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ORIGINAL ARTICLE

Role of Synchronized Lifestyle Modification Program and Physiotherapy in Peripheral Neuropathy in Insulin Dependent Type 2 Diabetics

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ABSTRACT

Background: Distal symmetrical polyneuropathy is the most common form of diabetic peripheral neuropathy. Management of peripheral neuropathy through dietary modification and exercise synchronized with circadian rhythm optimizes metabolic parameters, thus restoring nerve functions.
Aim: To determine the effect of Synchronized lifestyle modification program (SLP) and Physiotherapy on Michigan neuropathy screening instrument (MNSI), Fasting blood glucose (FBG), HbA1c, Lipid profile and Nerve conduction studies (NCS) in insulin dependent type 2 diabetic neuropathy patients.
Study Design: Randomized Controlled Trial
Place and Duration: Study was carried out in Physiology department of Islamic International Medical College (Riphah international University) in collaboration with Physiotherapy Department, Railway Hospital, Rawalpindi for a duration of 1 year from October 2020 to October 2021.
Methodology: 120 Type 2 diabetic neuropathic patients on insulin were recruited after written informed consent. Baseline evaluation included; assessment of lifestyle pattern, MNSI, FBG, HbA1c, lipid profile and NCS. Patients were divided into Group A (Control) and Group B (Experimental). Group B was subdivided into Group B1 who received SLP, Group B2 received combined SLP and Physiotherapy and Group B3 received Physiotherapy for 12 weeks. Analysis of parameters was done by repeated measure ANOVA. $p \leq 0.05$ was considered as significant.
Results: MNSI, FBG, HbA1c, serum cholesterol, TGs and LDLs were significantly improved in Group B2. HDL levels and Nerve conduction parameters were not found to be significant.
Conclusion: Combined Synchronized Lifestyle Modification Program and Physiotherapy is more effective in type 2 diabetic neuropathy patients on Insulin.
Keywords: Synchronized lifestyle modification programme, Diabetic peripheral neuropathy, Distal symmetrical polyneuropathy.

INTRODUCTION

Diabetic peripheral neuropathy (DPN) is a degenerative complication of diabetes, characterized by a progressive loss of nerve fibers, affecting about 50% of type 2 diabetics after 10 years of duration[1]. The major risk factors for development of DPN include; duration of diabetes, hyperglycemia, and age, followed by prediabetes, hypertension, dyslipidemia, and obesity[2,3].

Distal symmetrical polyneuropathy (DSPN) is the most common form of DPN and is defined as a symmetrical, length-dependent sensorimotor polyneuropathy which is attributed to metabolic and micro vessel alterations due to hyperglycemia[4]. It can engender disablement in touch and vibration sensation, and lower limb proprioception contributing to skin breakdown, amputation consequently lowering the quality of life.[5,6] Standard glycemic control is the most effective way of preventing and delaying the progression of DSPN through lifestyle modification and anti-diabetic drugs[7]. Importance of lifestyle modification is enhanced if it is synchronized with the circadian rhythm of the body as composition and timing of food intake are important regulators of circadian rhythm. Irregular eating patterns such as skipping breakfast and night eating drive disturbances in homeostatic control and is associated with the development of diabetes and its complications[8].

Thus, Synchronized Lifestyle Modification Program (SLP) is a personalized, homeostasis restoring, liver centric lifestyle modification program that works through the correction of body clock rhythm. While exercise improves three of the biggest risk factors for diabetic neuropathy including insulin sensitivity and glucose control, obesity, and dyslipidemia.[9,10] Insulin therapy is the cost beneficial intervention in patients who have not achieved their glycemic control despite taking oral hypoglycemic agents by increasing the uptake and utilization of glucose by peripheral tissues[11,12].

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Therefore, this study aims to determine the role of Synchronized lifestyle modification program and Physiotherapy in peripheral neuropathy in insulin dependent type 2 diabetics.

