Int J Trans Res Ind Med 2021, 3(2): (P) 31 - 36

Research Article ISSN 2582-0109

International Journal of Translational Research in Indian Medicine
www.ijtrim.com
Volume 3, Issue 2 – 2021

ANTI-SCIATIC POTENTIAL OF SIDDHA FORMULATION KIRAMBU CHOORANAM IN CHRONIC CONSTRICTION INJURY CAUSED BY SCIATIC NERVE COMPRESSION IN WISTAR RATS

L. Parwin[*1], J.Nikil Niva[2], M. Mahasundari@Sudha[3], N.Anbu[4]

*[*1,2&3] P.G Scholar, Department of General Medicine, Government Siddha Medical College, Arumbakkam, Chennai - 600 106, Tamil Nadu, India*
[4] Head, Department of General Medicine, Government Siddha Medical College, Arumbakkam, Chennai - 600 106, Tamil Nadu, India

ABSTRACT

Neuropathic pain (Sciatica) is manifested as a result of damage or lesions in the sensory nervous system. It is characterized by allodynia and hyperalgesia. It is one of the major devastating conditions with long-term impairment of the affected patients' social life and overall quality of life. This class of pain affects 7% to 9% of the world population. Conventional therapy for pain management in sciatica patients offers potential side effects which hindered the acceptability of conventional drugs. Traditional herbal medicines enriched with several bioactive compounds having physiologically important biomedical activities with minimal or no side effects. Kirambu chooranam (KC) is a siddha poly herbal formulation comprises of 14 versatile herbal therapeutics which possess numerous bioactive compounds. Still now there is no documentary evidence claiming the anti-sciatic potential of this novel formulation KC, hence the study aimed at investigating the neuroprotective efficacy of KC in chronic constriction injury caused by sciatic nerve compression in rats. It was observed from the results of the present study that there was significant decrease in reaction time on paw withdrawal response of the rats belongs to group II, which may be assign of chronic constriction injury caused by sciatic nerve compression. Treatment with KC at both the dose level reveals significant increase in reaction time as observed in the response of the treated rats subjected to Eddy's hot plate experiment. Histological data's further evident the anti-sciatic potential of Siddha formulation Kirambu chooranam by reducing the signs of degeneration.

KEY WORDS: ***Sciatica, Conventional therapy, Side effects, Siddha formulation, Anti- sciatic, Kirambu chooranam, Eddy's hot plate.***

Corresponding Author: S.Manju, P.G Scholar, Department of General Medicine, Government Siddha Medical College, Arumbakkam, Chennai - 600 106, Tamil Nadu, India.

1. Introduction

Peripheral nerve injury presents a lifelong disability where crush injury is the highest rated type among other injuries [1]. Sciatic nerve crush injury underlies a serious problem with an incidence of 2.8% in multiple-trauma victims and is diagnosed as allodynia, and heat and mechanical hyperalgesia. Among other therapeutic strategies, pharmacotherapy has been shown to be a promising approach to the neurorehabilitation, with the exploration of potential leads from nature being of increasing interest [2].

Traditionally, functional nerve defects have been remedied by many methods, including nerve transfer, nerve grafts and artificial nerve conduit bridging end-to-side neurorrhaphy [3]. However, these methods only provide a regenerative environment for injured nerves. Recovery of function depends on various local and systemic factors. Regeneration of axons from the proximal stump of an injured nerve to the distal nerve stump is one of the most important factors in re-innervation of peripheral tissue.

The search for a treatment for neuropathic pain with few or no complications has been intensified. Non-steroidal anti-inflammatory drugs, opiates, tricyclic antidepressant, and anticonvulsant drugs dominate the preferred choice used in clinical practices for the treatment of neuropathic pain. However, limited efficacy and unacceptable side effects have hindered the acceptability of these categories of drugs [4].

A variety of therapeutic options are available, but they remain unsuccessful in attaining desired functional recovery at an optimal cost and accessibility. Ongoing neuroscience research continues to reveal new and alternative therapeutic options that could minimize or eliminate the disabilities of patients from physical dependency by promoting the healing mechanisms underlying such injuries [5,6]. In this modern era also 75–80% of the world populations still use herbal medicine mainly in developing countries, for primary health care because of better cultural acceptability, better compatibility with the human body, and lesser side effects [7].

Siddha system of medicine is one of the oldest known traditional therapy that continuous to contribute the wellness of mankind since several centuries, Major proportion of siddha drugs are derived from herbal origin with possess numerus therapeutic moieties. Kirambu chooranam (KC) is a siddha poly herbal formulation comprises of 14 versatile herbal therapeutics which possess numerous bioactive compounds. Still now there is no documentary evidence claiming the anti-sciatic potential of this novel formulation KC, hence the study aimed at investigating the neuroprotective efficacy of KC in chronic constriction injury caused by sciatic nerve compression in rats.

2. Materials and Methods

2.1. Experimental Animals

Healthy adult wistar albino rats of either sex weighing between 220-240 g were used for the study. The animals were housed in poly propylene cages and were kept in well ventilated with 100% fresh air by air handling unit. A 12 light / dark cycle were maintained. Room temperature was maintained between 22± 2o C and relative humidity 50–65%. They were provided with food (Sai feeds, Bangalore, India) and water ad libitum. All the animals were acclimatized to the laboratory for 7 days prior to the start of the study. The experimental protocol was approved by The Institutional Animal Ethics Committee of Sathyabama Institute of science and technology, Chennai, Tamil Nadu, India. Approval ref number SU/CLATR/IAEC/XV/165/2020

2.2. Experimental Methodology

The animals were grouped into four groups of 6 animals each. Group I (Sham operated control group) –exposed to surgical procedure without nerve compression received normal saline 5ml/kg, p.o. Group II – Sciatic nerve compression induced group – in which animals are subjected to sciatic nerve compression by ligation method and serves as disease control. Animal belongs to group III (Low dose treatment group): Sciatic nerve compressed rats administered with 200mg/kg of KC, p.o for 21 days. Animal belongs to group IV (High dose treatment group): Sciatic nerve compressed rats administered with 400mg/kg of KC, p.o for 21 days.

2.3. Induction of peripheral neuropathy by chronic constriction injury [8,9]

Peripheral neuropathy in experimental rats were induced by chronic constriction injury method. The rats were anesthetized with thiopental sodium (35 mg/kg i.p.). The hair of the rat's lower back in thigh region of left paw was shaved, and sterilized with

povidone-iodine. The skin of the lateral surface of the left thigh was incised and a cut will made directly through the biceps femoris muscles to expose the sciatic nerve. Four ligatures (silk thread), placed around the nerve proximal part of the trifurcation with a distance of 1 mm between each ligature. After performing nerve ligation, muscular and skin layer was immediately sutured with thread and topical antibiotic was applied at once. Nociceptive threshold was assessed before and after performing surgery on different days i.e. 7, 14 and 21st day.

2.4. Heat Hyperalgeia test [10]

Heat hyperalgesia of the hind paw were assessed using Eddy's hot plate method, for assessing the reactivity to noxious and non-noxious thermal stimuli respectively. The rats was placed on the top of a controlled preheated (52.5 ± 0.5°C for hyperalgesia) and maintained hot plate surface, allowing access to the left hind paw withdrawal response to degree of the nociceptive threshold. The cut-off times of 45s for hyperalgesia were maintained.

2.5. Histopathological evaluation [11]

Samples of distal portion of sciatic nerve will be collected and the same is stored in the fixative solution (10% formalin) and cut into 10 µm thickness. Staining will be done by using hematoxylin and eosin. Nerve sections will be analysed qualitatively under light microscope (450 X) for axonal degeneration.

3.Results

3.1. Effect of Kirambu chooranam (KC) on paw withdrawal response of chronic constriction injury induced rats

It was observed from the results of the present study that there was significant decrease in reaction time on paw withdrawal response of the rats belongs to group II, which may be assign of chronic constriction injury caused by sciatic nerve compression. Treatment with Kirambu chooranam (KC) at both the dose level reveals significant increase in reaction time as observed in the response of the treated rats subjected to Eddy's hot plate experiment. Histological data's further evident the anti-sciatic potential of Siddha formulation Kirambu chooranam by reducing the signs of degeneration. Data's represented in the Table 1.

Table 1: Effect of *Kirambu chooranam (KC)* on paw withdrawal response of chronic constriction injury induced rats

Groups	Before Treatment	After Treatment		
		7th Day	14th Day	21st Day
	Reaction time in Sec	Reaction time in Sec	Reaction time in Sec	Reaction time in Sec
Group I	22.33 ± 0.55	8.333 ± 0.33	11.67 ± 0.88	12.17 ± 0.83
Group II	20.5±0.88	6.5± 0.56	9.167± 0.40	10.17±0.47
Group III	22.33 ± 0.55	8.333±0.33	11.67±0.88	12.17±0.83
Group IV	21.5 ± 0.88	10 ± 0.36	15.17 ± 0.79	17.5 ± 0.84

PW- Paw withdrawal | Values are mean ± S.E (n = 6 per group).

3.2. Effect of Kirambu chooranam (KC) on Histology of Rat Sciatic Nerve

Light microscopic observation of H&E stained section of sciatic nerves sample reveals dense network of Schwann cells with prominent regular architecture of myelin sheath were observed in sample belongs to group I. Significant increase in inter neuronal space with evidence of abnormal collagen deposition were observed in group II. Reduction in collagen deposition with reduced inter neuronal space were observed in group III. Rich dense network of fibres with no signs of degeneration or oedema were been observed in sample belongs to group IV. As shown in Figure 1.

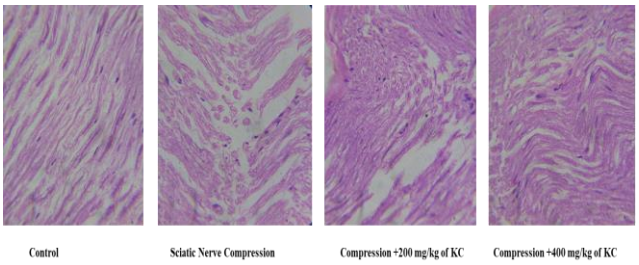

Figure 1: Effect of Kirambu chooranam (KC) on Histology of Control and drug treated Rat Sciatic Nerve

4.Discussion

Peripheral nerve injury is one of the major health concerns faced by the community at present. Till now, available therapeutic approaches are ineffective to fully heal a nerve injury and to assure the functional recovery entirely. Natural compounds can prove attractive and effective drug candidates to bridge up this gap. Traditionally, anti-inflammatory therapy has focused on the modulation of pro-inflammatory

mediators and/or adhesion molecule expression [12,13]. However, in the past few years it has been recognized that the inflammation resolution may be based on multi-target drugs [14]. Multiple signaling pathways are a way to improve the pro-inflammatory, immunomodulatory and pro-resolving cascades, which define the aspects of the inflammation [15].

In this context, natural products have played an important role in the development of new sources to treat inflammatory diseases [16]. Historically, the screening of sources for natural products led to the discovery of clinical drugs currently used in the pharmacological therapy [17]. Nonetheless, since natural products do not have a standard composition and they may provide compounds with a unique structural activity there is interest in identifying the potential biological therapeutic in new herbal derivatives [18].

