

EFFECT of HIGH TONE POWER THERAPY on NEUROPHYSIOLOGICAL MEASURES and FUNCTION OUTCOME in PATIENTS with DIABETIC NEUROPATHY

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Abstract:

Objective: Investigate high tone therapy effect on neurophysiological measures and function outcome in diabetic neuropathy.

Methods: Forty patients assigned randomly into high tone therapy and conventional therapy groups. Patients assessed by neurophysiological studies for median and sural sensory nerves and activities of daily living assessed by Katz Index of Independence.

Results: Neurophysiological measures for median and sural sensory nerves were significantly improved in high tone therapy group but not in conventional therapy group. The function outcome was significantly improved in both groups with the best results for high tone therapy group.

Conclusion: High tone therapy was able to improve neurophysiological measures and function outcome in diabetic neuropathy patients.

Keywords: *High tone power therapy, Neurophysiological measures, Diabetic neuropathy, Function outcome, Electrotherapy*

INTRODUCTION

Diabetic neuropathy (DN) represents 30 % up to 50% of chronic complication among diabetic patients due to progressive symmetrical nerve damage and impair of nerve regeneration subsequently leads to material morbidities as pains, foot ulcer, and low limb amputation (Pop-Busui, 2017). Although there are several pharmacological and non-pharmacological treatments for DN the approved pathogenic modifying therapies for DN not exit yet (Hicks and Selvin, 2019 and Brill et al., 2018). Even intensive glycemic control is not enough to prevent neuropathy in those with type 2 diabetes mellitus (T2DM) (Callaghan et al., 2018). Furthermore, constructed exercise training and encouraged physical activity for people with DN played big roles on primary prevention and delay the DN onset which can be challenging due to multiple comorbidity and peripheral insensitivity and could be led to injury. Painful DN pharmacotherapy is not entirely satisfactory as available treatments and often ineffective and/or led to many negative effects (Tesfaye, 2019).

Electro therapeutic modalities are used extensively for both research and clinic setting to decrease pain in general and neuropathy pain due to DN (**Shanmugam et al., 2017, Adehunoluwa et al., 2019 and Mokhtari et al., 2020**). High tone therapy (HTT) is a unique characteristic form of electrotherapy that introduce energy into the body to activate cells and to revitalize the body, producing a resonance effect that creates an oscillation or vibration in the cells, and tissues to promote metabolism and relieve pain, scattering the mediators of pain and inflammation, nutrients and waste substances and normalizing the cell and organism metabolism, and nerve regeneration (**Reichstein et al., 2005**). The main target is study HTT effects on neurophysiological parameter for those patients with symptomatic DN.

MATERIALS AND METHODS

Subjects

Forty DN patients were recruited by a specialized neurologist from the Outpatient Clinics of Neurology, Internal Medicine, Neurophysiology unit in Kasr Al- Aini Hospitals, Outpatient Clinic of Neurology, Faculty of Physical Therapy, Cairo University. The primary criteria and patients' characteristics shown in Table (1). All patients from both genders diagnosed as T2DM with a history of ≥ 10 years documented by Neuropathy disability score (NDS) (**Boulton, 2005**), general clinical evaluation sheet including vibration sense through used 128-Hz tuning fork from bony prominence of big toe, and tendon reflex (**Koutoukidis et al., 2017**). In addition, DN was documented by impaired sensory and/or motor conduction velocity in a minimum one nerve of lower limbs (**Preston and Shapiro, 2013**). Cases received glycemic control agents without changes at least through four weeks prior to recruitment and along the study. Furthermore, all patients instructed to do not use analgesics, anti-convalescents medications. Patients were excluded if they had uncontrolled blood glucose level with fasting plasma glucose ≥ 126 mg/dl and randomly plasma glucose ≥ 200 mg/dl (**ADA, 2014**), other neuromuscular abnormalities, musculoskeletal deformities, and disorders such as radiculopathy and amputations. All patients written informed consent before the study.

Study design: as shown in (Fig.1).

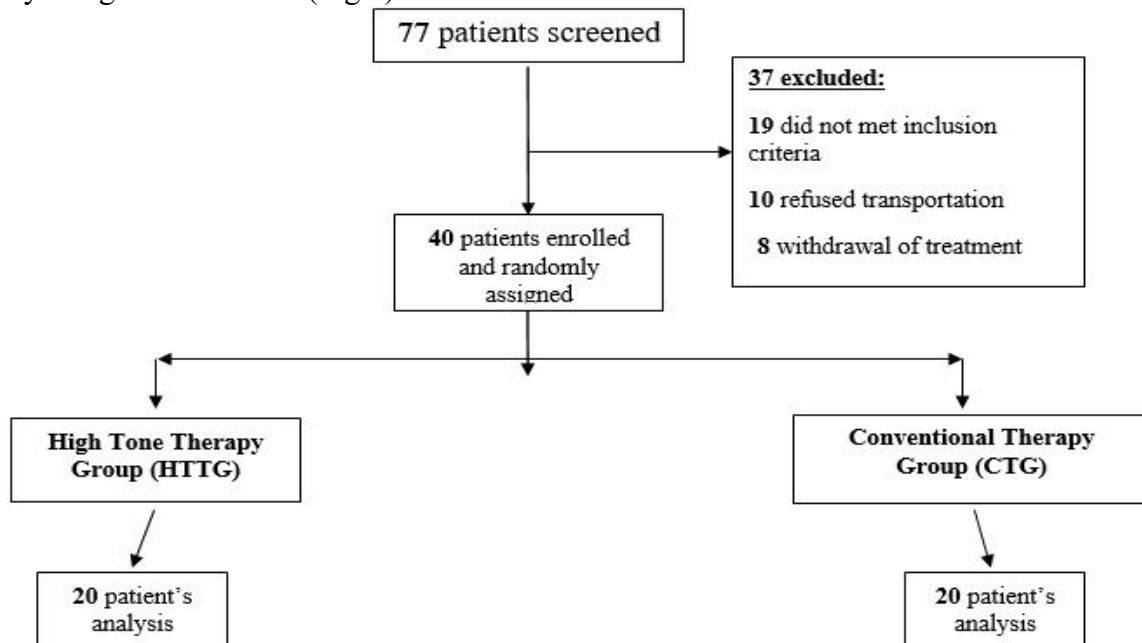


Fig. (1): Flow chart of the subjects

Design of study

A randomized controlled study and double blinded (all patients were assessed by the same physician before and after treatment. Neither the investigator nor the patients informed of the treatment assignments). Patients divided randomly using a secure system of opaque closed envelopes that was assigned either HTTG or CTG.

Procedure

Assessment

Electrophysiological Test for median and sural nerves sensory conduction studies were measured by a neurophysiologist. All measures performed by using (Nihon Kohen, Japan, MEB-9200/9300). Sural nerve conduction study does by put active pick-up electrode posterior and below lateral malleolus. Electrode put for three cm distal for active electrode and ground electrode put among stimulator cathode and active pickup electrode. Median sensory nerve conduction study achieved through putting stimulating electrode at wrist, cathode directed toward active recording electrode which is placed at 2nd digit (Distance between stimulating and recording sites 5 cm) and ground electrode put among stimulator cathode and active recording electrode.

Treatment Procedure

For HTT group

External muscles stimulation was performed by used HiToP191 device; (gbo Medizintechnik, Rimbach, Germany). From the technical point of view, HiToP191 device provided therapy with middle frequency sine waves. The therapy is free of direct current (D.C.) components. The amplitude and the frequency of carrier wave modulate simultaneous. Wave scanning frequencies from 4,096 Hz to 32,768 Hz and crossing the patient's electro-sensitive threshold curve leads to strong muscular stimulation through tetanic contraction for the trained muscles by 20 Hz (typical: 3 seconds ramp - 3 seconds stimulation. - 3 seconds pause). More energy could introduce correlated to individual electro-sensitive threshold curve. HTT electrodes placed on both quadriceps muscle. Electrical stimulation intensities adjusted for produce visible pleasant muscles contraction A typical value for the current intensity is 150 – 200 mA. The duration of HTT lasting for one hour every session. In addition to HTT, the patients in this group received gentle passive stretching and graduated active range exercise for both upper limbs and lower limbs, Balance training inform of Wobble board training, and graduated gait training for one hour.

For conventional therapy group

All patients in this group receive selective physical therapy program only as HTTG with same duration.

Primary outcome

Investigate high tone therapy effect on neurophysiological measures in diabetic neuropathy patients.

Secondary outcome

Investigate high tone therapy effect on function outcome in diabetic neuropathy patients assessed cases by Katz Index of Independence. A score of 6 indicated full function, 4

indicated moderate impairment, and 2 or less indicate many functionally impairment (Wallace and Shelkey, 2007).

Statistical analysis

Continuous results analyzed by SPSS version 25. Calculating mean and median values, and finally using Kolmogorov-Smirnov and Shapiro-Wilk tests. Baseline results throughout descriptive statistics and t-test. Neurophysiological measures and function outcome analyzed by MANOVA. Bonferroni's post hoc test use for pair-wise comparing among studied groups. $P < .05$.

RESULTS

Of the 77 patients screened for the study, 37 patients were excluded due to some of them did not met inclusion criteria and others denied. The remaining 40 cases randomly to HTTG (n = 20) or CTG (n = 20). Demographic data showed that, there were insignificant difference between both groups as shown in Table (1).

Table (1): Participant Descriptive Data.

General Characteristics	HTTG	CTG	MD	p-value	Sig
	$\bar{X} \pm SD$	$\bar{X} \pm SD$			
Age (years)	52.2 ± 4.87	51.2 ± 5.04	-0.07	0.96	NS
Weight (kg)	67.8 ± 2.74	68.15 ± 2.85	-1.74	0.43	NS
Height (cm)	170.8 ± 2.72	171.4 ± 3.06	-2.8	0.41	NS
BMI (kg/m ²)	23.2 ± 1.06	23.21 ± 1.15	0.12	0.88	NS
Gender					
Male	8	8			
Female	12	12			
Diabetes duration	≥ 10 years	≥ 10 years			

NS: Non-Significant BMI: Body mass index. \bar{x} : Mean SD: Standard deviation MD: Mean difference p-value: Probability value

Electrophysiological parameters

No significantly differ between both groups. At end of study the data showed a statistically significant improvement of median and sural sensory nerves peak latency in HTTG ($p = 0.0001$). While in CTG there were insignificant differences at end of study ($p = 0.36$) and ($p = 0.02$) for sural and median respectively. The percentage of improvement was 34.06 % in HTTG. However, CTG showed an improvement of 5.13 %.

For median and sural sensory nerves amplitude, CTG did not show any improvement at end of study compared with pre-treatment ($p = 0.64$) for median, ($p = 0.07$) for sural nerves. On the other side, significantly differ in median and sural sensory nerves amplitude of HTTG at post-treatment comparing with pre-treatment and among studied groups at end of study ($p = 0.0001$). The percent of change was 56.95 % in HTTG. However, CTG showed an improvement of 1.85 %, as presented in Table (2).

After four-weeks of treatment, HTTG showed a statistically significant improvement of median and sural sensory nerves NCV. Furthermore, there significantly differ among groups after ending our investigation ($p = 0.0001$) and ($p = 0.009$) for sural and median, respectively. Regarding to CTG the results revealed that there was no improvement of these parameters compared with pre-treatment ($p = 0.7$) for median and ($p = 0.38$) for sural nerves. The

percentage of improvement was 16.1 % in HTTG. However, CTG showed an improvement of 0.63 % as presented in Table (2).

Katz index

Both Groups showed an improvement regarding to Katz index with superiority of HTTG on CTG. The percent of change was 56.52% and 4.23% in HTTG and CTG, respectively, showed in Table (2).

Table (2): Comparison of Electrophysiological parameters and Katz index between both groups.

Variables	HTTG (n=20) $\bar{X} \pm SD$	CTG (n=20) $\bar{X} \pm SD$	MD	p- Value	Sig
MSNPL (ms) Pre Post	4.11 ± 0.97 2.71 ± 0.75	4.09 ± 0.94 3.88 ± 0.89	0.02 -1.17	0.93 0.0001	NS S
MSNA (µV) Pre Post	12.38 ± 4.71 19.43 ± 5.91	12.44 ± 4.3 12.67 ± 4.15	-0.06 6.76	0.96 0.0001	NS S
MSN-NCV (m/s) Pre Post	39.38 ± 7.11 45.72 ± 7	39.55 ± 6.81 39.8 ± 6.67	-0.17 5.92	0.93 0.009	NS S
SSNPL (ms) Pre Post	5.27 ± 1.18 4 ± 0.46	5.65 ± 0.88 5.49 ± 0.85	-0.38 -1.49	0.25 0.0001	NS S
SSNA (µV) Pre Post	4.64 ± 0.77 6.02 ± 1	4.26 ± 0.75 4.63 ± 0.76	0.38 1.39	0.12 0.0001	NS S
SSN-NCV (m/s) Pre. Post.	33.36 ± 3.21 38.71 ± 2.13	32.25 ± 2.7 32.73 ± 2.71	1.11 5.98	0.24 0.0001	NS S
Katz index Pre. Post.	3.45 ± 0.51 5.4 ± 0.59	3.55 ± 0.5 3.7 ± 0.47	-0.1 1.7	0.53 0.0001	NS S

NS: Non-Significant ($p > 0.05$) **MSNPL:** Median sensory nerve peak latency **MSNA:** Median sensory nerve amplitude **MSN-NCV:** Median sensory nerve NCV **SSNPL:** Sural sensory nerve peak latency **SSNA:** Sural sensory nerve amplitude **SSN-NCV:** Sural sensory nerve NCV.

DISCUSSION

The current study showed that treatment with HTT for 4 weeks improves neurophysiological measures which focus alternation of pathogenesis of DN patients. Furthermore, both groups showed improvement of function outcome with superiority of HTT group. The promising finding of the present study is HTT can modify DN progression without any side effects (**Reichstein et al., 2005**). The underlying mechanisms of the improvement in electrophysiological parameter is incompletely understood. The possible explanation of this improvement that electrical stimulation enhances myelin formations promotes nerve cell regenerations and stimulates Schwann cell for expressed neurotrophic factor in laboratory animals (**Zheng and Ma, 2019**).

Although aerobic exercises improved physical fitness, and insulin sensitivities diabetes cases, the HTTG showed an improvement of electrophysiological parameter that CTG did not show any improvement. Despite the recommendation of exercise training as a gold stander for DN patients, the outcomes of these studies focused on symptomatic pain relive, increase stability, strength rather than better outcomes of electrophysiological parameter (**Zilliox and Russell,**

2019) even rigorous glucose control has not shown for reduced incidence or progression of neuropathy in T2DM (**Kluding, 2017**). However, the treatment group in the current study received both HTT in addition to specific exercise training because exercise training may reduce the neuropathy pain due to regeneration of nociceptive fibers as a normal sequence due to application of HTT (**Willand et al., 2016 and Park et al., 2019**). The possible explanation of these improvements among DN patients who receive HTT are increase of ATP production, improve mitochondrial function, and activation of anti-oxidative stress (**Reichstein, 2005**). Reduced endurance and strength of skeletal muscles due to DN is well documented due to acceleration loss of motor axons (**Parasoglou et al., 2017**). In previous study conducted by **Requena et al., (2005)** concluded that HTT led to muscle contraction of large motor units resulting in stronger and deeper muscle contraction than a voluntary contraction resulting in reduced shear forces between muscle fibers subsequently reduce of insulin resistance.

Endothelial dysfunction impairment of nitric oxide (NO) production and activity consider as one of pathogenesis of DN. **Avogaro et al., 2011** reported that HTT improved endothelial function, micro vascular blood flow in peripheral nerves.

LIMITATIONS

The current study limited by small group size; more studies needed. The study was limited by assessing neurophysiological parameters, further studies needed to investigate the underlying mechanism of these improvements at cellular and sub cellular activities.

CLINICAL IMPLICATION

The study shell light into the visibility of neuro-regeneration in patients with diabetic neuropathy.

CONCLUSION

High tone power therapy could be considered a promising non-invasive method for improving neurophysiological measures and function outcome in diabetic neuropathy patients.

ACKNOWLEDGMENT

Authors thank patients, therapists, physicians and beloved colleagues in Clinical Neurophysiology unit, Faculty of Medicine, Cairo University for their endless love and unlimited support.

Ethical Committee: approved by physical therapy research ethical committee, Cairo university **number:** P.T.REC/012/002261 **at the date of:** 3/3/2019.

Clinical trial registration number: NCT03888872.

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