MATERIAL AND METHODS

It was a Randomized controlled trial conducted at Physiology Department of Islamic International Medical College (IIMC) and Physiotherapy Department of Railway Hospital, Rawalpindi carried out for one year, from October 2020 to October 2021, after the approval of Ethical Review Committee of IIMC, Rawalpindi. A total of 120 patients were recruited in the study through simple random sampling using random number method, including both males and females, aged 40–75 years with more than five years history of clinically diagnosed type 2 DPN. Type 1 diabetics, Type 2 diabetics on OHAs, patients less than 40 years and more than 75 years of age and a disease duration of less than five years, non-diabetic neuropathy patients and patients with correlated morbidities were excluded. **Lifestyle pattern** was assessed including timing and type of food taken in meals, intake of water, sleeping habits and physical activity through questionnaires. **Physical examination** was done including BMI (Weight-Kgs)/Height-meter^2) and blood pressure using Mercury sphygmomanometer (*TOSHIBA-Master K 303T*). **Assessment of neuropathy** was done MNSI that consisted of subjective assessment including a questionnaire and objective assessment including; feet inspection, ankle reflex performance using a reflex hammer (*Queen's square*) and vibration sensation bilaterally in big toes with a 128-Hz tuning fork (*LSA Surgical-50-010*). **Fasting blood glucose (FBG)** was measured in mg/dl by glucose oxidase strip method using glucometer (*Accu-Check Advantage®, Roche*) after at least 8-12 hours of fasting. **HbA1c** (%) was measured using glycated HbA1 kit by Ion exchange chromatograph. **Serum lipid profile** (mg/dl) was done including; total serum cholesterol by Cholesterol oxidase enzyme based method, serum triglycerides by Glycerol phosphate

enzyme based method, Serum HDLs by direct enzymatic immune-inhibition using Microlab analyzer *(China)* and serum LDLs were calculated using Friedewald equation (Total cholesterol (mg/dl) – HDL Cholesterol (mg/dl) − Triglycerides (mg/dl). **Nerve conduction studies (NCS)** of sural and peroneal sensory nerves was performed by using Keypoint work station machine (*Medtronic, France*). Patients were then randomly divided into **Group A** (Control Group) **and Group B** (Experimental Group). Group A didn't receive any intervention. Group B was subdivided into: **Group B1** who received Synchronized lifestyle modification program (SLP) for a duration of 12 weeks for which diet charts were handed over to patients comprised of; daily dietary intake with its timing and type of food taken in all meals, water intake, sleeping pattern and walk time. Patients were monitored weekly through telephonic calls and their hospital visits to reassure their compliance, **Group B2** received combined SLP and Physiotherapy (3 sessions/week) including; Aerobic exercise using treadmill and cycling (150min/week), Resistance exercise using dumbbells and resistance chairs, Flexibility exercise using hamstring and calf stretches, while balance exercise using one leg stance and tandem stance. **Group B3** received Physiotherapy only for 12 weeks after which post-experiment evaluation was done in all groups. **Statistical Analysis** of data was done using SPSS 21. Data was expressed as Mean±S.D. Comparison amongst groups was done by repeated measure ANOVA followed by Post Hoc-Tuckey test. p value ≤0.05 was considered as significant.

Clinical Trials ID: Study was clinically registered @ clinicaltrials.gov and the identification number is: NCT04813133.

Study Plan:

RESULTS

Demographic features of patients including age, gender, occupation, duration of diabetes, history of hypertension, and BMI (kg/m²) are shown in Table 1. Table 2 shows that on comparison through repeated measure ANOVA and Post-hoc Tuckey's test, the M±S.D of MNSI subjective and objective scoring of Group B2 (6.25±1.25*)* and (2.52±0.65) respectively is significant (p<0.001). Figures 2 and 3 show that the M±S.D of FBG (mg/dl) of Group B2 (138.45 ± 38.93) is significant (p<0.001) and the M±S.D of HbA1c (%) of Group B2 (6.65 ± 1.04) is significant (p<0.001). Table 3 shows that on comparison amongst the groups, the M±S.D of total serum cholesterol (154.60 ± 32.7), serum triglycerides (129.35 ± 57.2) and serum LDLs (100.27 ± 33.4) of Group B2 were reduced significantly (p ≤ 0.05) while the M±S.D of serum HDLs (37.11±5.82) didn't show any significant improvement (p=0.16). Table 4 shows that the M±S.D of right sural nerve peak latency (3.61±2.10), amplitude (2.23±1.41), conduction velocity (28.50±16.9), and M±S.D of left sural nerve peak latency (3.66±2.11), amplitude (2.32±1.43) and conduction velocity (28.60±16.9) of Group B2 were not significant (p=0.32). Similarly M±S.D of right peroneal sensory nerve peak latency (3.09±1.82), amplitude (2.00±1.20), conduction velocity (29.70±17.6), and M±S.D of left peroneal sensory nerve peak latency (3.23±1.97), amplitude (2.10±1.36) and conduction velocity (30.45±18.0) of Group B2 were not found to be significant (p=0.29)

Table 1: Demographic Features of Type 2 Diabetic Peripheral Neuropathy Patients on Insulin.