The rat sciatic nerve is commonly studied by researchers working on peripheral neuropathies not only for its anatomical features, but also for it length and consequently, the amount of tissue available for histological analysis. Several studies demonstrated that various transaction, ligation, and crushing of sciatic nerve and its branches induces an ipsilateral mechanical, cold, heat hyperalgesia and allodynia thereby indicating the induction of peripheral neuropathic pain [19]. These behavioural alterations are constantly present and last over 2–3 weeks, but their time course varying upon the model and species [20]. It was observed from the results of the present study that there was significant decrease in reaction time on paw withdrawal response of the rats belongs to group II, which may be assign of chronic constriction injury caused by sciatic nerve compression. Treatment with Kirambu chooranam (KC) at both the dose level reveals significant increase in reaction time as observed in the response of the treated rats subjected to Eddy's hot plate experiment.

Peripheral nerve encompasses all the nerve trunks and branches which lie outside the central nervous system. When a peripheral nerve is injured, the muscles supplied by that nerve do not receive messages from the brain. Therefore, they become weakened or paralysed [21, 22]. Traffic collisions usually induce traumatic nerve injuries resulting from disruption of the intraneural circulation [23]. This condition consequently induces demyelinization, remyelinization, axonal degeneration and axonal regeneration, focal, multifocal, or diffuse nerve fibre loss, and endoneural edema [24,25]. Light microscopic observation of H&E stained section of sciatic nerves sample reveals dense network of Schwann cells with prominent regular architecture of myelin sheath were observed in sample belongs to group I. Significant increase in inter neuronal space with evidence of abnormal collagen deposition were observed in group II. Reduction in collagen deposition with reduced inter neuronal space were observed in group III. Rich dense network of fibres with no signs of degeneration or oedema were been observed in sample belongs to group IV.

5. Conclusion

The findings of the current study suggest that the siddha formulation Kirambu chooranam accelerates the restoration of neuronal function following a mechanically induced injury to the sciatic nerve. Based on current observations, it can be suggested that these ameliorating effects can be accredited due to the bioactive phytocomponents present in the formulation further studies needs to be carried out to extrapolate the clinical application of the Kirambu chooranam in the management of sciatica.

Acknowledgement

We wish to acknowledge my thanks to The Tamil Nadu Dr. M.G.R. Medical University, Chennai, Tamil Nadu, India and The Noble research solutions, Chennai, Tamil Nadu, India for their support.

6. References

1. Zhang YG, Sheng QS, Wang HK, Lv L, Zhang J, Chen JM, et al. Triptolide improves nerve regeneration and functional recovery following crush injury to rat sciatic nerve. Neurosci Lett. 2014; 561: 198–202.
2. Zhao L, Liu Q, Chen H, Duan H, Bin P, Liu Q, et al. The effect of 2, 5-hexanedione on myelin protein zero expression, and its mitigation using Ginkgo biloba extract. Biomed Environ Sci. 2011; 24(4): 374–382.
3. Oberlin C, Beal D, Leechavengvongs S, Salon A, Dauge MC, Sarcy JJ. Nerve transfer to biceps muscle using a part of ulnar nerve for C5-C6 avulsion of the brachial plexus: anatomical study

