Sensory nerve conduction velocity changes in low level laser therapy irradiated diabetic neuropathy induced wistar rats

Running Title: Low Level Laser Therapy in Diabetic Neuropathy

Author:
[1]Prathap Suganthirababu
Professor Saveetha College of Physiotherapy
Saveetha Institute of Medical and Technical Sciences Chennai
orcid id- https://orcid.org/0000-0002-1419-266X

[2*]Lavanya Prathap
Associate Professor Department of Anatomy
Saveetha Dental College and Hospitals Saveetha Institute of Medical and Technical Sciences Chennai
https://orcid.org/0000-0002-9334-400X

[3]Kumaresan A
Professor Saveetha College of Physiotherapy
Saveetha Institute of Medical and Technical Sciences Chennai
https://orcid.org/0000-0002-5424-5463

[4]Vignesh Srinivasan
Assistant Professor Saveetha College of Physiotherapy
Saveetha Institute of Medical and Technical Sciences Chennai

[4]Jagatheesan Alagesan
Professor Saveetha College of Physiotherapy
Saveetha Institute of Medical and Technical Sciences Chennai

[5]Praveenkumar Kandakurti
Dean, College of Health Sciences, Gulf Medical University, Ajman, UAE

***Corresponding Author:**

Lavanya Prathap
Associate Professor Department of Anatomy Saveetha Dental College and Hospitals
Saveetha Institute of Medical and Technical Sciences Chennai
Email ID- lavanya.anatomist@gmail.com
https://orcid.org/0000-0002-9334-400X

ABSTRACT:

Background: Management of Diabetic neuropathy with physiotherapy is very limited and extensive research has to be done to address this problem conservatively in a physiotherapy perspective. The aim of the study is to analyze the effect of various dosage of low level laser irradiation on sensory nerve conduction velocity (SNCV) of experimentally induced diabetic neuropathy in wistar rats. **Materials and Methods:** We performed a randomized controlled trial using simple random sampling method in a CPCSEA Approved, Biomedical Research Unit & Laboratory Animal Centre, Chennai, India. The study carried out in two phases, in the phase I the selected experimental rats are treated with single dose on Alloxon 150mg/kg body weight after 12 hours of fasting. In the Phase II the samples with confirmed neuropathic status were divided into seven groups (six rats in each group) and irradiated with low level laser therapy with various dosages **Results:** The SNCV result analysis within the groups showed that laser dosage of 3,4j/cm2 are having more sensory regenerative effect as compared with 5-8j/cm2 dose and control group also did not show significant effect. The findings of the present study suggests nerve regeneration through nerve conduction velocity reports. **Conclusion:** It is evident from the results that an increase in nerve conduction velocity with selective dosages of laser proves that laser has neuroregenerative effects and by analyzing the results it can be concluded that low level laser of 3&4j/cm2 is found to be effective in regeneration of SNCV of experimentally induced diabetic neuropathy as compared with control group and with the dosage of higher energy with 5-8j/cm2.

Key words: Sensory nerve conduction velocity (SNCV); Low Level Laser Therapy; Diabetic Neuropathy; Alloxon;

INTRODUCTION

Diabetic neuropathy affects large population in our country which needs to be addressed efficiently. Diabetic neuropathy produces various symptoms like pain, sensory loss, weakness etc., particularly lower limb is mostly affected which is primary for locomotion and for activities of daily living, so this particular problem has to be addressed effectively and conservatively to provide relief to persons affected by this problem. Neuropathy is also expected to be prevalent in 19.1 percent of type 2 diabetics in South India. (1) Diabetic neuropathy is prevalent in 26.1 percent of Type 2 diabetics in metropolitan (Chennai) south Indian populations. (2–4) Diabetic neuropathy is a worldwide problem which affects all the classes, management for this problem in field of medicine is only aimed to clear the symptom rather than the nerve pathology. Medicines like insulin supplements and nerve vitamin and mineral supplements are added to manage these problems. Researches are going all over the world to treat the diabetes and its complications effectively in the field of medicine. Management of Diabetic neuropathy with physiotherapy is very limited and extensive research has to be done to address this problem conservatively in a physiotherapy perspective.

Consulting an expert physiotherapist can help give each patient a chance at the most positive outcome for functional improvements. LASER as a therapeutic modality in the field of physiotherapy has undergone various researches since early 1960's and many therapeutically significant results have been obtained from LASER. The present study focuses on the Neuro regenerative effect of therapeutic low level LASER on diabetic neuropathy.

