Original Article

The Role of Hyperlipidemia on Nerve Conduction

Shaymaa J. Al-Shareefi (M.B.Ch.B, M.Sc.)*
Hedef D. El-Yassin (Ph.D post Doctorate)**
Abdul-Raheem H. Dawoud (M.B.Ch.B, Board.)*

Summary:

Background:
Previous reports suggested a connection between hyperlipidemia and neuropathy to cause focal neuropathy or generalized poly neuropathy. Only few cases were reported and these often involved individuals with other illnesses that themselves can cause neuropathy such as diabetes mellitus, hypertension, hyperuricemia and fatty liver.

Objectives:
This study was carried out to confirm the association of peripheral neuropathy with hyperlipidemia and to detect the type of that peripheral neuropathy, its distribution and whether the proximal or distal segment of the nerve is more affected.

Patients and methods:
Sixty eight patients (38 males and 30 females) aged 25-77 years with a mean age of (48.9±13.5) years. Forty two healthy subjects (24 males and 18 females) of matching age were involved in this study as control. Biochemical investigations included lipid profile, post parandial blood glucose, blood urea, serum creatinin and uric acid. Electrophysiological investigations included:

1.Sensory nerve conduction study: with measurement of sensory latency, amplitude and conduction velocity for median, ulnar, common peroneal and posterior tibial nerves for both right and left side of the body.

2.Motor nerve conduction study: which measures latency amplitude and conduction velocity of the CMAP for median ulnar, common peroneal and posterior tibial nerves for both right and left side of the body.

3.F-wave conduction study: that measures minimal f-wave latency and conduction velocity of median, common peroneal nerves bilaterally.

Results:
The results of sensory nerve conduction study reveled variable levels of significance between measured parameters of the same nerve and between different nerves. As for the motor nerve conduction study and f-wave conduction study they were all normal and with no abnormality that could be elicited.

Conclusion:
Hyperlipidemia could be associated with subclinical peripheral neuropathy which may occur more frequently in patients with very high levels of TG, TC and LDL. The type of peripheral neuropathy that occurs is mainly a sensory type, although motor neuropathy still cannot be excluded.

Keywords: fat disorder, hyperlipidemia, peripheral neuropathy, nerve conduction study

Fac Med Baghdad
2008; Vol. 50, No. 1
Received Oct. 2007
Accepted Nov.2007

**Department of Physiology, College of Medicine, University of Al-Basra*
***Department of Physiological Chemistry, College of Medicine, University of Baghdad*

Introduction:

Hyperlipidemia is a common metabolic disease characterized by abnormal lipid metabolism in which one of the major plasma lipoids-cholesterol (free esterified form) and triglycerides is /are elevated [1]. Recently the incidence and prevalence of hyperlipidemia increased greatly which increases the risk of coronary heart disease. and because metabolic disease affect all systems in the body including the peripheral nervous system but this in fact still not proved and there is a controversy whether to consider hyperlipidemia as a cause of peripheral neuropathy[2]. Many reports had suggested that hyperlipidemia can cause focal mono-neuropathy or generalized ploy-neuropathy. However only few cases where reported and these often involved individuals with other illnesses that may cause neuropathy like diabetes mellitus, hypertension, hyperuricemia and fatty liver[3].

The proportion of hyperlipidemic patients with poly-neuropathy is unknown and based on pervious literature reviews [4] . Therefore this study was carried out to confirm the association of peripheral neuropathy with hyperlipidemia and to detect its distribution and whether the proximal or distal segment of the nerve is affected more [5].

Patients and methods:

This is a prospective study conducted at the neurophysiology unit in Basra Teaching hospital and the Department of Physiological Chemistry, College of Medicine, University of Baghdad for the period July2005-April 2006. it includes 68 patients who attended the out patient clinic of the unit (38 males and 30 females) with age range between 25-77 years with a mean age (48.9±13.5) years. No one had any medical condition to be associated with poly neuropathy, unusual dietary habits, family history of peripheral nerve disease, or exposed to alcohol or to drugs with potential neurotoxic effects. And no one received any lipid lowering agents before the electrophysiological examination. They were carefully examined by a senior physician and showed no neurologica or dysautonomic symptoms. Forty two healthy subjects (24 males and 18 females of matching age were involved in this study as control.

Biochemical investigations included lipid profile post parandial blood glucose, blood urea, serum creatinin and uric acid. Electrophysiological investigations were conducted in a room temperature between 25-30°C and their body temperature was between 36.5-37.5°C measured by a thermometer at the axilla. All subjects were comfortably lying in a supine position with upper limps abduction 10-15° and lower limp flexion 10-15° at the knee joint. Computerized Micromed EMG system plus myoquick was used in all the electrophysiological analyses using surface stimulating and recording electrodes.