and report of four cases. Journal of Hand Surgery. 1994;19(2):232–237.
4. Muthuraman A, Singh N, Jaggi AS, Ramesh M. Drug therapy of neuropathic pain: current developments and future perspectives. Curr Drug Targets. 2014;15:210–53.
5. Hussain, G. , Wang, J. , Rasul, A. , Anwar, H. , Qasim, M. , Zafar, S. , Aziz, N. , Razzaq, A. , Hussain, R. , de Aguilar, J.-L. , & Sun, T. (2020). Current status of therapeutic approaches against peripheral nerve injuries: A detailed story from injury to recovery. International Journal of Biological Sciences, 16, 116–134.
6. Razzaq, A. , Ahmad, S. , Farhan, M. , Ali, S. , Rasul, A. , Qasim, M. , Hussain, M. (2020). Moringa oleifera Lam. ameliorates the muscles function recovery following an induced insult to the Sciatic nerve in a mouse model. Food Science and Nutrition, 8, 1–8
7. B. Debjit, C. Chiranjib, K. K. Tripathi, Pankaj, and K. P. Sampath Kumar, "Recent trends of treatment and medication peptic ulcerative disorder," International Journal of PharmTech Research, vol. 2, no. 1, pp. 970–980, 2010.
8. Arunachalam Muthuraman and Nirmal Singh. Attenuating effect of Acorus calamus extract in chronic constriction injury induced neuropathic pain in rats: an evidence of anti-oxidative, anti-inflammatory, neuroprotective and calcium inhibitory effects. Muthuraman and Singh BMC Complementary and Alternative Medicine 2011, 11:24.
9. Paul J. Austin, Ann Wu, and Gila Moalem-Taylor. Chronic Constriction of the Sciatic Nerve and Pain Hypersensitivity Testing in Rats. J Vis Exp. 2012; (61): 3393.
10. N. B. Eddy and D. Leimback, "Synthetic analgesic II. Diethlenyl butenyl and dithienyl butylamines," Journal of Pharmacology and Experimental Therapeutics, vol. 107, pp. 385–393, 1953.
11. Suvarna, S.K., C.Layton and J.D. Bancroft. 2013. Bancroft's theory and practice of histological techniques. 7th edn, Churchill Livingstone, London.
12. Rainsford KD. Anti-inflammatory drugs in the 21st century. Subcell Biochem. 2007;42: 3–27. Available: http://www.ncbi.nlm.nih.gov/pubmed/17612044
13. Georgakopoulou EA, Scully C. Systemic use of non-biologic corticosteroids in orofacial diseases. Oral Dis. 2014;20: 127–35.
14. Koeberle A, Werz O. Multi-target approach for natural products in inflammation. Drug Discov Today. 2014;19: 1871–82.
15. Kohli P, Levy BD. Resolvins and protectins: mediating solutions to inflammation. Br J Pharmacol. 2009;158: 960–71.
16. Cragg GM, Grothaus PG, Newman DJ. New horizons for old drugs and drug leads. J Nat Prod. 2014;77: 703–23.
17. Gasparetto JC, Martins CAF, Hayashi SS, Otuky MF, Pontarolo R. Ethnobotanical and scientific aspects of Malva sylvestris L.: a millennial herbal medicine. J Pharm Pharmacol. 2012;64: 172–89.
18. Ishtiaq M, Hanif W, Khan MA, Ashraf M, Butt AM. An ethnomedicinal survey and documentation of important medicinal folklore food phytonims of flora of Samahni valley, (Azad Kashmir) Pakistan. Pakistan J Biol Sci PJBS. 2007;10: 2241–56.
19. Kaur G, Jaggi AS, Singh N. Ameliorative potential of pralidoxime in tibial and sural nerve transection-induced neuropathic pain in rats. Biol Pharm Bull. 2010;13(8):1331–1336.
20. Crips T, Giles JR, Cruce WL, McBurney DL, Stuesse SL. The effects of aging on thermal hyperalgesia and tactile-evoked allodynia using two models of peripheral ononeuropathy in the rat. Neurosci Lett. 2003;13(2):103–106.
21. Chiu D. T. W., Ishii C. Management of peripheral nerve injury. Orthopedic Clinics of North America. 1986;17(3):365–373.
22. Navarro X., Vivó M., Valero-Cabré A. Neural plasticity after peripheral nerve injury and regeneration. Progress in Neurobiology. 2007;82(4):163–201.
23. Lundborg G. Intraneural microcirculation. Orthopedic Clinics of North America. 1988;19(1):1–12.
24. Zachodne D. W., Ho L. T. Endoneural microenvironment and acute nerve crush injury in the rat sciatic nerve. Brain Research. 1990;535:43–48.

25. Bagdatoglu C., Saray A., Surucu H. S., Ozturk H., Tamer L. Effect of trapidil in ischemia/reperfusion injury of peripheral nerves. Neurosurgery. 2002;51(1):212–220.