Laser as a therapeutic modality since its invention has produced many clinically significant result. Laser is used worldwide in physiotherapy for many clinical conditions like pain, inflammation, tissue healing etc, and much research is being conducted on nerve regeneration properties of laser, with this correlations laser can be effectively studied in the management of diabetic neuropathy. According to a thorough assessment of the literature, there are few investigations on the role of low-level laser therapy's neuro-regenerative effects in experimentally generated diabetic neuropathy. (5,6) The management options for this particular condition are equally limited, necessitating a study using low-level irradiation, which is well-known for its tissue-healing qualities around the world.. Developed countries with their modern setup “know how” progressing rapidly in exploring the possibilities of low level laser to supplement the medical management and facilitate early recovery. The aim of the study is to analyze the effect of various dosage of low level laser irradiation on sensory nerve conduction velocity (SNCV) of experimentally induced diabetic neuropathy in wistar rats.

MATERIALS & METHODS

We performed a randomized controlled trial using simple random sampling method in a CPCSEA approved, Biomedical Research Unit & Laboratory Animal Centre, Chennai, India. We commenced the study after getting approval from Institutional Animal Ethical Clearance - Ethical Committee Clearance Number: IAEC. NO. BPT/001/2008. The Materials required includes 1. Laser Unit – Physitalia (Unilaser Scan – 2000), Class-1, Type-B, 230V-50Hz, 2. Nerve Conduction Velocity Unit – BIOTECK-NEUROCARE, 3. Glucometer: one touch ultra (Johnson & Johnson, USA). The inclusion criteria includes 1. Species: Rattus norvegicus , 2. Age : 2-3months, 3. Weight: 180-200gms, 4. Sex : Male, 5. Study Duration: 3 months

Procedure

Phase I

The experimental rats of 42 numbers were selected based on the inclusion criteria and were kept on fasting for 12 hours prior to experimentation and were induced for diabetes by a single dose of intra- peritoneal injection of Alloxan 150 mg/kg body weight by dissolving in normal saline.(7)

Blood glucose level of the rats were measured prior to Alloxan induction and after 24hrs post induction and all the rats were screened for blood glucose levels and rats with blood glucose levels of more than 200 mg/dl were selected for further intervention. Diabetes was confirmed with help of Glucometer readings by obtaining blood samples from tail vein of the rat .Diabetic levels of the rats were monitored prior to Alloxan induction and on day 1, 15, 30 and 60 after Alloxan induction. Booster dose of 50 mg/kg body weight of Alloxan was administered on the 30th day to maintain diabetic status.

Nerve Conduction Study:

Nerve conduction velocities were recorded initially pre Alloxan administration and 30 days and 60 days post induction. Experimental animals were anesthetized with Ether solution and electrode placement areas were shaved and cleaned with alcohol. The anode was placed on the

third toe of the foot, while the cathode was put on the heel of the foot, for sural nerve SNCV recordings. The frequency range consisted of recordings of both inclusive and antidromic sensory potentials at a frequency of 2 Hz.After analyzing sensory nerve conduction velocity tests values, the neuropathic status deficits was confirmed and the rats were grouped into study and control group for next phase of experimentation.

Phase II:

The experimental animals with sensory degeneration which confirmed neuropathic status were divided into seven groups (six rats in each group) and irradiated with low level laser therapy with various dosages.

Laser Therapy:

Low level He-Ne laser therapy of 632.8nm was irradiated at the site of sciatic notch of the rat where the nerve is superficial and the irradiation was given for 4 days in a week for 4 weeks with various dosage of laser ranging from 3 to 8j/cm2. The effect of laser induced nerve regeneration was again measured with sensory nerve conduction velocity to find regeneration status of the nerve.

Groups:

I Group- 3 j/cm2

II Group- 4 j/cm2

III Group- 5 j/cm2

IV Group- 6 j/cm2

V Group- 7 j/cm2

VI Group- 8 j/ cm2

VII Group is kept as control

Outcome Meassure includes 1. Blood glucose values measured from one touch ultra-Glucometer. 2. SNCV values measured from EMG-NCV from Bioteck-Neurocare

RESULTS:

The Paired‘t’ test analysis was made for comparison within the groups and One way ANOVA & Post hoc analysis was made for comparison between the groups.

Post hoc comparisons of the groups SNCV values showed significant p values in Group I (3j/cm2) and Group II (4j/cm2), rest of the groups from 5-8j/cm2 and control Group did not show significant p value with 95% confidence interval.

Blood glucose: Table 1 Blood glucose levels were initially noted on the day 0 with M= 82.42 , on day1 after alloxan induction as M=261.71,on day 15 as M=342.07, on day 30 as M=389.14 and on day 60 as M=401.42 as shown in fig1.

SNCV recording for confirming sensory degeneration: Table 2 SNCV results of Sural nerve in all the animals were recorded on day 0 prior alloxan induction with M=54.2 and on day 30 after Alloxan induction which showed M=47.4 and on 60th day which confirmed M=38.56 and statistical analysis were made with values of day 0 and day 60 which showed significant changes in SNCV with p value <0.0001 of t value20.045 & 14.145 as shown in table 3.

