also present in many other studies. The underlying pathophysiology of the neuropathy that appears in this study might be the affection of the blood supply of the involved nerves with the same pathology that already causes the patient to be hypertensive. This is also evident in the results of Yokoyama et al., (2007) who concluded that multifactorial intervention to inhibit progression of the atherosclerotic process may slow the progression of neuropathy. What further support this suggestion is the finding of Quattrini et al., (2007) who stated that inappropriate local blood flow may have a role in the pathogenesis of diabetic neuropathy.

On the other hand, there is a reported relationship between the antihypertensive drugs and variable forms of neuropathy within hypertensive patients and subsequently such drugs might be the cause of the neuropathy that appears in these patients. Finally, our results show a positive relationship between HRT and variable forms of neuropathy that is also well reported by many other studies and researches.

References:


