DOI: https://doi.org/10.53350/pjmhs22165199

ORIGINAL ARTICLE

Effect of Synchronized Lifestyle Modification Program and Physiotherapy in Improving Type 2 Diabetic Neuropathy patients having Increased Body Mass Index

RUBAB RAMEEZ[1], SHAZIA ALI[1], TAYYABA ANIS CHAUDHRY[1], SIDRA SHAUKAT[2], AYESHA ZAFAR[1], FATIMA IQBAL[1]
[1]Department of Physiology, Islamic International Medical College, Riphah International University, Rawalpindi, Pakistan
[2] Department of Physiology, Army Medical College, National University of Medical Sciences, Rawalpindi, Pakistan.
Correspondence to: Dr. Rubab Rameez, Tel: +923314337057. Email: rubabarshed54@gmail.com

ABSTRACT

Background: Prevalence of diabetic neuropathy (DPN) is associated with increased Body Mass Index (BMI). Synchronized lifestyle modification program attempts to synchronize the circadian rhythm of the body through diet and exercise.
Objective: Determine the role of Synchronized Lifestyle Modification Program (SLP) and Physiotherapy on fasting blood glucose (FBG), HbA1c, lipid profile, and degree of neuropathy in Type 2 DPN patients on Oral Hypoglycemic Agents (OHAs) having increased BMI.
Materials and Methods: Randomized-controlled trial. Evaluation of 120 DPN patients on OHAs included, MNSI, BBS, FBG, HbA1c, Lipid profile and NCS. Participants divided into Group A and B, then divided into A1 and B1, that were overweight and A2 and B2, that were obese. B1 was divided into 1, 2 and 3 and B2 was divided into 4, 5 and 6. Groups 1 and 4 received SLP, Groups 2 and 5 received both SLP and Physiotherapy and Groups 3 and 6 received Physiotherapy for 12 weeks. p≤0.05 was considered significant.
Results: MNSI, BBS, FBG, HbA1c, Total Cholesterol, TGs, HDL and LDL were significantly improved in Group 2.
Conclusion: Combined Synchronized Lifestyle Modification Program and Physiotherapy is effective in DSPN patients that were overweight.
Keywords: Diabetic neuropathy, Synchronized lifestyle modification program, Physiotherapy.

INTRODUCTION

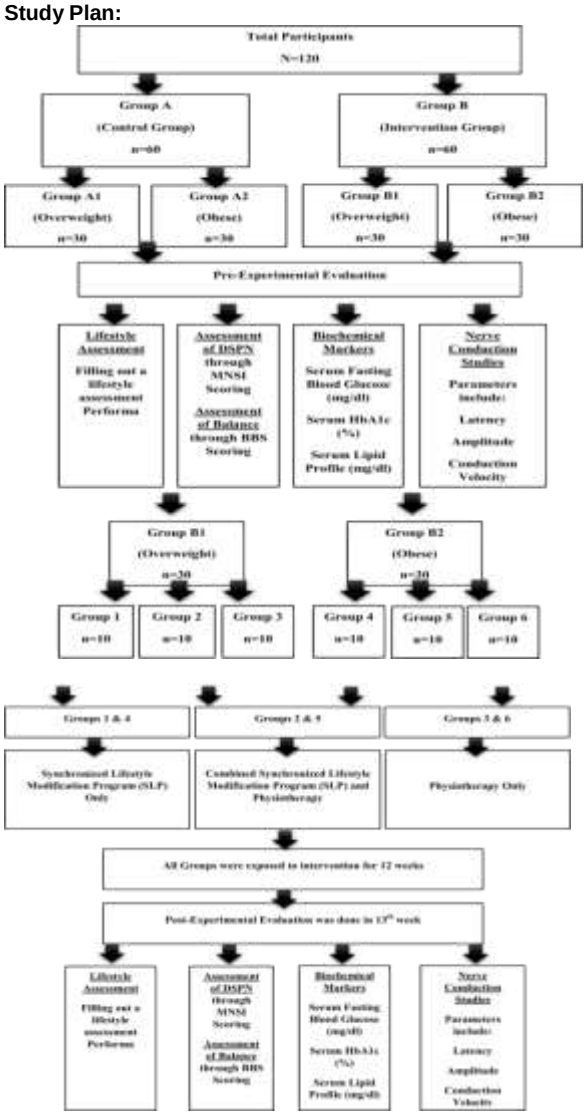
Distal symmetric sensorimotor polyneuropathy (DSPN) is characterized as a distal, symmetric sensorimotor polyneuropathy caused by hyperglycemia and microangiopathy causing demyelination of peripheral nerve fibers leading to parasthesias, loss of vibration, proprioception, touch, pressure, pain, and temperature perceptions.[1] Risk factors include aging, diabetes duration, HbA1c >7.0%, increased BMI, hyperlipidemia including; low HDL, high LDL levels and hyperglycemia.[2,3] Several studies indicated a significant correlation between excess weight and increased risk \s of death, placing the overweight group at a 40% higher and the obese group at up to 300 % higher risk of death than persons whose BMI is normal[4,5,6]. Proper history, examination and presence of symptoms with clinical abnormalities in peripheral nerve functions in diabetic patients along with changes in Nerve Conduction Studies (NCS) confirms the diagnosis.[7,8,9] Lifestyle modification and improving glycemic control are considered the best approaches to prevent and treat DSPN.[10] In terms of lifestyle changes, according to the statement released by American Diabetic Association (ADA), in 2017, a number of exercises were recommended such as aerobic training, weight-bearing, static and dynamic balance training, strength training exercises and flexibility exercises.[11,12,13] The study of how daily habits and activities affect disease prevention and treatment is termed as lifestyle medicine.[14] Synchronized Lifestyle Modification Program (SLP) is a personalized, homeostasis restoring, liver centric lifestyle modification program that works through the correction of body clock rhythm.[15] Suprachiasmatic nucleus (SCN) is a pacemaker in the hypothalamus that maintains the body's circadian rhythm and is affected by the alternating light/dark cycle, eating and sleeping habits, and physical activity.[16] Changes in lifestyle improve pancreatic islet cell function and insulin release in diabetics.[17,18] The aim of this study is to determine the combined effect of SLP along with Physiotherapy in Type 2 diabetic neuropathy patients that are overweight and obese.

MATERIALS AND METHODS

Randomized Controlled Trial (RCT) conducted at the Islamic International Medical College (IIMC) Al-Mizan campus along with the Physiotherapy Department, Railway Hospital, Rawalpindi. The study lasted one year, from October 2020 to October 2021, after the Ethical Review Committee (ERC) of IIMC approved it. Males and females aged 40–75 years with a five-year history of diagnosed Type 2 Diabetic neuropathy patients were enrolled in the study after written consent. Type 1 diabetics, Type 2 diabetics less than 40 and greater than 75 years of age with diagnosed disease duration of less than five years, having normal BMI and underweight, with neuropathies due to other causes, having foot ulcers were excluded. **Lifestyle Pattern** was assessed by a questionnaire, including the timing and type of food eaten, water intake, and physical activity. **BMI** was then computed by using the formula i.e. weight(kg) / height (m2). BMI was classified as: 18.5 (underweight), 18.5–24.9 (normal weight), 25–29.9 (overweight), 30–34.9 (class I obesity), 35–39.9 (class II obese), and >40 kg/m2 (class III obese). **DSPN** was assessed by using Michigan Neuropathy Screening Instrument (MNSI). **Fasting blood glucose** was measured in mg/dl by using the glucometer (Accu-Check Advantage®, Roche) after fasting for 8-12 hours. **Serum Triglycerides** (mg/dl), **Total cholesterol** (mg/dl) and **High density lipoproteins** (mg/dl) were measured by using Microlab 300 analyzer (China), while **Low density lipoproteins** (mg/dl) was calculated using Friedewald equation. **Serum HbA1c** (%) levels were measured by using a glycated HbA1 kit (AMP diagnostics). **NCS** were performed by Keypoint work station (Medtronic, France). Participants were randomly divided into a control group (Group A) and an experimental group (Group B). Group A was further divided into Group A1 that were overweight and Group A2 that were obese. Group B was further divided into Group B1 that were overweight and Group B2 that were obese. Group B1 was subdivided into Group 1, Group 2 and Group 3 and Group B2 was subdivided into Group 4, Group 5 and Group 6. Groups 1 and 4 received SLP only, for 12 weeks, Groups 2 and 5 received both SLP and Physiotherapy, for 12 weeks and Groups 3 and 6 received Physiotherapy only, for 12 weeks. For **SLP,** diet charts were given, and patients were monitored through phone calls thrice weekly and Physiotherapy included**,** aerobic exercise- treadmill (150 minutes/week), resistance exercise-dumbbells, flexibility exercise-hamstring and calf stretch (10-30 seconds) and balance exercise-one leg stance. **Statistical Analysis** was done by SPSS 21. Comparison amongst the groups was done by Repeated Measure Design ANOVA followed by Post Hoc-Tuckey test. Results were expressed as mean±standard deviation. p – value less than or equal to 0.05 was considered as statistically significant.

Received on 14-10-2021
Accepted on 22-04-2022

Study Plan:



Clinical Trials ID: Study was clinically registered @ clinical trials.gov. The identification number is: NCT04813146.

RESULTS

Demographic features of the patients are shown in Table 1. Table 2 shows that on comparison, through Post-hoc Tuckey's test, the M±S.D of MNSI subjective and objective scoring of Group 2 (6.23±1.24) and (3.52±1.03) respectively, is significant ($p<0.001$). Figure 1 shows that the BBS scoring of Group 2 (45.7±3.30) is significant ($p<0.05$). Figures 2 and 3 show that the M±S.D of FBG (mg/dl) of Group 2 (130.45±4.5) are significant ($p < 0.001$) and M±S.D of HbA1c (%) of Group 2 (6.65±1.39) is significant ($p < 0.05$). Table 3 shows that on comparison amongst the groups, the M±S.D of HDL and Triglyceride of Group 1(43.95±7.49) and (124±31.2) respectively, while the M±S.D of LDL and Total Cholesterol of Group 2(100.35 ± 57.2) and (154.60 ± 32.7) respectively, are significant. Table 4 shows that M±S.D of NCS are not significant ($p>0.05$).

Table 1: Shows demographic features of Type 2 DSPN in Percentages.

Demographics	Group A(n=120)	Group B(n=120)
Age (years)	58.15±8.8	61.70±10.8
Gender	Male=46 (38%) Female=74 (62%)	Male=46 (38%) Female=74 (62%)
Occupation	Housewife=62(52%) Retired=22(18%)Private job=14(12%)Others=22(18%)	Housewife=58 (48%) Retired=22 (18%) Private job=14 (12%) Others=26 (22%)
BMI (kg/m²)	Overweight=80 (67%) Obese=40 (17%)	Overweight=76 (63%) Obese=44 (23%)
Smoking	Smoker=22 (18%) Non-smoker=98 (82%)	Smoker=32 (27%) Non-smoker=68 (57%)

Group A= Control group, Group B= Experimental group

Figure 1: Comparison of post-hoc analysis of M±SD of Berg Balance Scale Scoring of Type 2 DSPN patients

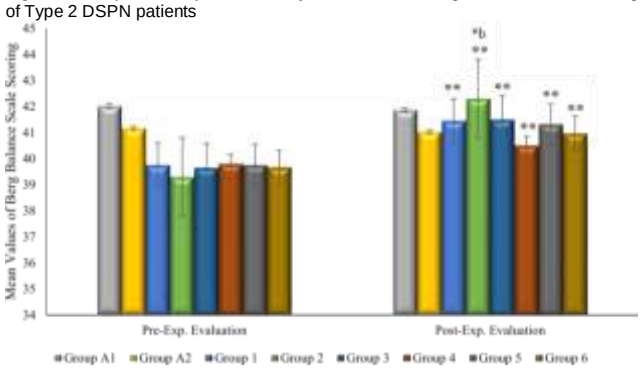


Table 2: Comparison of M±S.D of MNSI Subjective and Objective scores of Type 2 DSPN patients of all the Groups at baseline and after 12 weeks.

MNSI(Subjective)	GroupA1	GroupA2	Group 1	Group 2	Group 3	Group 4	Group 5	Group 6
Pre-Exp.Evaluation	9.12±1.09	9.33±1.24	9±1.02	9.23±1.02	9.3±1.21	9.45±1.08	9.06±1.09	9.35±1.06
Post-Exp.Evaluation	9.35±1.05	9.67±1.03	7.6±1.36**	6.23±1.24***b	7.78±1.26**	6.73±1.12**	7.16±1.21*	7.9±1.11*
MNSI(Objective)-Pre-Exp.Evaluation	5.97±0.71	5.79±1.32	6.7±1.45	5.7±1.02	7±1.02	6.2±0.77	5.76±0.78	6.9±0.78
Post-Exp.Evaluation	6.35±0.72	6.32±1.26	4.57±1.43**	3.52±1.03** *b	6.23±1.00**	5±0.68**	4.5±0.68**	6.4±0.72**

***=p < 0.001 **=p < 0.01 *=p < 0.05

Figure 2: Comparison of post-hoc analysis of M±SD of Serum FBG (mg/dl) levels.

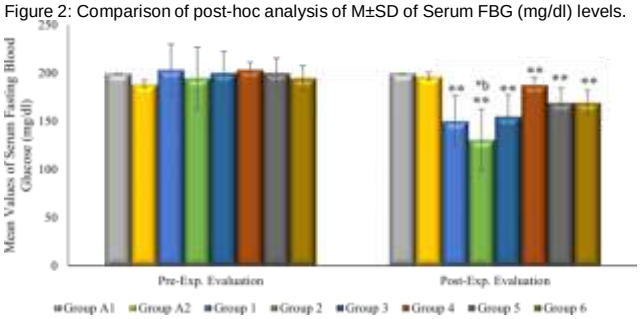


Figure 3: Comparison of post-hoc analysis of M±SD of Serum HbA1c (%) levels of Type 2 DSPN patients

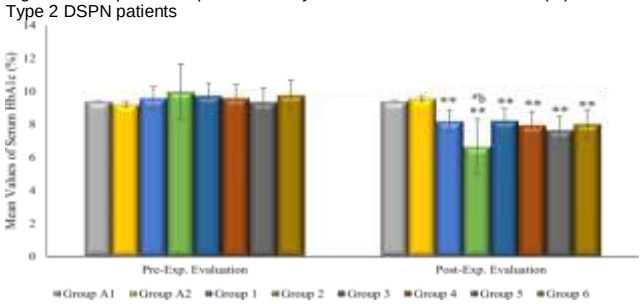


Table 3: Comparison of Mean±SD of Serum Lipid Profile of Type 2 DSPN patients of all the Groups at baseline and after 12 weeks.

Serum HDL	Group A1	Group A2	Group 1 n=30	Group 2 (n=30)	Group 3(n=30)	Group 4	Group 5	Group 6
Pre-Exp. Evaluation	33.92 ±6.41	40.1±10.1	41±10.1	33.46 ±5.90	37.24±7.79	35.12 ±5.01	38.8±6.60	35.24 ±3.90
Post-Exp.Evaluation	33.85 ±6.42	213.2±55.5	44±7.49**a	34.63 ±5.79*	44.67±10.3*	34.63 ±5.79	40.86±6.23*	36.80 ±3.92
Serum LDL-Pre-Exp. Evaluation	126.82 ±88.1	134.5±51.2	135.1±70	127.95 ±59.3	134.5±31.8	139.95 ±59.3	127.5±31.8	138.1±70
Post-Exp. Evaluation	126.33 ±88.2	135.5±56.1	131.8±51*	100.35 ±57.2**b	129.8±51*	129.35 ±57.2*	121.8±29.1*	112.10±41.8*
Serum Total Cholesterol-Pre-Exp.	183.38 ±55.3	212.4±55.8	229.1±64.7	184.45 ± 39.4	214±59.4	184.45 ± 39.4	187.60 ± 32.6	230.5±48.8
Post-Exp. Evaluation	183.45 ±55.3	213.2±55.5	159.8±32*	154.60 ±32.7**b	159.8±32*	166.95 ±31.8*	210±48.2*	166.95 ±31.8*
Serum TG-Pre-Exp. Evaluation	161.82 ±88.1	157.5±51.2	184.5±31.8	159.95±59.3	184.5±31.8	159.20 ±81.2	162.50±45.5	178.1±70
Post-Exp. Evaluation	162.05 ±88.2	185.5±56.1	124±31.2**a	139.30±48.5*	142.8±51*	146.10±41.8*	179.8±29.1*	146.10±41.8*