SNCV recording for confirming Neuro regeneration: Results shown in Table 4 were statistically analyzed with paired t test comparing the pre and post laser irradiation among all the 7 groups and the results showed that Group I with 3j/cm2 showed extremely statistically significant changes with p value =0.0003 of t value= 8.9299 and Group II with 4j/cm2 also showed extremely statistically significant changes with p value =0.0005 of t value=7.8523 and Group III with 5j/cm2 showed No significant changes with p value=0.3220 of t value=1.0985 and Group IV with 6j/cm2 also no significant changes with p value = 0.1810 of t value=1.5536 and Group V with 7j/cm2 showed non-significant changes with p value =0.6514 of t value=0.4802 and Group VI with 8j/cm2 showed non-significant changes with p value =0.2173 of t value=1.4112 and Group VII which were kept as control without laser irradiation also showed statistically non significant effect with p value=0.0096 of t value=4.0737 as shown in table 5.

Comparison of SNCV values between the groups after laser irradiation using one way ANOVA & Post Hoc test.

Analysis of variance of SNCV values Post laser irradiation revealed significant p value <0.0001 with F value 48.875 (Table 6) and post hoc analysis revealed that groups 1,2 showed significant improvement and groups 3,4,5,6,7 did not show statistical significance for 95% confidence interval as shown in table 7and 8.

DISCUSSION:

In the present study comparison was done on various dosage of low level laser therapy to find out its neuroregenerative effect in experimentally induced diabetic neuropathy in wistar rats. The diabetes status was confirmed by repeated measures of blood glucose analysis from day 0, day1, day15, day30 and day60.The dosage to induce diabetes was selected as 150mg/ kg b.w of Alloxan intraperitonealy based on Szkudelski in 2001.(8–12)

The SNCV result analysis within the groups showed that laser dosage of 3,4j/cm2 are having more sensory regenerative effect as compared with 5-8j/cm2 dose and control group also did not show significant effect.. This proves that if dosage is not selected properly it can inhibit the nerve regeneration process like higher dosage can have photo inhibitory effect. In the present study nerve regeneration is confirmed through nerve conduction velocity studies.

Eliasson (1964) & Dharmesh kumar (2008) in their study considered 200mg/dl as base line value for their study and Butler (1995) stated that around 90 mg/dl of blood is normal blood

glucose levels for 15-24 hrs fasted rats and they also stated that in diabetic induced rats it may go up to 200-400mg/dl in 3-4 weeks after diabetic induction.(13–18) As per the earlier studies by Coste (2003) and Dharmeshkumar (2008) confirmed that diabetic neuropathy will start by 15 days of uncontrolled diabetes and PK Thomas 1981 recorded neuropathic changes after 8 weeks and Biessels (1999) also confirmed this by proving that impairments of sciatic nerve conduction velocities developed fully during the first 2-3 months of diabetes. J. G. R. Jefferys 1978 proved in his experiment that normal nerve conduction velocity of wistar rats was around 52m/sec ranged from 46 m/sec to 57m/sec.(14,19,20)

Induction of experimental diabetes in rats by pancreatectomy or alloxan administration resulted in decreased sciatic motor and sensory nerve conduction velocities within 2 weeks, according to Eliasson (1964). (13) Eliasson, on the other hand, was unable to prevent or impact the development of reduced nerve conduction velocities by administering insulin to a single nerve in vitro. Despite two reports indicating that insulin treatment can improve impaired nerve conduction velocity in rats with experimental diabetes, it has not been possible to prevent the disease from developing, and Sharma and Thomas concluded that "the influence of insulin on conduction velocity in diabetic animals is so far uncertain.".

Anders et al. conducted a study on the neuro regenerative and neuro protective effects of low-level laser in 2004 and found massive axonal sprouting as well as an increase in various molecules such as growth associated protein-43 (GAP-43), calcitonin gene related (CGRP), and transforming growth factors betal. They came to the conclusion that laser irradiation stimulates the proliferation of Schwann cells, which are important for nerve healing.(21)

Prathap etal 2018 2019 conducted studies with LLLT on human subjects with 3-4j/cm2 dosage of Laser irradiation on Diabetic Neuropathy induced pain and foot ulcers and the results were significant..Future studies on Functional impairments associated with Diabetic Neuropathy can be also considered for experimentation with Low Level Laser irradiation(22–26)

Prathap et al in 2011 conducted study on diabetic neuropathy induced motor nerve conduction velocity changes and its alterations after low level Laser application and concluded that 3-4j/cm2 dosage showed significant improvements, which is also similar dosage as proved in this SNCV recording. Although this study found that low-level laser therapy (LLLT) improved sensory nerve conduction velocity in diabetic neuropathy, the observed trend requires additional exploration. The results of the study demonstrated that LLLT with 3-4 joules of irradiation improved the condition significantly, with no major adverse effects recorded in any of the groups. As a result, LLLT could be safely administered to diabetic neuropathy patients. (27)

Recommendations:

Future studies can be done on human subjects with 3-4j/cm^2 dosage of Laser irradiation on Diabetic Neuropathy. Functional impairments associated with Diabetic Neuropathy can be also considered for experimentation with Low Level Laser irradiation

CONCLUSION

In the present study it is proved that sensory nerve conduction velocity in diabetic neuropathy can be improved with low level laser irradiation. An increased nerve conduction velocity with selective dosages of laser proves that laser has neuroregenerative effects and by analyzing the results it can be concluded that low level laser of 3&4j/cm2 is found to be effective in regeneration of SNCV of experimentally induced diabetic neuropathy as compared with control group and with the dosage of higher energy with 5-8j/cm2. The present investigation highlights the possible utility of Helium-Neon Laser with appropriate energy density as an adjunctive modality for diabetic neuropathy in clinical practice.

Table 1: Mean and SD of Blood glucose levels at pre Alloxan (Day 0)administration and various days post Alloxan Administration

N	Day 0 (mg/dl)		Day 1 (mg/dl)		Day 15 (mg/dl)		Day 30 (mg/dl)		Day 60 (mg/dl)	
42	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
	82.42	3.46	261.71	3.49	342 .07	3.74	389.14	3.87	401.42	14

Table 2 :Sensory Nerve Conduction Velocity Values (m/sec) of Experimentally Diabetes Induced Wistar Rats

N	Pre test (Day 0) (m/sec)		Post test (30 days) (m/sec)		Post test (60 days) (m/sec)	
42	Mean	SD	Mean	SD	Mean	SD
	54.2	2.19	47.4	1.35	38.56	2.25

Table 3 : Comparison of SNCV values between day 0 (Pre Alloxan) to Day 30 and Day 60 (Post Alloxan) by Paired‘t’ test

S.no	Comparison	Nos.	Pre Alloxan (m/sec)		Post Alloxan (m/sec)		T value	P value
			Mean	SD	Mean	SD		
1	Day0 vs Day 30	42	54.2	2.19	47.4	1.35	20.045	<0.0001
2	Day0 vs Day 60	42	54.2	2.19	38.5	2.25	14.145	<0.0001

Table 4: SNCV Values Pre & Post Laser Irradiation

Groups(n=6)	Pre laser irradiation (m/sec)		Post laser irradiation (m/sec)	
	Mean	SD	Mean	SD
Group I-3j/cm2	37.9	1.766	45.3	1.370
Group II- 4j/cm2	37.6	2.593	48.2	1.926
Group III- 5j/cm2	40.4	1.097	41.2	1.996
Group IV -6j/cm2	38.9	1.879	40.6	1.599
Group V -7j/cm2	38.9	1.058	39.2	1.724
Group VI-8j/cm2	38.4	1.332	37.2	0.951
Group VII- control	37.7	0.991	35.06	1.297

Table 5: Comparison of SNCV values pre and post laser irradiation using paired t test

Groups(n=6)	Pre laser irradiation (m/sec)		Post laser irradiation (m/sec)		T value	P value
	Mean	SD	Mean	SD		
Group I-3j/cm2	37.9	1.766	45.3	1.370	8.929	0.0003
Group II- 4j/cm2	37.6	2.593	48.2	1.926	7.852	0.0005
Group III- 5j/cm2	40.4	1.097	41.2	1.996	1.098	0.3220
Group IV -6j/cm2	38.9	1.879	40.6	1.599	1.553	0.1810
Group V -7j/cm2	38.9	1.058	39.2	1.724	0.480	0.6514
Group VI-8j/cm2	38.4	1.332	37.2	0.951	1.411	0.2173
Group VII- control	37.7	0.991	35.06	1.297	4.073	0.0096

Table 6: SNCV values Post laser irradiation Results Analysis with One way ANOVA

Comparison	Sum of squares	Df	Mean square	F-value	P value
Between Groups	740.912	6	123.485	48.875	0.000
Within groups	88.430	35	2.527	-	-

Table 7: Post hoc Analysis for SNCV values comparison between the Groups

S.No	Comparison	Mean 1	Mean 2	Mean1 - Mean2	95% CI of difference
1	Group I-3j/cm2	37.9	45.3	7.4	4.8 to 10.0
2	Group II- 4j/cm2	37.6	48.2	10.6	8.0 to 13.2
3	Group III- 5j/cm2	40.4	41.2	0.8	1.8 to 3.4
4	Group IV -6j/cm2	38.9	40.6	1.7	0.9 to 4.3
5	Group V -7j/cm2	38.9	39.2	0.3	2.3 to 2.9
6	Group VI-8j/cm2	38.4	37.2	1.2	1.4 to 3.8
7	Group VII- control	37.7	35.6	2.1	0.5 to 4.7

