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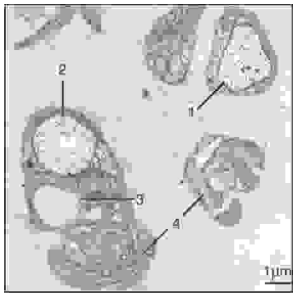
# DIABETIC POLYNEUROPATHY;

## EFFECT OF OMEGA-3 FATTY ACIDS ON NERVE CONDUCTION VELOCITY (NCV) AND F-WAVE LATENCY

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**ABSTRACT … Introduction:** Diabetes mellitus with the prevalence rate of 8.9-12.3% in human population, ultimately leads to the peripheral nervous system involvement in many patients. It causes various types of polyneuropathies which may manifest abnormalities such as impaired nerve conduction velocity (NCV) and prolonged F-wave latency. The aim of this study was to investigate the effect of omega-3 fatty acids on NCV and F-wave latency. **Material and Methods:** This clinical trial was performed on diabetic patients referring to the Diabetes Center of Shahid Bahonar Hospital in Kerman/Iran. Subjects were randomly divided to Omega-3 and Control (no treatment) group. Patients in the case group received three capsules of omega-3 daily and for the duration of 12 weeks. NCV and F-wave latency were determined in all patients before and after the treatment period. The rate of alterations in these variables in the two groups was analyzed by using statistical tests. **Results:** Controlling for baseline NCV and F- wave latency measures, follow up results showed no significant difference between the Omega-3 and the no-treatment group in accordance to somatic nerve measures. **Conclusion:** No significant difference in electro diagnostic indices was found before and after Omega-3 administration. This result may be due to using the combination of docosahexaenoic acid (DHA) and eicosapentaenoic acid(EPA).Short term administration and lack of sufficient time for drug efficacy can be other probable reason. Further studies with the administration of pure forms of EPA or DHA and longer period of administration are suggested.

**Key words:** Diabetes mellitus, Omega-3, Neuropathy.

## INTRODUCTION

Diabetes is one of the major diseases with various complications. The prevalence rate is 8.9%- 12.3% in human population. It leads to various complications in long term. Neuropathy is one of the most common diabetic complications[1]. Of the symmetrical diabetic neuropathies, distal symmetrical polyneuropathy, a predominantly axonal ,length dependent neuropathy is most prevalen[2]. The frequency of this complication in patients with long-term diabetes is approximately 50% which can observe in both insulin-dependent and non-insulin dependent patients. The diagnosis is based on history taking, physical exam, nerve conduction study (NCS), electromyoghraphy (EMG) and finally nerve biopsy[1].

Initially, there is no definite and approved treatment for this complication by FDA[3]. Fatty acids metabolism disturbance in diabetes has been determined and this phenomen is very important in the occurrence of peripheral neuropathy. Therefore, the administration of unsaturated fatty acids especially omega-3 has gained considerable attention recently. The effect of omega-3 fatty acid on the treatment of coronery arteries atherosclerosis has been shown[4]. Consumption of Omega-3 fatty acids in animal models would be effective in restoring nerve conduction velocity (NCV)[5-8]. The current study was undertaken to investigate the efficacy of Omega-3 fatty acid on diabetic peripheral neuropathy and its effects on NCV and F-wave latency in patients with non-insulin dependent (type II) diabetes mellitus.

## MATERIALS AND METHODS

The study was a randomized, single blind clinical trial. The studied population was diabetic patients referring to the Diabetes Center of Shahid Bahonar Hospital, Kerman, Iran. First, each patient was given written information about the study. Informed consent was obtained verbally and in writing from all participants and ethical approval was obtained from Ethics Committee then the referring patients were studied clinically by Internal Medicine and neurologist. The results of physical examinations as well as age, sex, type of diabetes, and the duration of disease were recorded. Then, in order to approve the diagnosis, those with the clinical diagnosis of symmetrical motor-sensory neuropathy were referred to the electro diagnosis clinic for performing NCV and EMG. After confirming the diagnosis of symmetrical motor-sensory neuropathy by NCV, EMG and F-wave latency recording, patients were randomly divided to two groups. The first administered three Omega-3 capsules daily and controls received placebo. Patients were following up for 12 weeks period. After that, they were referred for the second time to electro diagnosis clinic for performing NCV/EMG and recording NCV and F-wave latency. Electromyography findings of both groups containing motor NCV, Sensory NCV and F-wave latency prior and after omega-3 administration. Data were collected and analyzed with SPSS software ,Version 10 for Windows.

Results were summarized using mean ±SE for continuous variables and frequency for categorical variables. For the comparison of background qualitative and quantitative variables, t-test and Chi square test were used.

## RESULTS

Of the 22 subjects in the treatment group all were assessed for follow up and of 22 patients in the control group 17 were studied at follow up. The subjects in the treatment group were comparable to the control group according to demographic variables(i.e. age and sex), and mean duration of diabetes (Table I).

**Table-I. Comparison of baseline characteristics in the two groups**

| | Treatment (n=22) | Control (n=17) | P value |
|---|---|---|---|
| Age mean (SD) | 58.0(2.0) | 53.8 (1.9) | 0.15 |
| Male / Female | 2/18 | 3/14 | 0.50 |
| Duration of diabetes years mean (SD) | 12.8 (1.3) | 11.2 (1.7) | 0.45 |

All of the study subjects had diabetes type II. Controlling for baseline NCV and F wave latency measures the follow up results are compared between the two groups.