* p ≤ 0.05 * = Group 1, 2, 3, 4 vs A, *a = Group 1b vs all the intervention groups, *b = Group 2b vs all the intervention groups, Group A1= Control group having BMI 25.0-29.9 kg/m^2, Group A2= Control group having BMI 30-40 kg/m^2, Group 1= SLP group having BMI 25.0-29.9 kg/m^2, Group 2= SLP & Physiotherapy group having BMI 25.0-29.9 kg/m^2, Group 3= Physiotherapy group having BMI 25.0-29.9 kg/m^2, Group 4= SLP group having BMI 30-40 kg/m^2, Group 5= SLP & Physiotherapy group having BMI 30-40 kg/m^2, Group 6= Physiotherapy group having BMI 30-40 kg/m^2

Table 4: Comparison of Mean ± SD of NCS of Sural Sensory Nerve of Right and Left Lower Limbs of patients at baseline and after 12 weeks.

Parameters	Sural(Sensory)	GroupA1	GroupA2	Group1	Group2	Group3	Group4	Group5	Group6
Peak Latency	Right	3.30±2.30	3.30±2.30	3.66±2.17	3.61±2.10	3.56±2.11	3.64±2.13	3.70±2.19	3.67±2.11
	Left	3.25±2.33	3.25±2.33	3.69±2.15	3.66±2.11	3.57±2.11	3.65±2.19	3.68±2.18	3.64±2.10
Amplitude	Right	2.00±1.51	2.00±1.51	2.01±1.20	2.23±1.41	2.11±1.26	2.18±1.40	1.75±1.04	2.09±1.32
	Left	2.12±1.51	2.12±1.51	2.12±1.26	2.32±1.43	2.01±1.20	2.38±1.54	1.78±1.06	2.28±1.47
Conduction Velocity	Right	24.96±17.83	24.96±17.83	28.72±17.04	28.50±16.94	28.54±16.94	28.50±16.9	28.43±16.85	28.45±16.88
	Left	25.48±18.24	25.48±18.24	28.79±17.09	28.60±17.0	29.06±17.25	28.79±17.09	29.13±17.28	28.50±16.93

Group A1= Control group having BMI 25.0-29.9 kg/m^2, Group A2= Control group having BMI 30-40 kg/m^2, Group 1= SLP group having BMI 25.0-29.9 kg/m^2, Group 2= SLP & Physiotherapy group having BMI 25.0-29.9 kg/m^2, Group 3= Physiotherapy group having BMI 25.0-29.9 kg/m^2, Group 4= SLP group having BMI 30-40 kg/m^2, Group 5= SLP & Physiotherapy group having BMI 30-40 kg/m^2, Group 6= Physiotherapy group having BMI 30-40 kg/m^2