Mean Square= 2.527 DF= 35

Table 8: Significance levels of groups with SNCV values Post Laser Irradiation

S.No	Comparison	Significance (P <0.05?)	T
1	Group I-3j/cm2	0.0005-Yes	8.063
2	Group II- 4j/cm2	<0.0001-Yes	11.550
3	Group III- 5j/cm2	0.4231-No	0.872
4	Group IV -6j/cm2	0.1232-No	1.852
5	Group V -7j/cm2	0.7569-No	0.327
6	Group VI-8j/cm2	0.2481-No	1.307
7	Group VII- control	2.288- No	2.288

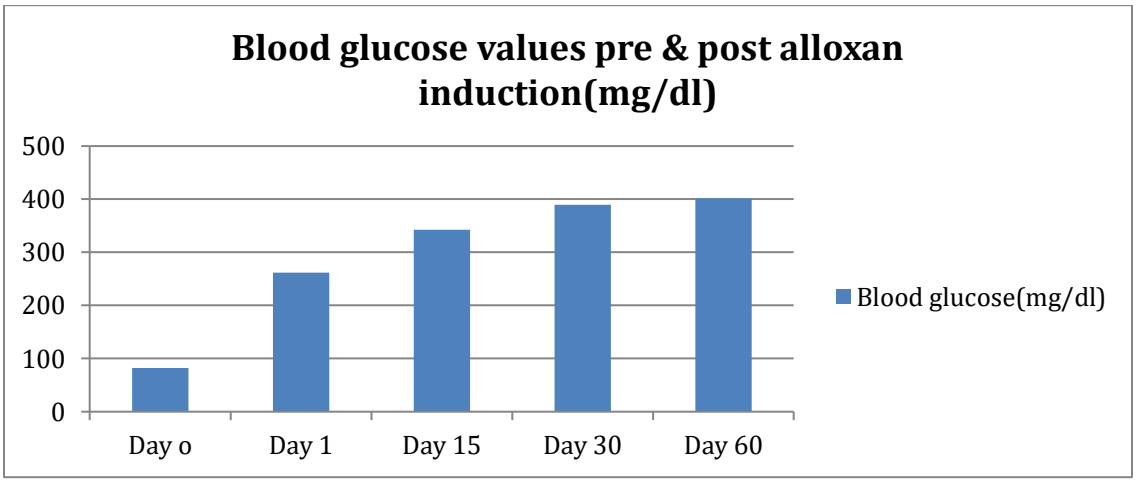

Fig 1: Blood glucose values Pre & Post Alloxan induction in mg/dl

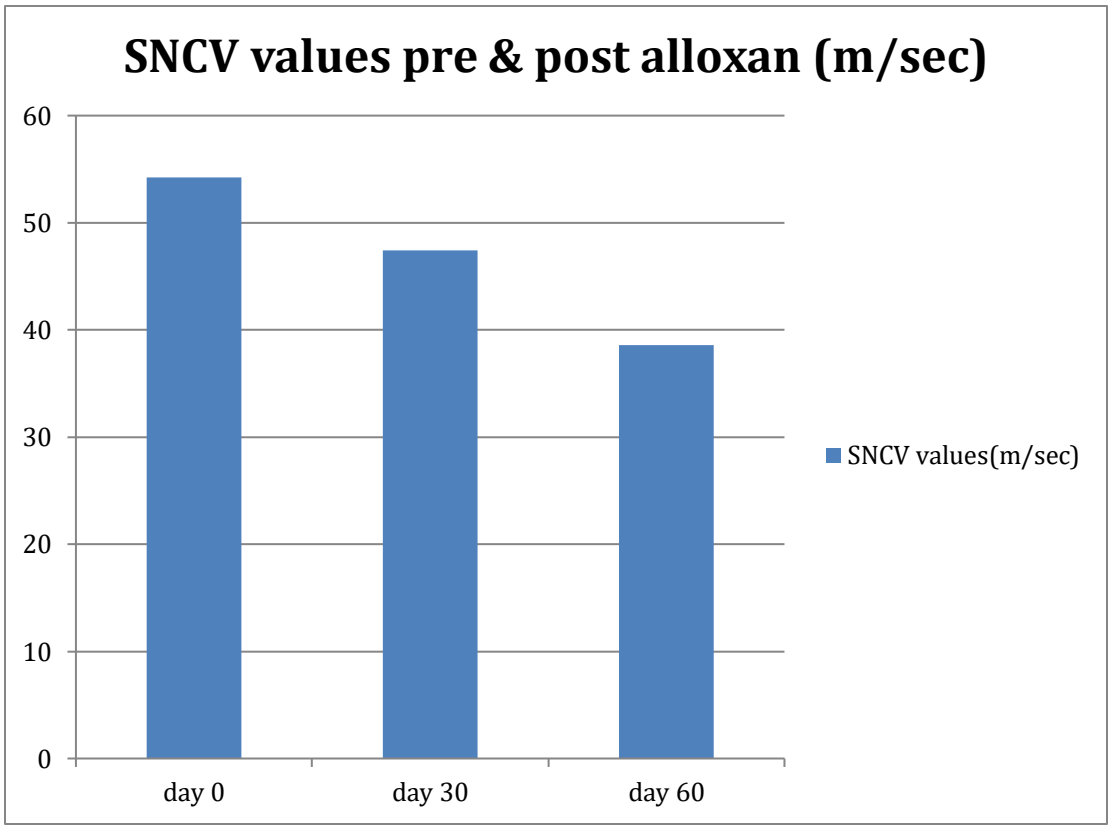

Fig 2 : Sensory Nerve Conduction Velocity Values (m/sec) of Experimentally Diabetes Induced Wistar Rats

