

# Hypertriglyceridemia and peripheral neuropathy in neurologically asymptomatic patients

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## Abstract

**OBJECTIVES:** In this study we intended to find a correlation between hypertriglyceridemia and peripheral neuropathy (PN) in patients with a high triglyceride level and no neurological complaints.

**Methods:** We recruited 24 patients (21 males and 3 females) having a triglyceride level above 300 mg/dl with no neurologic complaints and none of the other common causes of PN and they underwent an electroneurographic study. The distal motor or sensory latencies (DL), motor or sensory conduction velocities (CV), and motor or sensory amplitudes (AMP) were collected for the peroneal, posterior tibial, sural, median, and ulnar nerves and were considered abnormal if they fall above or below 2 standard deviations of reference values.

**RESULTS:** Our results show that 70.8% of the patients had a significant delay in the DL of the sural nerves and 66.7% had a significant delay in the DL of the median sensory fibers. 54.2% of the patients had a significant decrease in the motor CV in the posterior tibial nerves and 33.3% had a significant decrease in the sensory CV in the sural nerves. The means of the DL and CV were significantly different from reference values in most of the nerves. Amplitudes were the least if at all affected.

**CONCLUSION:** The pattern of the abnormalities affecting more the DL, the sensory nerves and the longer nerves of the lower extremities is suggestive of an early axonal polyneuropathy. We conclude that hypertriglyceridemia affects conduction parameters in peripheral nerves in a trend suggestive of early peripheral neuropathy.

## Introduction

Peripheral neuropathy is a common, often distressing, and sometimes disabling disease. One of the frequent causes of peripheral neuropathy is diabetes mellitus. Diabetic neuropathy is a painful neuropathy involving sensory, motor and autonomic fibers [4,5]. Patients with peripheral

neuropathy usually complain of altered sensation, muscle weakness and atrophy, pain and autonomic symptoms. The overall prevalence of the condition is about 2400 per 100 000 population (2.4%), but in people older than 55 years, the prevalence rises to about 8000 per 100 000 (8%) [4]. Although

symptomatic peripheral neuropathy is a common neurologic problem, its cause may not be identified in at least one-fourth of patients, especially those with the clinical features of small fiber neuropathy. An association between lipid abnormalities and neuropathy has been reported previously [3,10]. Some reports did not find any association between these two entities [1]. However, only few reports have investigated the correlation between hypertriglyceridemia and peripheral neuropathy. In this study we intend to investigate this correlation in patients with high levels of triglycerides and no symptomatic manifestations of neuropathy.

## Material and methods

We recruited 24 patients from the hyperlipidemia clinic having a triglyceride level above 300 mg/dl with no neurologic complaints. The institutional review board of the institution approved the study and the patients gave their informed consent. These were patients with newly discovered hypertriglyceridemia and none of them was on any lipid lowering therapy before the electrophysiological examination. The patients were recruited after screening for common causes of polyneuropathy and excluding patients having one or more of the following conditions: diabetes, carcinoma, lymphoma, myeloma, gammopathy, HIV positive, hypothyroidism, vitamin B12 deficiency, uremia, chronic liver disease, exposure to neurotoxic drugs and more than twice per week of moderate alcohol intake.

All patients underwent an electroneurographic study in the classical manner described in the literature [7]. The peroneal, posterior tibial, sural, median, and ulnar nerves were studied in both lower extremities and in the left arm. Patients with carpal tunnel syndrome were excluded from the study.

The peroneal nerves were stimulated at the ankle and the fibular head recording from the extensor digitorum brevis muscles. The posterior tibial nerves were stimulated behind the medial malleolus and at the popliteal fossa with recording from the abductor hallucis muscles. The sural nerves were stimulated between the heads of the gastrocnemii with recording from the lateral malleolus. The median and ulnar nerves were stimulated at the wrist and elbows with recording from the abductor pollicis brevis and abductor digit quinti muscles respectively. The distal motor or sensory latencies (DL), motor or sensory conduction velocities (CV), and motor or sensory amplitudes (AMP) were collected for each of the above nerves.

Results were compared to normal values reported in the literature [7] and considered abnormal if they fall above or below 2 standard deviations (SD) of reported normal distal latencies, amplitudes, and conduction velocities. Means were compared to the normal values using the one-sample t test. Triglycerides level was correlated to the different electrophysiological parameters using the Pearson correlation coefficient. P value <0.05 was considered significant.

## Results and discussion

We recruited 24 patients (21 males and 3 females) having an average age of  $43.0 \pm 12.3$  years, an average weight of  $80.6 \pm 15.6$  kg, an average blood cholesterol level of  $234.4 \pm 58.7$  mg/dl and an average triglyceride level of  $583.4 \pm 388.9$  mg/dl.