The electrophysiological study included:

1. Sensory nerve conduction study (SNCS) with measurement of sensory latency, amplitude and conduction velocity for median, ulnar, common peroneal and posterior tibial nerves for both right and left side of the body.
2. Motor nerve conduction study (MNCS) which measures latency amplitude and conduction velocity of the (compound muscle action potential (CMAP) for median ulnar, common peroneal and posterior tibial nerves for both right and left side of the body.
3. F-wave conduction study that measures minimal f-wave latency and conduction velocity of median, common peroneal nerves bilaterally.

Results:

From the total number of patients studied (68 patients), 21 patients (31%) of them were with abnormal electrophysiological results as seen in table 1.

Table 1: Percentage of patient with abnormal NCS results in each age group.

Age group	Male		Female		Total	
	No.	%	No.	%	No.	%
15-34	2	9.52	1	4.76	3	**14.28**
35-65	9	42.58	5	23.8	14	**66.66**
> 65	2	9.52	2	9.52	4	**19.04**
Total	**13**	**61.9**	**8**	**38.09**	**21**	**100**

A comparison is made between the data obtained from the right side of the body with those of the left side; no significant difference can be noticed in all the parameters measured and for all tested nerves.

The results of SNCS revealed variable levels of significance between measured parameters of the same nerve and between different nerves. Variation from the normal evoked response is due either to prolongation of distal sensory latency, reduction in amplitude, decrease in conduction velocity or combination of all in comparison with the same measured parameters of control group.(Table 2).

Table2: Results of SNC study of patients and controls with their level of significance.

	subject	no	Rt. Median N mean±SD	Rt. Ulnar N mean±SD	Rt. Com. P.N. mean±SD	Rt Post T.N. mean±SD
DSL (msec)	**Patients**	**68**	**2.65 ± 0.58**	**2.44 ± 0.5**	**3.52 ± 0.88**	3.6 ± 0.69
	Control	**42**	**2.44 ± 0.17**	**2.29 ± 0.16**	**3.05 ± 0.22**	3.12 ± 0.27
	P value		**S**	**NS**	**HS**	HS
Amplitude(μv)	**Patients**	**68**	**22.63 ± 5.5**	**20.75 ± 3.6**	**9.65 ± 2.97**	9.92 ±3.75
	Control	**42**	**25.25 ± 2.2**	**22.04 ±1.7**	**11.07 ± 1.37**	11.66 ± 1.81
	P value		**HS**	**S**	**HS**	HS
C.V. (m/sec)	**Patients**	**68**	**57.34 ± 7.1**	**57.55 ± 6.7**	**47.7 ± 8.19**	47.88± 8.01
	Control	**42**	**59.67 ± 3**	**59.41 ± 3.4**	**51.48 ± 4.55**	51.61 ± 3.97
	P value		S	NS	HS	HS

Fifteen patients were with abnormal results of posterior tibial nerve, 14 patients with abnormal common peroneal nerve results, 8 patients with abnormal median and 5 patients with abnormal ulnar nerve results, (table 3).

Table3: SNCS of each tested nerve

Nerve	DSL		Amplitude		C.V.	
	No.	%	No.	%	No.	%
Rt Median N	8	11.76	8	11.76	8	**11.76**
Rt. Ulnar N	5	7.35	5	7.35	5	**7.35**
Rt.Com. P.N.	14	20.58	14	20.58	14	**20.58**
Rt Post T.N.	**15**	**22.05**	**15**	**22.05**	**15**	**22.05**

Regarding MNCS and F-wave conduction study, they were all normal and no abnormality could be elicited.

The results of the biochemical assay revealed highly significant differences in mean values of lipid profile for the two patients' subgroups as compared with the control group , (table 4).

Table 4: Comparison of lipid profile between patients' subgroups and control group.

	Control mean±SD (no.=41)	Patients with normal sensory NCS mean±SD (no.=47)	Patients with abnormal sensory mean±SD (no.=21)
TC	**109.85 ± 15.01**	**243.27 ± 23.58****	251.09±16.32**
TG	**93.26 ± 17.88**	**323.25 ± 40.35****	329.42±35.87**
LDL	**17.55 ± 12.9**	**137.117 ± 24.13****	145.60±16.53**
HDL	**73.64 ± 7.43**	**41.51 ± 7.153****	39.61±7.01**
LDL/HDL	**0.24 ± 0.18**	**3.46 ± 1.09****	3.83±1.02**
VLDL	18.65 ± 3.57	64.64 ± 8.04**	65.87±7.17**

** Highly significant differences in comparison with control group $p<0.01$.

Discussion

The data from the studied series clearly demonstrate that sensory neuropathy may occur in patients with Hyperlipidemia but usually of subclinical type, which can be presented more frequently in patients with very high mean serum level of TG, TC and LDL. However, although motor neuropathy could not be traced in the patients included in this study, but this can not be ruled out completely especially at very high triglycerides and cholesterol levels. Meanwhile duration of the disease process might affect the results because the turnover rate of lipids of the myelin is slow. The amplitude of the sensory nerve action potential was affected more than the distal sensory latency and conduction velocity which was the first parameter to be affected [6,7,8].