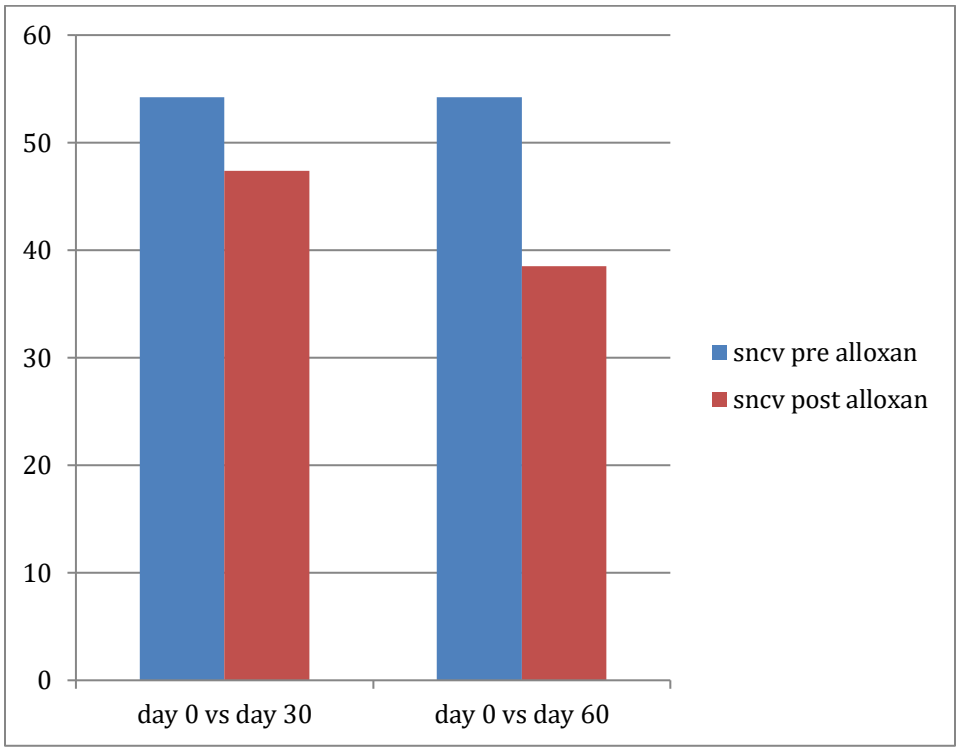

Fig 3: Comparison of SNCV values between day 0 (Pre Alloxan) and day 60 (Post Alloxan)