At follow up the treatment group showed no significant difference comparing to control group in accordance to somatic nerve function measures (Table II & III). No serious side effects were observed the therapeutic Trial.

**Table-II. Comparison of NCV between two groups**

| Nerve Group | Treatment group | Controls | P value |
|---|---|---|---|
| Median (motor) | 47.67 | 47.18 | 0.4 |
| Ulnar (motor) | 50.05 | 49.31 | 0.28 |
| Deep peroneal (motor) | 37.71 | 37.7 | 0.9 |
| Tibial (motor) | 37.66 | 37.48 | 0.75 |
| Median (sensory) | 11.11 | 10.58 | 0.5 |
| Ulnar (sensory) | 13.16 | 11.93 | 0.09 |

**Table-III. Minimum latency of F wave in two groups**

| Nerve Group | Treatment group | Controls | P value |
|---|---|---|---|
| Median | 26.79 | 27.26 | 0.2 |
| Ulnar | 29 | 28.94 | 0.9 |
| Deep peroneal | 51.33 | 51.47 | 0.84 |
| Tibial | 51.58 | 55.18 | 0.15 |

Although the study did not show significant statistical differences, the primary end-point measure, namely, improve NCV and F. wave latency.

## DISCUSSION

Many mechanisms have been advanced for the pathogenesis of diabetic neuropathy ,including I). metabolic processes directly affecting nerve Fibers, II). endoneurial micro vascular disease, III). auto immune inflammation ,and (IV) deranged neuropathic support. Attempts to treat diabetic neuropathy by manipulating nerve metabolism have been disappointing. Advances in treatment of diabetic neuropathy are focusing on at least four areas: neuropeptide manipulation ,antioxidant treatment ,NMDA antagonist therapy ,and essential fatty acid supplementation.

The longitudinal use of objective reproducible measures is critical to judge the course of diabetic neuropathy and especially response to therapy. As to the role of essential fatty acid in diabetic neuropathy, experimental evidence suggesting that the conversion of linoleic to gamma linoleic acid (GLA) is impaired in human diabetes[2]. Diabetes impairs essential fatty acid metabolism by decreasing activities of ?6 and ?5 de-saturates, enzymes that convert dietary linoleic acid (LA) and α-linolenic acid to long–chain polyunsaturated fatty acids (PUFA),including ý-linolenic acid (GLA) ,arachidonic acid (AA), eicosapentanoic acid (EPA) ,and docosahexanoic acid (DHA)[3,9,10].

Fatty acid imbalance contributes to reductions in peripheral nerve conduction velocity and blood Flow[4]. This fatty acid imbalance may be corrected by dietary supplements[11]. This result could be explained in part by a normalization of eicosanoid synthesis ,which is depressed in diabetic nerve, and/or by a direct effect on in corporation of these fatty acid into the plasma membranes[3]. By changing membrane properties ,PUFA can modify the activity of trans-membrane enzymes, such as Na,K-Atpase, which is implicated in the propagation of nerve impulses[7].

Dines and et al. examined the efficacy of a number of GLA sources, such as borage oil ,black current oil ,and evening primrose oil in correcting motor and sensory deficits in the rat diabetic model and found that omega-3 fatty acids dietary improves NCV of sciatic nerve in rat[5]. Gerbi and coworkers, too showed an improvement in NCV in rat following omega-3 fatty acid –containing diet[7]. Jarahi and coworkers found the beneficial effects of omega-3 containing diet on NCV in diabetic rats. That is, their administered diet prevented NCV decrease in diabetic rats[8]. Okuda et al. showed significant beneficial effects of highly purified eicosapentaenoic acid on diabetic peripheral neuropathy and serum lipids as well as other diabetic complications such as nephropathy and microangiopathy[12]. In other hand, Coste et al. showed Fish oil supplementation (n-3)fatty acids containing

docosohexaenoic acid (DHA) and eicosapentaenoic acid (EPA) ,were less effective on diabetic neuropathy that (n-6) fatty acids[3].

This partial effect of (n-3) fatty acids might be attributed to the presence of EPA ,a competitor of arachidonic acid ,which enhanced the diabetes induced decrease of this fatty acid in serum and tissues. They determined a supplementation with DHA alone could prevent neuropathy in stereptozotocin induced diabetic rats. thus they suggest, treatment with DHA phospholipids could be suitable for evaluation in clinical trials[3].

Considering the above contraversies, in this study we used a combination of omega-3 fatty acids: Eicosapentaoenoic acid C20:5 omega-3(EPA), 2-Docosahexaenoic C22:6 omega-3 acid (DhA). Meanwhile for the first time we applied electro diagnostic indices of NCV & F-wave latency in this clinical trial. In Shimida and coworkers study in 1998 ,NCV and F-wave latency have been introduced as the best criteria for studying diabetic neuropathy in clinical trials[13]. No significant difference in electro diagnostic indices was found before and after Omega-3 administration. This result may be due to using the combination of DHA and EPA as it has been shown in Coste et al study. Short term administration and lack of sufficient time for drug efficacy can be other probable reason. Further studies with the administration of pure forms of EPA or DHA and longer period of administration are suggested.

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