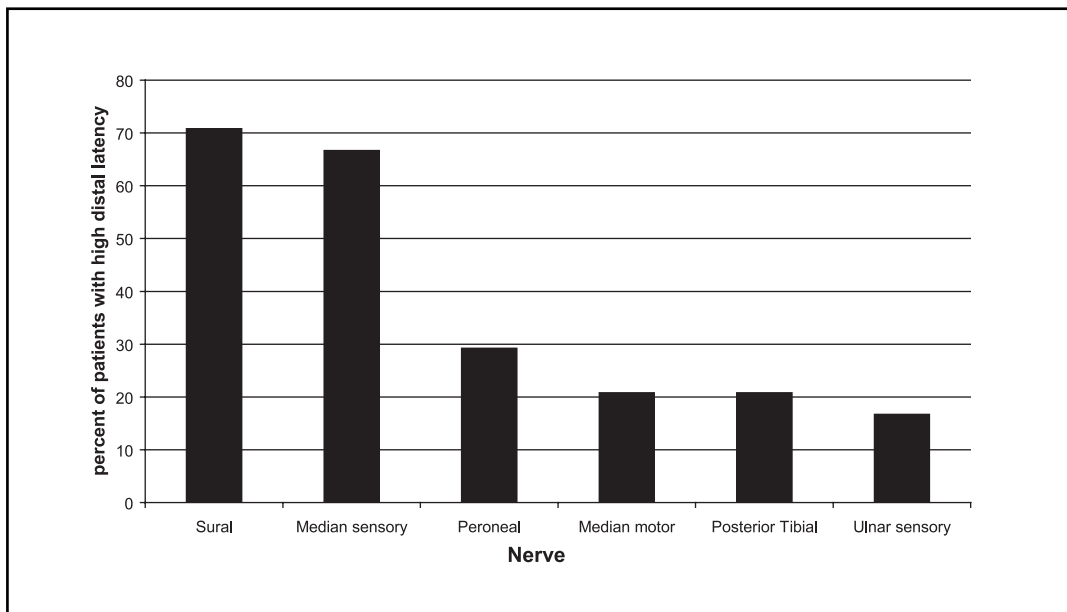
Our results show that 70.8% of the patients had a significant delay in the distal latencies of the sural nerves and 66.7% had a significant delay in the distal latencies of the median sensory fibers. The distal latencies of the peroneal, posterior tibial, median motor and ulnar nerves were also significantly delayed in 16.7 to 29.2% of the patients (Figure 1). The means of the distal latencies were significantly higher than the reference values in all the nerves ( $3.8 \pm 0.9$  vs.  $2.7 \pm 0.4$  msec for the sural nerve;  $3.0 \pm 0.5$  vs.  $2.5 \pm 0.2$  msec for the sensory fibers of the median nerve;  $4.2 \pm 0.7$  vs.  $3.3 \pm 0.6$  msec for the peroneal nerve;  $4.2 \pm 0.7$  vs.  $3.9 \pm 0.4$  msec for the posterior tibial nerve;  $3.7 \pm 0.5$  vs.  $3.2 \pm 0.4$  msec for the motor fibers of the median nerve) except the sensory branch of the ulnar nerve ( $2.3 \pm 0.4$  vs.  $2.4 \pm 0.2$  msec). The difference in the means was most pronounced in the peroneal and sural nerves (Figure 2).

54.2% of the patients had a significant decrease in the motor conduction velocity in the posterior tibial nerves and 33.3% had a significant decrease in the sensory conduction velocity in the sural nerves. The conduction velocities on the median nerve and peroneal nerves were decreased in around 20% of the patients (Figure 3). The means of the measured conduction velocities were significantly lower than the reference values in the posterior tibial nerve ( $47.9 \pm 4.0$  vs.  $52.5 \pm 2.5$  m/s), sural nerve ( $50.3 \pm 4.7$  vs.  $56.1 \pm 4.5$  m/s), sensory branch of the ulnar nerve ( $55.6 \pm 5.5$  vs.  $64.0 \pm 6.9$  m/s), and motor fibers of the median nerve ( $54.4 \pm 5.7$  vs.  $59.5 \pm 4.4$  m/s) but not in the peroneal and median sensory fibers (Figure 4).