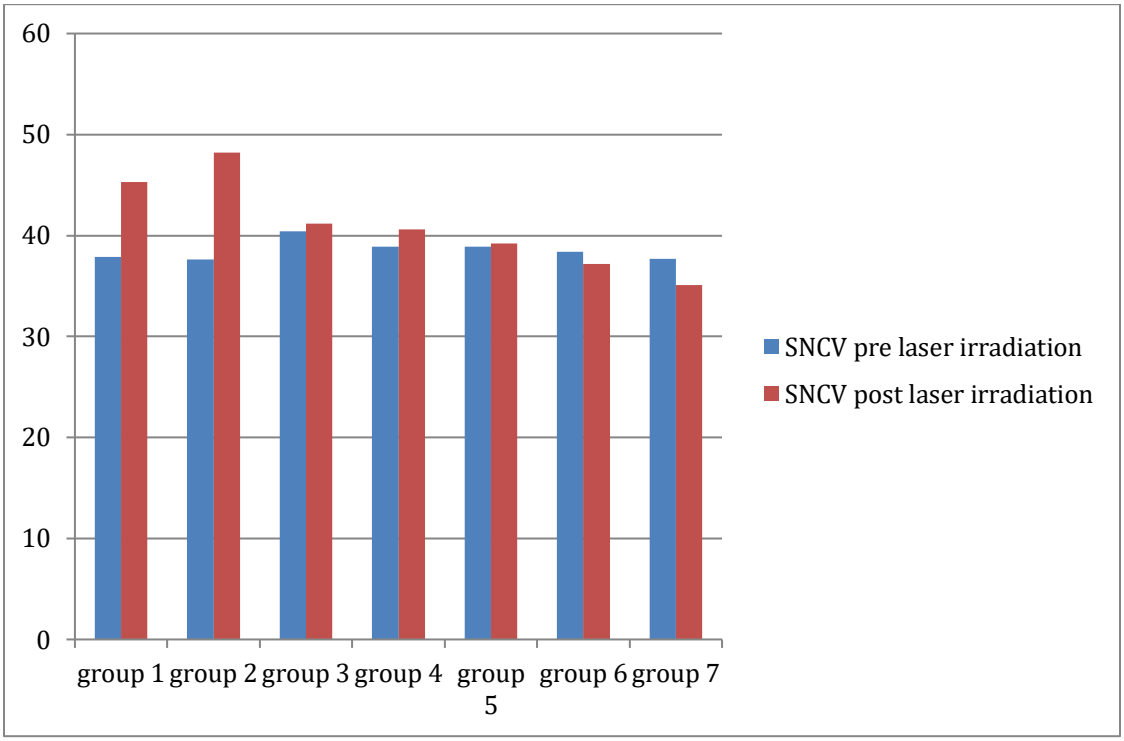

Fig 4: SNCV Values Pre & Post Laser Irradiation

Acknowledgement:

We thank Saveetha Institute of Medical and Technical Sciences for the successful completion of the research work.

Conflict of Interest: The authors declare no potential conflict of interest

Funding Source: Self

.**REFERENCES**:

1. Ashok S, Ramu M, Deepa R, Mohan V. Prevalence of neuropathy in type 2 diabetic patients attending a diabetes centre in South India. J Assoc Physicians India. 2002 Apr;50:546–50.

2. Pradeepa R, Rema M, Vignesh J, Deepa M, Deepa R, Mohan V. Prevalence and risk factors for diabetic neuropathy in an urban south Indian population: the Chennai Urban Rural Epidemiology Study (CURES-55). Diabet Med. 2008 Apr;25(4):407–12.

3. Diabetic neuropathy [Internet]. Diabetes. 2012. p. 88–97. Available from: http://dx.doi.org/10.1201/b15227-10

4. Tamar M. Association Between Diabetic Peripheral Neuropathy and Hypertiglyceridemia in Patients with Type2 Diabetes in Georgia. 2017.

5. Abdel-Wahhab KG, Daoud EM, El Gendy A, Mourad HH, Mannaa FA, Saber MM.

Efficiencies of Low-Level Laser Therapy (LLLT) and Gabapentin in the Management of Peripheral Neuropathy: Diabetic Neuropathy. Appl Biochem Biotechnol. 2018 Sep;186(1):161–73.

6. Hasegawa T, Kosaki A, Shimizu K, Matsubara H, Mori Y, Masaki H, et al. Amelioration of diabetic peripheral neuropathy by implantation of hematopoietic mononuclear cells in streptozotocin-induced diabetic rats. Exp Neurol. 2006 Jun;199(2):274–80.

7. Spadella CT, Machado JLM, Caramori CA, Gregório EA. Successful islet transplantation does not prevent the development of neuropathy in alloxan-induced diabetic rats [Internet]. Vol. 34, Transplantation Proceedings. 2002. p. 1296–300. Available from: http://dx.doi.org/10.1016/s0041-1345(02)02769-0

8. Gorray KC, Baskin D, Brodsky J, Fujimoto WY. Responses of Pancreatic B Cells to Alloxan and Streptozotocin in the Guinea Pig [Internet]. Vol. 1, Pancreas. 1986. p. 130–8. Available from: http://dx.doi.org/10.1097/00006676-198603000-00004

9. Szkudelski T, Nogowski L, Szkudelska K. Short-Term Regulation of Adiponectin Secretion in Rat Adipocytes [Internet]. Physiological Research. 2011. p. 521–30. Available from: http://dx.doi.org/10.33549/physiolres.931971

10. P RBLG, Ram Bindurani L G, Singh A. ANTIDIABETIC EVALUATION OF ISOLATED COMPOUNDS FROM TINOSPORA CORDIFOLIA IN ALLOXON INDUCED DIABETIC RAT MODEL [Internet]. Vol. 8, Journal of Biomedical and Pharmaceutical Research. 2020. Available from: http://dx.doi.org/10.32553/jbpr.v8i6.695

11. Protective Effect of Kombucha on Diabetic Nephropathy in Streptozotocin - Induced Diabetic Rats [Internet]. Vol. 5, International Journal of Science and Research (IJSR). 2016. p. 945–8. Available from: http://dx.doi.org/10.21275/v5i3.nov161951

12. J M, Mohamad J. Antidiabetic Activity of Pereskia Bleo Aqueous Extracts in Alloxan Induced Diabetic Rats [Internet]. Vol. 1, Open Access Journal of Pharmaceutical Research. 2017. Available from: http://dx.doi.org/10.23880/oajpr-16000137

