MANAGEMENT OF DIABETIC PERIPHERAL NEUTOPATHY (DPN) USING LOW FREQUENCY PULSED ELECTRO MAGNETIC FIELD (LF-PEMF)

POSTER # 272

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ABSTRACT

Abstract

Objective: To evaluate the effectiveness of LF - PEMF in the management of DPN symptoms.

Methods: A comparative observational study of 60 patients, male and female (1:1) aged 60 to 85 years. Enrolment criteria - known diabetics, HbA1c 7 to 9 and DPN of 1-5 years. Patients were randomized into 2 treatment groups G1 and G2. The study period was 4 weeks with results assessed at baseline and bi-weekly follow-ups using diabetic neuropathy symptom (DNS) score.

G1: 30 patients with an established DPN were treated with LF-PEMF therapy - frequency of 10Hz, thru two emitters of 20 mTl and 6 mTl, keeping north polarity was towards the body. A total of 15 sitting of 20 (10 + 10) minutes - one per day.

G2: 30 patients with an established DPN were continued on oral symptomatic treatment options like - amitriptyline, duloxetine, gabapentin, pregabalin and tramadol.

Patients in both the groups were on Vitamin B 12 + Alpha Liponic Acid which was continued.

Results: In **G1** application of LF-PEMF therapy significantly facilitated the regression of the main clinical symptoms of DPN. Patient scores were more differentiated on DNS score. Complete relief in the symptoms of DPN DNS0 score was achieved in 4 patients at W2 which sustained at 4 patients at W4. DNS1 score was achieved in 10 patients. DNS2 score was achieved in 8 patients at W2 which was sustained at W4. Overall 22 patients had a relief of main clinical symptoms on the DNS score.

In **G2** there was a mild regression of the main clinical symptoms of DPN. Complete relief in the symptoms of DPN on DNS0 score was achieved in 0 patients at W2 and in 1 patient at W4. DNS1 score was achieved in 2 patients at W2 which sustained at 2 patients at W4. DNS2 score was achieved in 7 patients at W2 which increased to 11 patients at W4. Overall 9 patients had a relief of main clinical symptoms on the DNS score at W2 which increased to 15 patients at W4 with continuation of oral symptomatic drugs.

Conclusion: The present study provides convincing data regarding the effectiveness of LF-PEMF therapy, on patients with DPN symptoms. The usage of oral symptomatic drugs is limited due to the high frequency of adverse events, lack of evidence of long term efficacy and concern about dependence. Considering the benefits and safety, in comparison to oral symptomatic drugs, LF-PEMF can be used as an adjacent in the management of diabetic neuropathy cases. A bigger study is warranted to determine whether DPN can be modulated with LF-PEMF and how it can influence nerve regeneration. Limitations of this study include small sample size, short duration of treatment and non-availability of follow-up data.

BACKGROUND

DPN is one of the most common and serious complications of both T1DM and T2DM, and one of the major cause of nontraumatic amputations. Prolonged exposure of peripheral nerves to hyperglycemia in long standing diabetics predisposes them to development of neuropathy. The role of glycemic control in development as well as progression of DPN is supported by the available evidence

A widely-accepted definition of diabetic peripheral neuropathy is “the presence of symptoms and / or signs of peripheral nerve dysfunction in people with diabetes after exclusion of other causes”. Depending on criteria, DPN is estimated to occur in 50–90% of individuals with diabetes for more than 10 years. The etiology of DPN is not well understood because it is based on the clinical symptoms of individuals.

DPN can cause symptoms that last for years and severely impair quality of life, and it’s prevalence is 26.4% in DM.