Demographic Features	Group A (n = 60)	Group B (n = 60)
Age (Years)	60.12 ± 9.53	59.80 ± 8.16
Gender	Male= 26 (44%) Females= 34 (56%)	Male= 21 (35%) Females= 39 (65%)
Occupation	Retired= 15 (25%) Housewives= 33 (55%) Employee = 12 (20%)	Retired = 14 (23%) Housewives = 38 (63%) Employee= 10 (17%)
Duration of Diabetes	11.57 ± 3.12	10.95 ± 3.08
History of Hypertension	Positive = 34 (57%) Negative = 26 (43%)	Positive= 46 (77%) Negative= 14 (23%)
BMI (kg/m²)	Underweight = 3 (5%) Normal weight = 20 (33%) Over weight = 19 (32%) Obese = 18 (30%)	Underweight = 4 (7%) Normal weight = 19 (32%) Overweight = 23 (385) Obese = 14 (23%)

Table 2: Comparison of Mean±S.D of MNSI Subjective and Objective Scoring.

Parameters	Group A	Group B1	Group B2	Group B3
MNSI Subjective Score				
Pre-experiment	9.12±1.09	8.80±0.89	9.30±1.21	9.06±1.06
Post-experiment	9.35±1.05	7.72±0.99*	6.25±1.25***	7.90±0.98*
MNSI Objective Score				
Pre-experiment	4.10±0.71	4.07±0.67	4.00±0.53	3.95±0.55
Post-experiment	4.20±0.72	3.41±0.68*	2.52±0.65***	3.30±0.57*

*** = p < 0.001, * = p < 0.05

Table 3: Comparison of Mean±S.D of Serum Lipid Profile (mg/dl).

Parameters	Group A	Group B1	Group B2	Group B3
Cholesterol-Baseline	183.38±55.3	183.38±55.3	184.45±39.4	187.60±32.6
Post-experiment	184.45±55.5	184.45±55.5	154.60±32.7*	166.95±31.8*
TGs- Baseline	161.82±88.1	159.95±59.3	159.20±81.2	162.50±59.5
Post-experimental	162.05±88.2	139.30±48.5*	129.35±57.2*	146.10±41.8*
HDLs-Baseline	33.92±6.41	33.46±5.90	35.12±5.01	35.24±3.90
Post-experiment	32.85±6.42	34.63±5.79	37.11±5.82	36.80±3.92
LDLs- Baseline	126.15±30.7	127.73±39.6	125.61±29.4	122.18±28.3
Post-experiment	131.33±30.7	109.47±41.5*	100.27±33.4*	112.18±27.9*

*** = p < 0.001, * = p < 0.05

Table 4: Comparison of Mean±S.D of Nerve Conduction Parameters of Right and Left Sural and Peroneal Sensory Nerves before and after 12 weeks of Intervention.