DISCUSSION

Results of subjective and objective scoring of MNSI in the current study showed improvement in Group 2 (overweight having BMI in the range of 25.0-29.9 kg/m^2, on SLP and Physiotherapy for 12 weeks) and findings are consistent with a LOOK Ahead Trial (2017), showing significant improvements in MNSI scoring.[19] AE Brunner et al., (2015) observed that plant-based diet for 20 weeks did not improve the MNSI scoring.[20] Results were contradictory due to the fact that pain-related calcium channels have circadian oscillation confirmed by a study.[21] Similar findings were reported by Kluding et al. and Zilliox et al., and Russell et al., (2019).[22,23] Group 2 showed significant improvement in BBS scoring after 12 weeks. Similar results were reported by Khallaf et al., (2020), Kashif. et al (2021), and Ajitha. et al (2020).[24,25,26] No study was found that could reflect the role of diet on BBS score improvement to the best of my knowledge. Group 2 showed a significant reduction in fasting blood glucose (mg/dl) levels after 12 weeks and findings were consistent with those of E. Barreira et al., (2017) and Pot GK et al., (2019), and Köing. et al (2014).[27,28,29] Various studies emphasized the role of the central circadian clock (SCN) on the pancreatic β-islet cells.[16,18,30] Serum HbA1c (%) levels of Group 2 showed significant improvement and findings are consistent with a study by Che.et al (2021), Lubia et al., Abril et al., (2016) and Köing.et al (2014).[31,32] Serum total cholesterol (mg/dl) levels are significantly reduced in Group 2. Findings are consistent with those of Asif et al., (2014) and E. Barriera et al., emphasizing the role of diet in the overweight individuals.[33,34] Serum TG (mg/dl) are significantly reduced in Group 1 (Type 2 DSPN, SLP-group, having BMI in the range of 25.0-29.9 kg/m^2), that are consistent with the results stated by E. Barriera et al.[34] HDL (mg/dl) levels of Group 1 are significantly improved and our findings were similar with studies conducted by Lazarevic et al., and Kasumov et al.[35, 36] LDL cholesterol (mg/dl) of Group 2 have shown significant improvement. These findings are consistent with those reported previously by Cater et al., and Garg et al.[37] NCS of sural sensory nerves of both lower limbs of all the groups were improved but these changes were not found to be significant. Results are consistent with a study conducted by Gholami et al., and Bedi et al., (2018)

CONCLUSION

SLP and Physiotherapy are found to be more effective in improving the degree of neuropathy, balance and biochemical parameters in Type 2 DSPN patients having BMI in the range of 25.0-29.9 kg/m^2.

REFERENCES

1. Ziegler D, Papanas N, Schnell O, Nguyen BDT, Nguyen KT, Kulkantrakorn K, et al. Current concepts in the management of diabetic polyneuropathy. J Diabetes Investig. 2021 Apr 1;12(4):464–75.
2. Liu X, Xu Y, An M, Zeng Q. The risk factors for diabetic peripheral neuropathy: A meta- analysis. PLoS One. 2019;14(2):1–16.
3. Papanas N, Ziegler D. Risk factors and comorbidities in diabetic neuropathy: An update 2015. Rev Diabet Stud. 2015;12(1–2):48–62.
4. Wing RR. Achieving weight and activity goals among diabetes prevention program lifestyle participants. Obes Res. 2004;12(9):1426–34.
5. Xin Y, Wang Y, Chi J, Zhu X, Zhao H, Zhao S, et al. Elevated free fatty acid level is associated with insulin-resistant state in nondiabetic Chinese people. Diabetes, Metab Syndr Obes Targets Ther [Internet]. 2019 Jan 17 [cited 2021 Jun 30];12:139–47. Available from: http://dx.doi.org/10.2147/DMSO.S186505
6. Lin X, Xu Y, Pan X, Xu J, Ding Y, Sun X, et al. Global, regional, and national burden and trend of diabetes in 195 countries and territories: an analysis from 1990 to 2025. Sci Rep [Internet]. 2020;10(1):1–11. Available from: https://doi.org/10.1038/s41598-020-71908-9
7. Kasznicki J. Advances in the diagnosis and management of diabetic distal symmetric polyneuropathy. Arch Med Sci [Internet]. 2014 [cited 2021 Jul 15];10(2):345. Available from: /pmc/articles/PMC4042056/
8. Yang H, Sloan G, Ye Y, Wang S, Duan B, Tesfaye S, et al. New Perspective in Diabetic Neuropathy: From the Periphery to the Brain, a Call for Early Detection, and Precision Medicine [Internet]. Vol. 10, Frontiers in Endocrinology. Frontiers Media S.A.; 2020 [cited 2021 Jun 30]. p. 929. Available from: www.frontiersin.org
9. Manoj Abraham M, Tyng TS, Rekha K, Shanmugananth E, Kiruthika S. Comparison of four screening methods for diabetic peripheral neuropathy in type 2 diabetes mellitus patients: A cross sectional study. Res J Pharm Technol. 2018 Dec 1;11(12):5551–8.
10. Iqbal Z, Azmi S, Yadav R, Ferdousi M, Kumar M, Cuthbertson DJ, et al. Diabetic Peripheral Neuropathy: Epidemiology, Diagnosis, and Pharmacotherapy. Clin Ther [Internet]. 2018;40(6):828–49. Available from: http://dx.doi.org/10.1016/j.clinthera.2018.04.001
11. Kluding PM, Bareiss SK, Hastings M, Marcus RL, Sinacore DR, Mueller MJ. Physical training and activity in people with diabetic peripheral neuropathy:

Paradigm shift. Phys Ther [Internet]. 2017 Jan 1 [cited 2020 Aug 31];97(1):31–43. Available from: /pmc/articles/PMC6256941/?report=abstract
12. Evert AB, Boucher JL, Cypress M, Dunbar SA, Franz MJ, Mayer-Davis EJ, et al. Nutrition Therapy Recommendations for the Management of Adults With Diabetes. Diabetes Care [Internet]. 2013 Nov 1 [cited 2021 Dec 20];36(11):3821–42. Available from: https://care.diabetesjournals.org/content/36/11/3821
13. Inzucchi SE, Bergenstal RM, Buse JB, Diamant M, Ferrannini E, Nauck M, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach: position statement of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). Diabetes Care. 2012 Jun 1;35(6):1364–79.
14. Rippe JM. Lifestyle Medicine : The Health Promoting Power of Daily Habits. 2018;12(6):499–512.
15. Living As Nature Intended: Feroz, Dr. Shagufta: 9789695440223: Amazon.com: Books [Internet]. [cited 2022 Mar 24]. Available from: https://www.amazon.com/Living-Nature- Intended-Shagufta-Feroz/dp/9695440223?asin=9695440223&revisionId=&format=4&depth=1
16. Bae SA, Fang MZ, Rustgi V, Zarbl H, Androulakis IP. At the Interface of Lifestyle, Behavior, and Circadian Rhythms: Metabolic Implications. Front Nutr. 2019;6(August).
17. Sci-Hub | Circadian clocks and insulin resistance. Nature Reviews Endocrinology | 10.1038/s41574-018-0122-1 [Internet]. [cited 2021 Aug 25]. Available from: https://sci- hub.se/10.1038/s41574-018-0122-1
18. Onaolapo AY. Circadian dysrhythmia-linked diabetes mellitus: Examining melatonin's roles in prophylaxis and management. World J Diabetes [Internet]. 2018 [cited 2021 Aug 25];9(7):99–114. Available from: http://www.f6publishing.com
19. Horton ES, Chen H, Nathan DM, Pi-Sunyer X, Knowler WC, Gregg EW, et al. Effects of a long-term lifestyle modification programme on peripheral neuropathy in overweight or obese adults with type 2 diabetes: the Look AHEAD study. Diabetologia [Internet]. 2017 Jun 1 [cited 2022 Mar 23];60(6):980. Available from: /pmc/articles/PMC5423967/
20. Bunner AE, Wells CL, Gonzales J, Agarwal U, Bayat E, Barnard ND. A dietary intervention for chronic diabetic neuropathy pain: A randomized controlled pilot study. Nutr Diabetes [Internet]. 2015;5(5):e158-6. Available from: http://dx.doi.org/10.1038/nutd.2015.8
21. Burish MJ, Chen Z, Yoo S-H. Emerging relevance of circadian rhythms in headaches and neuropathic pain.
22. Zilliox LA, Russell JW. Physical Activity and Dietary Interventions in Diabetic Neuropathy: A Systemic Review HHS Public Access. Clin Aut Res. 2019;29(4):443–55.
23. Kluding PM, Pasnoor M, Singh R, Jernigan S, Farmer K, Rucker J, et al. The Effect of Exercise on Neuropathic Symptoms, Nerve Function, and Cutaneous Innervation in People with Diabetic Peripheral Neuropathy. J Diabetes Complicat. 2012;26(5):424–9.
24. Khallaf M, Fayed EE. Improving Planter Pressure Distribution Could Reduce the Risk of Fall in Patients with Diabetic Neuropathy Improving quality of life among PD patients View project Management of UL after stroke View project. 2020 [cited 2021 Aug 25]; Available from: https://doi.org/10.17756/jnen.2020-064
25. Iram H, Kashif M, Hassan HMJ, Bunyad S, Asghar S. Effects of proprioception training programme on balance among patients with diabetic neuropathy: A quasi-experimental trial. J Pak Med Assoc. 2021 Jul 1;71(7):1818–21.