The treatment options are limited, which may explain why up to 50% of patients have not requested or received treatment for the condition. Analgesics, antidepressants and anticonvulsants are often prescribed, with varied responses but have significant side effects and addiction profiles. In some PEMF studies, the experimental groups showed improvement in distal latency, which can be attributed to indirect effect of PEMF, that is it augments angiogenesis by stimulating endothelial release of fibroblast growth factor beta-2. Some studies showed that PEMF stimulate the arteriolar microvessel diameters in rat cremester muscle, which further support that it improves the microenvironment for the tissues leading to regeneration. One of the approaches which is currently of clinical interest includes LF-PEMF, which have analgesic, neurostimulatory, trophic, and vasoactive actions. The efficacy of LF-PEMF which induces quasirectangular currents that can depolarize, repolarize, hyperpolarize neurons and can potentially modulate neuropathic pain and nerve impulse. It stimulates the cell power stations and enhances cell metabolism resulting in higher mucosal content of RNA, DNA and improve the microcirculation due to an increased release of calcitonin gene related peptide, a bioactive messenger responsible for the formation of capillaries in wound area. The most common presenting symptom of DPN is burning / aching pain in one or both lower limbs. Pricking sensation was the next common symptom followed by unsteadiness on walking and numbness in that order.

OBJECTIVES

To evaluate the effectiveness of LF-PEMF in the management of DPN symptoms. To compare LF-PEMF treatment with the oral symptomatic treatment drugs (analgesics, antidepressants and anticonvulsants).

MATERIALS & METHODS

Study Design (Figure 1):

A comparative observational study of 60 patients, male and female (1:1) aged 60 to 85 years. Enrolment criteria - known diabetics, HbA1c 7 to 9 and DPN of 1-5 years. Patients were randomized into 2 treatment groups G1 and G2 (Table 1). The study period was 4 weeks with results assessed at baseline and bi-weekly follow-ups using diabetic neuropathy symptom (DNS) score. All patients were having a starting DNS score of 3 or 4.

G1: 30 patients with an established DPN, with DNS score of 4 – 16 patients and DNS score of 3 – 14 patients, who were treated with PEMF therapy.

G2: 30 patients with an established DPN, with DNS score of 4 – 14 patients and DNS score of 3 – 16 patients, were continued on oral symptomatic treatment options like – pregabalin, gabapentin, duloxetine, tramadol and amitriptyline.

Patients in both the groups were on Vitamin B 12 + Alpha Liponic Acid, which were continued in both groups.

Time Frame: Study period is from October 1st 2016 to November 15th 2016. The first patient was enrolled on October 1st 2016 and the last patient was enrolled on 15th October 2016.

Target population: Elderly Diabetic population aged 60-85 Male to Female 1:1, HbA1C 7 – 9 and DPN of 1 – 5 years with DNS score of 4 and 3.

Exclusion criteria: Patients with electronic implants like pace maker or insulin pump, oncology, bleeding disorders, hemorrhage and coagulopathy, acute period of myocardial infarction, tuberculosis, infection or ischemic and hemorrhagic stroke,

Device used: Almag-02 manufactured by Elamed, Russia. Two sets of emitters of 20 and 6 mTl were used. frequency: 10Hz, keeping north polarity towards the body. A total of 15 sitting of 20 (10 + 10) minutes - one per day.

End points: To review the effect of treatment with LF- PEMF treatment on pain and sensitivity in patients with DPN compared with oral symptomatic drugs (Table 1). The DNS score (Table 2) is a validated and widely accepted scoring system for screening of diabetic neuropathy. It comprises four questions in relation to the symptoms of diabetic neuropathy. 1. Burning, aching pain or tenderness in legs or feet, 2. Prickling sensations, 3. Numbness in legs or feet and 4. Unsteadiness in walking. It is calculated on the basis of total positive replies. DNS greater than one is considered as presence of diabetic peripheral neuropathy. This score is also valid to be used for predictive purpose or prognostics

Figure 1: Study design.