Nerves	Parameters	Time	Group A	Group B1	Group B2	Group B3
Right Sural Nerve	Peak Latency (ms)	Pre Post	3.30±2.30 3.25±2.27	3.69±2.12 3.64±2.13	3.71±2.09 3.61±2.10	3.72±2.20 3.67±2.11
	Amplitude (uV)	Pre Post	2.00±1.52 2.00±1.51	2.14±1.39 2.18±1.40	2.19±1.39 2.23±1.41	2.08±1.29 2.09±1.32
	CV (m/sec)	Pre Post	25.01±17.824.96±17.8	28.10±16.628.50±16.9	27.90±16.528.50±16.9	28.05±16.628.45±16.8
Left Sural Nerve	Peak Latency (ms)	Pre Post	3.25±2.32 3.27±2.33	3.71±2.20 3.65±2.19	3.70±2.20 3.66±2.11	3.68±2.18 3.64±2.10
	Amplitude (uV)	Pre Post	2.12±1.61 2.12±1.57	2.33±1.53 2.38±1.54	2.26±1.42 2.32±1.43	2.21±1.42 2.28±1.47
	CV (m/sec)	Pre Post	25.50±18.225.48±18.2	28.40±16.828.60±17.0	28.45±16.828.60±16.9	28.25±16.7 28.50±16.9
Right Peroneal Sensory Nerve	Peak Latency (ms)	Pre Post	2.80±2.01 2.81±2.02	3.28±1.91 3.16±1.89	3.18±1.80 3.09±1.82	3.24±1.90 3.18±1.87
	Amplitude (uV)	Pre Post	1.96±1.61 1.95±1.57	2.07±1.45 2.14±1.45	1.93±1.19 2.00±1.20	2.00±1.33 2.07±1.34
	CV (m/sec)	Pre Post	25.83±18.4 25.80±18.3	28.95±17.129.30±17.3	29.15±17.329.70±17.6	29.30±17.429.85±17.7
Left Peroneal Sensory Nerve	Peak Latency (ms)	Pre Post	2.87±2.01 2.88±2.02	3.17±1.88 3.08±1.88	3.33±1.95 3.23±1.97	3.45±2.00 3.39±2.03
	Amplitude (uV)	Pre Post	1.93±1.41 1.96±1.60	2.16±1.38 2.20±1.40	2.03±1.34 2.10±1.36	1.97±1.22 2.04±1.34
	CV (m/sec)	Pre Post	26.76±19.1 26.70±19.0	30.05±17.830.45±17.8	29.95±17.730.45±18.0	30.05±17.830.20±17.9

Figure 1: Comparison of post-hoc analysis of Mean±S.D of Fasting Blood Glucose (mg/dl).

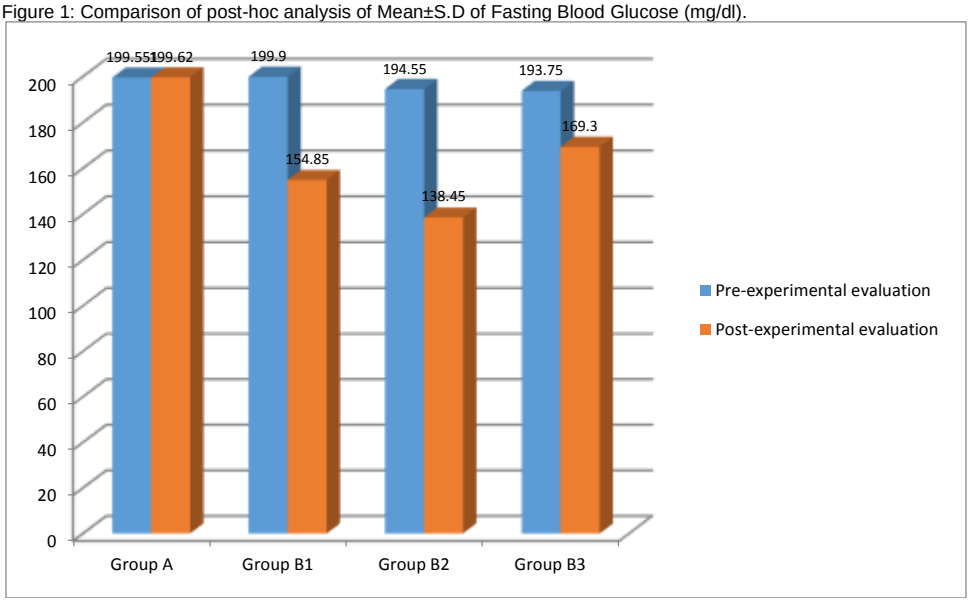
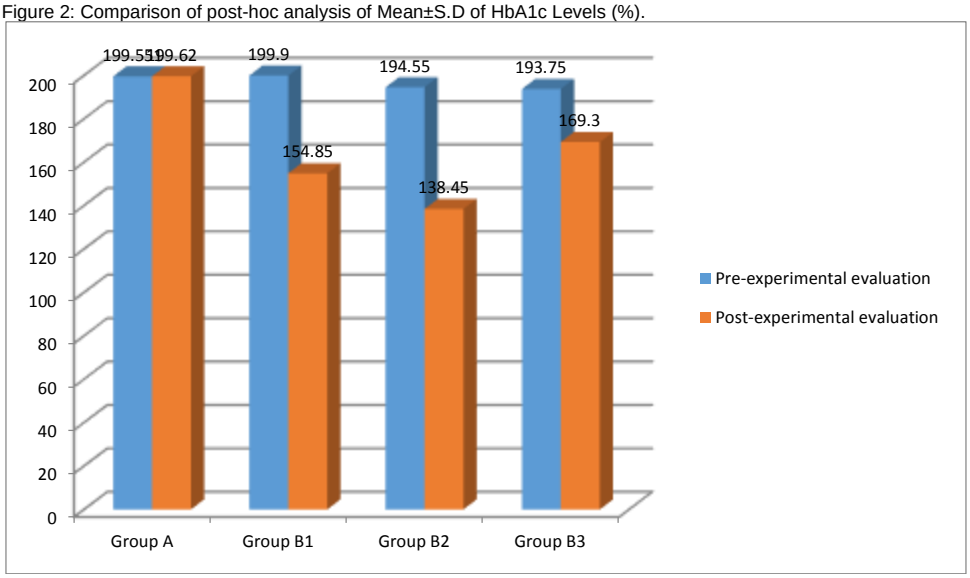