26. Pilot Study of Exercise Therapy on Painful Diabetic Peripheral Neuropathy [Internet]. [cited 2020 Aug 31]. Available from:https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4673891/
27. Thiel DM, Al Sayah F, Vallance JK, Johnson ST, Johnson JA. Association between Physical Activity and Health-Related Quality of Life in Adults with Type 2 Diabetes. Can J Diabetes [Internet]. 2017;41(1):58–63. Available from: http://dx.doi.org/10.1016/j.jcjd.2016.07.004
28. Pot GK, Battjes-Fries MC, Patijn ON, Pijl H, Witkamp RF, Visser M de, et al. Nutrition and lifestyle intervention in type 2 diabetes: pilot study in the Netherlands showing improved glucose control and reduction in glucose lowering medication. BMJ Nutr Prev Heal [Internet]. 2019 May 14 [cited 2021 Aug 25];2(1):bmjnph-2018-000012. Available from: https://nutrition.bmj.com/content/early/2019/05/13/bmjnph-2018-000012
29. König D, Kookhan S, Schaffner D, Deibert P, Berg A. A meal replacement regimen improves blood glucose levels in prediabetic healthy individuals with impaired fasting glucose. Nutrition [Internet]. 2014 Nov 1 [cited 2022 Mar 23];30(11–12):1306–9. Available from: https://pubmed.ncbi.nlm.nih.gov/25194963/
30. Kurose T, Hyo T, Yabe D, Seino Y. The role of chronobiology and circadian rhythms in type 2 diabetes mellitus: implications for management of diabetes. 2014 [cited 2021 Aug 25];4–41. Available from: http://dx.doi.org/10.2147/CPT.S44804
31. Che T, Yan C, Tian D, Zhang X, Liu X, Wu Z. Time-restricted feeding improves blood glucose and insulin sensitivity in overweight patients with type 2 diabetes: a randomised controlled trial. Nutr Metab [Internet]. 2021 Dec 1 [cited 2022 Mar 23];18(1):1–10. Available from: https://nutritionandmetabolism.biomedcentral.com/articles/10.1186/s12986-021-00613-9
32. Velázquez-López L, Violeta Muñoz-Torres A, García-Peña C, López-Alarcón M, Islas- Andrade S, Escobedo-de la Peña J. Research Article. 2016 [cited 2021 Aug 25]; Available from: http://dx.doi.org/10.1155/2016/2980406
33. Asif M. The prevention and control the type-2 diabetes by changing lifestyle and dietary pattern. J Educ Health Promot [Internet]. 2014 [cited 2021 Aug 25];3(1):1. Available from: /pmc/articles/PMC3977406/
34. Stino AM, Rumora AE, Kim B, Feldman EL. Evolving concepts on the role of dyslipidemia, bioenergetics, and inflammation in the pathogenesis and treatment of diabetic peripheral neuropathy. J Peripher Nerv Syst. 2020 Jun 1;25(2):76–84.
35. Lazarevic G, Antic S, Cvetkovic T, Vlahovic P, Tasic I, Stefanovic V. A physical activity programme and its effects on insulin resistance and oxidative defense in obese male patients with type 2 diabetes mellitus. Diabetes Metab. 2006 Dec 1;32(6):583–90.
36. Kasumov T, Solomon TPJ, Hwang C, Huang H, Haus JM, Zhang R, et al. Improved insulin sensitivity after exercise training is linked to reduced plasma C14:0 ceramide in obesity and type 2 diabetes. Obesity [Internet]. 2015 Jul 1 [cited 2021 Aug 26];23(7):1414–21. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/oby.21117
37. Cater NB, Garg A. The Effect of Dietary Intervention on Serum Lipid Levels in Type 2 Diabetes Mellitus. Curr Diab Rep. 2002;2:289–94.