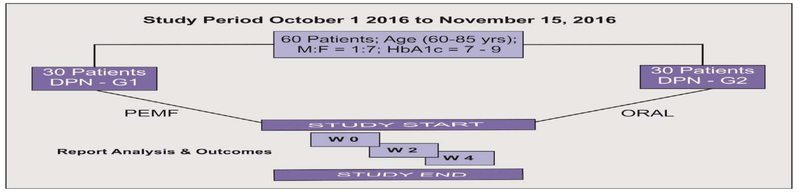


Table 1:

Treatment		No. of Patients
G2 + Oral symptomatic Drugs	Pregabalin	8
	Gabapentine	8
	Duloxitine + Tramadol	6
	Gabapentine + Amytriptyline	8
G1 + Pulsed Electro Magnetic Field		30

Number of patients on LF-PEMF and oral symptomatic drugs

Table 2:

DNS items	Rate
Unsteadiness in walking	0 = absent, 1 = present
Numbness	0 = absent, 1 = present
Prickling sensations	0 = absent, 1 = present
Burning, aching pain or tenderness in legs or feet	0 = absent, 1 = present

Diabetic neuropathy symptom score (DNS 0 to 4)

RESULTS

Patient scores were differentiated on DNS score .DNS score of 0 and 1 was considered a satisfactory result – moderate relif in neuropathic symptoms , score 2 as mild relief ,score 3 and 4 considered as no relief in the symptoms.

In **G1** (Table 3), application of LF - PEMF therapy significantly facilitated the regression of the main clinical symptoms of DPN. Out of 30 patients with DNS score of 4 and 3 we achieved a DNS score of 0 in 4 patients, DNS score of 1 in 10 patients, DNS score of 2 in 8 patients and DNS score 3 in 2 patients, There was no relief in the symptoms or DNS score of 4 in 6 patients at W2 which sustained to W4. Overall 22 patients had some relief from main clinical symptoms on the DNS score.

In **G2** (Table 4), there was a mild regression of the main clinical symptoms of DPN. Out of 30 patients with DNS score of 4 and 3 we achieved a DNS score of 0 in 0 patients at W2 and in 1 patient at W4. DNS score of 1 was achieved in 2 patients at W2 which sustained at 2 patients at W4. DNS score of 2 was achieved in 7 patients at W2 which increased to 11 patients at W4. Overall 14 patients had a relief of main clinical symptoms on the DNS score.

Table 3:

G1		Low Frequency - Pulsed Electro Magnetic Field																													
Patient #		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
DNS Scoring	W0	4	4	3	3	3	4	4	4	3	3	3	4	4	4	4	3	4	3	3	4	4	4	3	3	4	3	4	3	3	4
	W2	4	2	1	0	1	2	4	4	2	1	1	4	2	3	1	2	3	1	0	2	4	4	1	1	0	1	2	1	0	2
	W4	4	2	1	0	1	2	4	4	2	1	1	4	2	3	1	2	3	1	0	2	4	4	1	1	0	1	2	1	0	2

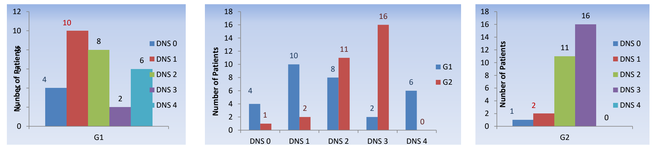
Individual DNS score of patients on LF-PEMF in G1

Table 4:

G2		Pregabalin								Gabapentin								Duloxitine + Tramadol						Gabapentine + Amitriptylline							
Patient #		1	2	3	4	5	6	7	8	1	2	3	4	5	6	7	8	1	2	3	4	5	6	1	2	3	4	5	6	7	8
DNS Scoring	W0	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	3	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	W2	2	3	3	2	3	3	2	3	3	2	2	3	3	3	3	2	3	1	4	3	3	3	3	4	3	1	3	3	2	3
	W4	2	3	3	2	3	3	2	3	3	2	2	3	3	3	3	2	3	1	3	2	2	3	3	3	2	1	3	2	0	2

Individual DNS score of patients on oral symptomatic drugs in G2

Figure 2:



Number of patients achieving DNS 0, DNS 1, DNS2 , DNS 3 and DNS 4 in G1 and G2. at W4