Figure 2: Comparison of post-hoc analysis of Mean±S.D of HbA1c Levels (%).



DISCUSSION

In current study, results of MNSI scoring showed a significant reduction in both subjective and objective scoring in all intervention groups. These results are in accord with study carried out by Edward S. Horton et al., (2017) which stated that intensive lifestyle intervention program for 24 weeks had reduced MNSI subjective scoring in DPN patients but results are contradictory to same study for objective scoring showing no significant reduction[13]. This contradiction may be due different composition of food, and timing of food that we synchronized with the circadian rhythm of body leading to increased insulin response[14,15]. Group B2 showed 85% improvement in subjective scoring and 60% improvement in objective scoring. These results are similar to study carried out by Patricia M. Kluding et al., (2012) showing that subjective and objective scoring had reduced significantly after combined lifestyle intervention program and physiotherapy for 10 weeks in type 2 DPN patients[16]. In present study, a significant reduction in Fasting blood glucose levels (mg/dl) was observed in all intervention groups but Group B2 showed more significant reduction. This finding is in consistent with the study carried by S. Hun Kim et al., (2006) which found that intensive lifestyle modification and supervised physiotherapy intervention for 6 months reduced the FBG with optimal glycemic control[17]. This decrease may be due to consumption of food at right circadian phase during which beta pancreatic cells release increased amount of insulin, with increased insulin sensitivity, and avoiding food late at night, when the insulin secretion and sensitivity decreases[18]. Current study have shown a significant reduction in HbA1c levels (%) in all intervention Groups. These findings are in accord to the study carried out by Anfal N Al-Mallah et al., (2020) and S. Hun Kim et al., (2006)[17,19]. but Group B2 showed more significant decrease in HbA1c levels (%) and these findings are consistent with a study carried out by Lubia et al., (2016) that showed a significant reduction in HbA1c levels of DPN. Present study also showed a significant reduction in lipid profile including; serum cholesterol, TGs, and LDLs with no significant improvement in serum HDLs. These findings conform to the study carried out by Nakhilesh

Pradhan et al., (2018) and L. Nankling Michael et al., (2006) which stated that structured lifestyle modification programme for 12 weeks significantly reduced serum cholesterol, and TGs levels but results are contradictory to same study that showed a significant increase in serum HDLs that can be due to different type of diet (caloric restricted diet)[20]. Results of present study are consistent with Chen et al., (2012), G.S. Mannul et., (2013) who did not find a significant increase in serum HDL levels following lifestyle intervention programme[21]. Present study did not show significant improvement in sensory NCS and these findings are in accord with the study carried out by A. Gordon Smith et al., (2006) which observed that lifestyle intervention for 6 months did not improve nerve conduction parameters in DPN patients[22]. Findings of present study are also consistent with study carried out by Evan B. Stubbs et al., (2019) which stated that physiotherapy for 24 weeks did not improve any of the nerve conduction parameter in DPN patients[23].

CONCLUSION

Combined Synchronized lifestyle modification program and Physiotherapy is more effective in improving distal symmetrical polyneuropathy in type 2 diabetics on Insulin.

Limitation of study: The results of serum lipid profile of patients could create discrepancy as some patients were taking statin drugs. As NCS assess large nerve fiber dysfunction, but cannot assess small fiber damage. Therefore, we could not find out the extent of damage of small nerve fiber conduction parameters at baseline and the extent of improvement after intervention

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Conflicts of interest: The authors have no conflict of interest.

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