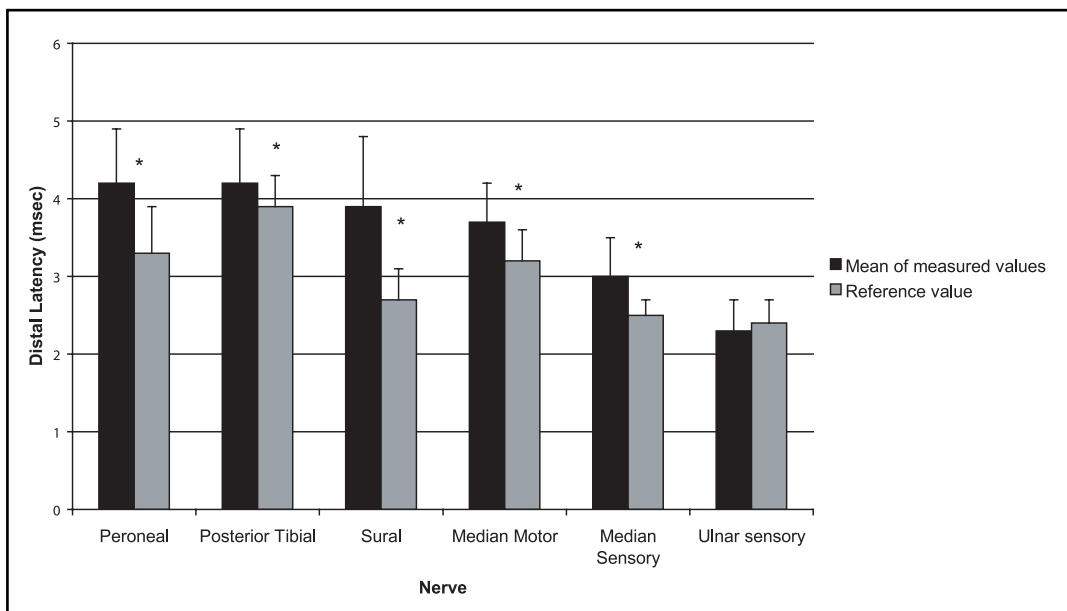
Amplitudes were the least if at all affected. Only two patients had the amplitudes of the sensory fibers of the median nerve considerably lower than the reference value.

Using the Pearson correlation coefficient, there was no significant correlation between the triglycerides levels and any of the measured electrophysiological parameters.

We studied a group of patients with very high triglyceride blood levels and no neurologic complaints. We found that a considerable number of our patients had delayed DL in 2 out of 6 nerves in the upper and lower extremities. In fact the means of the DL for 5 out of the 6 nerves studied in the patients population were significantly higher than the controls suggesting a tendency for delay in conduction distally in the nerves of patients with hypertriglyceridemia. Moreover, the means of the CV were significantly lower in 4 out of 6 nerves in the patient's population compared to the controls and more than half the patients had a decrease in the CV in the posterior tibial nerve. The pathology was most advanced in the nerves of the lower extremities (sural and posterior tibial) and both abnormal DL



**Figure 1.** Effects of amylin on PRL after intracerebroventricular (icv) administration. \*\* $p < 0,05$



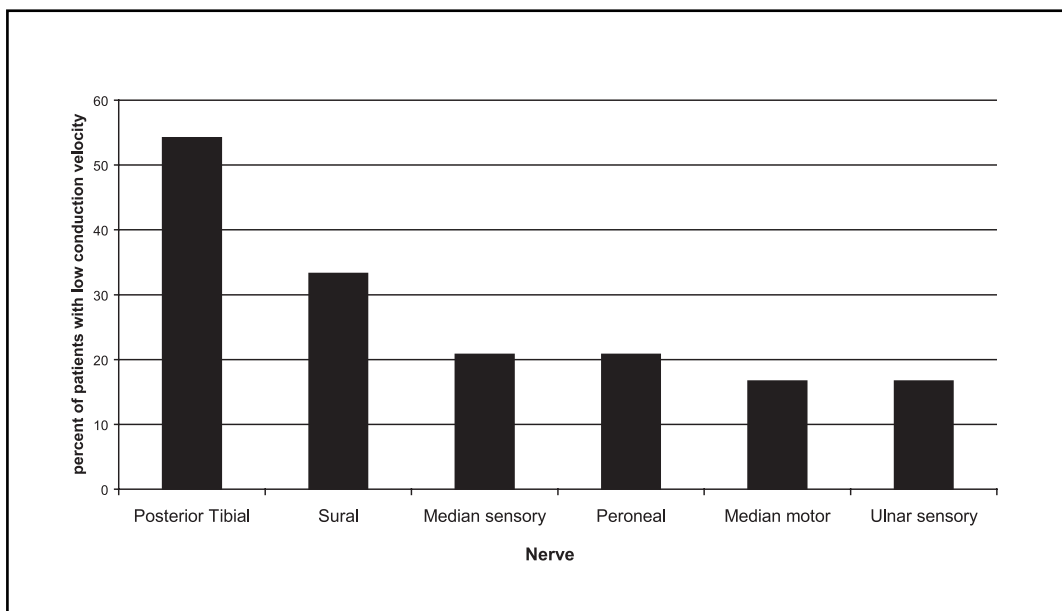
**Figure 2.** Comparison between the means of the measured distal latencies and the reference values reported in the literature for the different nerves.

and CV pointed out to a delay in conduction across the different segments studied. In addition it was noted that the pathology predominated in the sensory fibers (sural and median sensory) and in the longest nerves (posterior tibial). The nerve least affected was the ulnar nerve. All of the above complies with the definition of a polyneuropathy. Similar findings were reached by Drory et al who found a subclinical polyneuropathy in patients with extremely high levels of triglycerides. The study demonstrated that hypertriglyceridemia might be associated with mild axonal polyneuropathy [2].