13. Eliasson SG. Nerve Conduction Changes in Experimental Diabetes* [Internet]. Vol. 43, Journal of Clinical Investigation. 1964. p. 2353–8. Available from: http://dx.doi.org/10.1172/jci105109

14. Prajapati DD, Patel NM, Savadi RV, Akki KS, Mruthunjaya K. Alleviation of alloxan-induced diabetes and its complications in rats by Actinodaphne hookeri leaf extract [Internet]. Vol. 3, Bangladesh Journal of Pharmacology. 2008. Available from: http://dx.doi.org/10.3329/bjp.v3i2.946

15. Konsue A, Picheansoonthon C, Talubmook C. Fasting Blood Glucose Levels and Hematological Values in Normal and Streptozotocin-Induced Diabetic Rats of Mimosa pudica L. Extracts [Internet]. Vol. 9, Pharmacognosy Journal. 2017. p. 315–22. Available from: http://dx.doi.org/10.5530/pj.2017.3.54

16. Addepalli V, Suryavanshi SV. Catechin attenuates diabetic autonomic neuropathy in streptozotocin induced diabetic rats [Internet]. Vol. 108, Biomedicine & Pharmacotherapy. 2018. p. 1517–23. Available from: http://dx.doi.org/10.1016/j.biopha.2018.09.179

17. Pethe M, Yelwatkar S, Manchalwar S, Gujar V. Evaluation of Biological Effects of Hydroalcoholic Extract of Hibiscus Rosa Sinensis Flowers on Alloxan Induced Diabetes in Rats. Drug Res . 2017 Aug;67(8):485–92.

18. Gül N, Özsoy N. The ultrastructure of the capillaries in the gingiva of alloxan-induced diabetic rats [Internet]. Vol. 21, Cell Biochemistry and Function. 2003. p. 311–5. Available from: http://dx.doi.org/10.1002/cbf.1033

19. Coste TC, Gerbi A, Vague P, Pieroni G, Raccah D. Neuroprotective Effect of Docosahexaenoic Acid-Enriched Phospholipids in Experimental Diabetic Neuropathy [Internet]. Vol. 52, Diabetes. 2003. p. 2578–85. Available from: http://dx.doi.org/10.2337/diabetes.52.10.2578

20. Jefferys JG, Palmano KP, Sharma AK, Thomas PK. Influence of dietary myoinositol on nerve conduction and inositol phospholipids in normal and diabetic rats [Internet]. Vol. 41, Journal of Neurology, Neurosurgery & Psychiatry. 1978. p. 333–9. Available from: http://dx.doi.org/10.1136/jnnp.41.4.333

21. Anders JJ, Geuna S, Rochkind S. Phototherapy promotes regeneration and functional recovery of injured peripheral nerve. Neurol Res. 2004 Mar;26(2):233–9.

22. Suganthirababu P, Sai Sowjanya BV, Prathap L, Kumaresan A, Jannu C, Chandupatla VD. Low-level laser therapy in the management of diabetic sensorimotor polyneuropathy [Internet]. Vol. 9, Indian Journal of Public Health Research & Development. 2018. p. 147. Available from: http://dx.doi.org/10.5958/0976-5506.2018.01823.5

23. Devi CV, Jannu C, Suganthirababu P, Puchchakayala G. Effect of Therapeutic Laser in the Management of Diabetic Foot Ulcer [Internet]. Vol. 10, Indian Journal of Public Health Research & Development. 2019. p. 217. Available from: http://dx.doi.org/10.5958/0976-5506.2019.01881.3

24. Ch VD, Jannu C, Suganthirababu P, Puchchakayala G. Comparison of Ultrasound and Low Level Laser Therapy in the Management of Diabetic Foot Ulcer [Internet]. Vol. 10, Indian Journal of Public Health Research & Development. 2019. p. 204. Available from: http://dx.doi.org/10.5958/0976-5506.2019.02797.9

25. Jannu C, Devi V, Suganthirababu P, Puchchakayala G. EFFECT OF THERAPEUTIC LASER IN THE MANAGEMENT OF DIABETIC NEUROPATHY PAIN. Ethiopian Journal of Health Development [Internet]. 2019 [cited 2020 Aug 26];33(2). Available from: https://www.ajol.info/index.php/ejhd/article/view/188857

26. Suganthirababu P, Alagesan J, Prathap L, Manikumar M, Kumaresan A, Banu N. Action of Ultrasound Therapy in Altering Motor Nerve Conduction Velocity of Ulnar Nerve [Internet]. Vol. 12, Biomedical and Pharmacology Journal. 2019. p. 843–8. Available from:

http://dx.doi.org/10.13005/bpj/1708

27. S Prathap, A Maiya, JD Saraswathi, Effect of low level laser irradiation on motor nerve conduction velocity of experimentally induced diabetic neuropathy in wistar rat. Journal of Pharmaceutical and Biomedical Sciences (JPBMS) 13 (13) 2011