The underlying mechanism of that is mixed axonal degeneration and segmental demyelination. However segmental demyelination is thought to be secondary to the axonal degeneration[9] . The electrophysiology abnormalities were found to affect both sides of the body equally, which indicate that the peripheral neuropathy associated with Hyperlipidemia is of symmetrical type[10]. Comparison of the nerve show that the median nerve was affected more frequently than ulnar nerve, while the common peroneal and posterior tibial nerves are affected to a certain degree equally. Beside

that the affection of nerve of lower extremities was more that that of the upper extremities, indicating that the effect of hyperlipidemia on the long nerves is more that that of the short nerves[11].

At the same time the effect was found to be distally while the proximal segment spared unaffected as its function was assesed by measurement of F-wave latency and conduction velocity which give normal results, many theories had been made to explain the possible relationship between lipid disorders and peripheral neuropathy, one of them assumes that the structural lipids are involved because of the abnormal serum lipid as in Bassen-Korzweing syndrome [7]. Since the turn over of lipids in the outer layers of the myelin sheath is considered to be more rapid than the inner layers, so there is a great possibility that serum lipid abnormality have a direct effect on cell membrane and might influence the structure of the more rapidly turning over outer layers of myelin sheath[12]. Another study suggests that the function and structure of the nerve could be affected by abnormal serum lipids by two mechanisms: one of them is by the action of lipoproteins as enzyme cofactors and as bound intermediate in the biosynthesis of polysaccharide and proteins, or because abnormal serum lipids could mediate nerve infarction via fat embolism o lipid induced platelet aggregation[13].

References

1. Smith GD and Ebrahim S." Is it time to call it a day" Int. J. of Epidemiology 2001; 30(1): 1-11.

2. Kimura J. " Electrodiagnosis in diseases of nerve and muscle. Principle and practice " 3rd ed Oxford press Inc. 2001.

3. Al-Rubayi HAA, El-Yassin HD and Al-Ani W. "Fat disorders and subclinical peripheral neuropathy". J Fac. Med. Bghdad 2001; 43(1): 91-94.

4. Ball RD " Electrodiagnostic evaluation of the peripheral nervous system In: Delisa J. Rehabilitation medicine Principle and Practice " 3rd ed. Lippincott company , Philadelphia 1993.

5. Vrancken AF, Franssen H, Wkke JH, Teunissen LL and Notermans NC. "Chronic idiopathic axonal polyneuropathy and successful aging of the peripheral nervous system in elderly people" Arch Neurol 2002; 59: 533-540.

6. Seley R, Stephens T and Tate P." Functional organization of nervous system In: anatomy and physiology" 4th ed. McGraw Hill company.

7. Drory V.E. Groozman GB , Rubinstien A and Korczyn AD. "Hypertriglyceridemia may cause subclinical peripheral neuropathy". Electromyog Clin neurophysiology 1999; 39: 39-41.

8. Court FA, Sherman DL, Pratt T and Garry EM." Restricted growth of schwann cells lacking cajal bands slows conduction in myelinated nerves" Nature 2004; 431: 191-195.

9. kassem HS, Azar ST, Zantout MS and Sawaya RA." Hypertriglyceridemia and peripheral neuropathy in neurologically asymptomatic patients" Neuroendocrinol. Lett. 2005; 26(6): 775-779.

10. Canron MH, Bouillot S, Favereaux A, Perty K and Vital A. "Structure of neuron" J PNS 2003; 8(1): 1-7.

11. Riboni LVA, Bassi R, Giussani P, Viani P and Tettamanti G." Sphingoid mediators in brain function and dysfunction" J Neuro Chem 2003; 85(2): 11-12.

12. Vincent AD, Robert C. Sergott T. James J, et al."Ischemic optic neuropathy as the first manifestation of elevated serum cholesterol level" Ophth. 2003; 110: 1041-1045.

13. Aravindan PD, Lioyed M." Scalp pain and hyperlipidemia" Int. J lin Pract 2000; 54(7): 478-490.