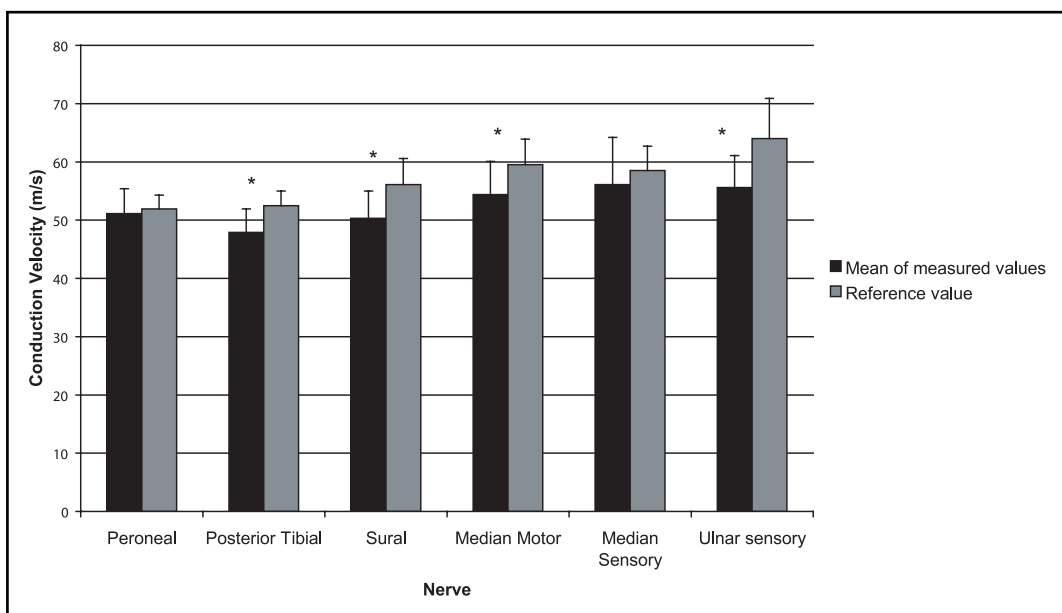
In addition, in 1994 McManis P.G. et al also described six patients with painful polyneuropathy who had markedly increased levels of triglycerides. It was concluded that hypertriglyceridemia caused

the peripheral neuropathy in these patients and the author recommended that serum lipid levels should be measured in patients with unexplained peripheral neuropathy to identify a potentially curable cause for this condition [8].

Another recent study that attempted to investigate the etiology of chronic idiopathic axonal polyneuropathy (CIAP), found that there were significantly higher triglycerides concentrations in the patients with CIAP as compared to control subjects from the same region. The authors documented that a logistic regression analysis identified environmental toxin exposure and hypertriglyceridemia as significant risk factors that should be further investigated as possible causes of CIAP [6].



**Figure 3.** Percent of patients with low conduction velocities (more than 2 standard deviations below the reference values) in the different nerves studied.



**Figure 4.** Comparison between the means of the measured conduction velocities and the reference values reported in the literature for the different nerves.

In this study, the sural nerve was one of the most commonly affected nerves with a delay in conduction velocity and a low distal latency. In 1971 Sandbank et al. observed severe electron microscopic alterations of myelin sheaths in the sural nerve obtained by biopsy in a patient with hyperlipemia and peripheral neuropathy [9]. The degree of abnormality in the nerves of our patients differed from the reference values much more in the measurements of the DLs than the measurements of the CVs and much more in the longer nerves of the lower extremities than the shorter nerves of the arm. These findings suggest an axonal pathology rather than focal demyelination. It is not possible without needle EMG analysis or nerve biopsy to ascertain whether

there is actual axonal damage or only metabolic dysfunction secondary to elevated triglycerides levels.

We conclude from this study that hypertriglyceridemia affects conduction parameters in peripheral nerves and the effect is more commonly seen distally and primarily in the sensory nerves. This is consistent with early peripheral neuropathy. These changes were present despite the fact that the patients were newly diagnosed with hypertriglyceridemia and asymptomatic neurologically. Therefore it might be useful to check TG serum levels in patients with a clinical or electrophysiological picture of a peripheral neuropathy especially if no other etiology is present. Prospective

studies are needed to establish the long-term effect of hypertriglyceridemia on peripheral nerves and whether treatment of the hypertriglyceridemia may improve the neuropathy.

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