SUMMARY

In the present study, we achieved better relief in the symptoms of DPN with LF-PEMF as compared to oral symptomatic drugs. In PEMF group we achieved an overall relief in the symptoms of DPN as per DNS score of 0-1 in 14 patients and 0-2 in 22 patients. Whereas in the oral symptomatic drugs group the relief in the symptoms of DPN as per DNS score of 0-1 in 3 patients and 0-2 were in 11 patients. The above results of the study suggest that treatment with LF-PEMF gives a faster and better improvement in the symptoms of DPN as compared to oral symptomatic drugs. DPN is best classified as axonal neuropathy, in that, predominant neuropathic feature is nerve fiber loss. The effects of LF-PEMF is to trigger a biologic response such as cell proliferation that represent the basic effect to explain some relevant results. Recently, it has been observed that PEMF modulates the neurite growth *in vitro* and nerve regeneration *in vivo,* which further explains the improvement obtained in G1.

In DPN, the pain may result due to various reasons such as increase in different signals from degenerating nociceptive afferent fibers, depolarization because of dysregulation of normal sodium, calcium and potassium channel activities. It is well known that a biological system exposed to a physical stimulus (LF-PEMF) is able to detect its presence and to modify its own biological activity depending on the characteristic of the applied stimulus such as mechanic, electric, or magnetic. In particular, static and time varying magnetic fields have been shown to alter animal and human behaviors such as pain perception. The pain relief in G1 could be attributed to the effect that magnetic fields affects pain perception by direct effects in form of neuron firing, calcium ion movement, endorphin levels, acupuncture action, and nerve regeneration. The LF-PEMF influence diabetic neurons and cell membrane of cutaneous nociceptors thereby inducing change in the cellular and pericellular microenvironment. Other probable reason for the improvement may be that it stimulates neurotrophic factors that are known to play an important role in the development, maintenance, and survival of neuronal tissues. Few studies suggested that endoneurial capillaries in peripheral nerves of diabetics are thickened and perineurial basement membrane widened. A permeability disorder at the blood nerve or blood perineurial barrier in diabetics could lead to endoneurial metabolic derangements, possibly resulting in neuropathy. LF-PEMF by targeting increased circulation and anti inflammatory effects combined with the pain relief and restoration of normal nerve conduction lead to reversal of the damage that cause DPN.

LIMITATIONS

Limitations of this study include small sample size, short duration of treatment, and non-availability of follow-up data. The limited number of studies involving electromagnetic stimulation, the different treatments studied, the different parameters used and the low quality of included studies demonstrate the need for further randomized clinical trials designed with greater methodological rigor to establish the true efficacy of these therapies in diabetic neuropathy.

CONCLUSION

The present study provides convincing data regarding the effectiveness of LF - PEMF therapy, on patients with DPN symptoms. The usage of oral symptomatic drugs is limited due to the high frequency of adverse events, lack of evidence of long term efficacy and concern about dependence. Considering the benefits and safety, in comparison to oral symptomatic drugs, LF - PEMF can be used as an adjunct in the management of diabetic neuropathy cases. A bigger study is warranted to determine whether DPN can be modulated with LF - PEMF and how it can influence nerve regeneration. It can be concluded that available data provides evidence that LF-PEMF treatment has the potential to modulate neuropathic pain and nerve impulse. Considering its benefit and safety, LF-PEMF can be used as an adjunct in the management of DPN cases.

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Abbreviations: LF-PEMF – low frequency pulsed electro magnetic field; DPN – diabetic polyneuropathy; HbA1C - glycosylated haemoglobin; G1 – group 1; G2 – group 2; Hz – hertz; mTl – microtesla; DNS – diabetic neuropathy symptom; T1DM – type 1 diabetes mellitus; T2DM – type 2 diabetes mellitus; M – male; F – female; W – week;.

Disclaimer: There was a typo error in the result part of the abstract which has been rectified.

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