



PREVENTIVE APPROACH TO DIABETIC NEUROPATHY: THE AYURVEDIC REFLECTIONS

Madhavi Mahajan¹, Ritaja Nitin Sathe^{2*}, Satyam³

¹M.D., Ph.D. (Kayachikitsa), Asso. Professor, Department of Kayachikitsa, Bharati Vidyapeeth (Deemed to be University) Pune, College of Ayurved, Pune; Email: drmadhavi.m@gmail.com

²Post Graduate Scholar, Department of Kayachikitsa, Bharati Vidyapeeth (Deemed to be University) Pune, College of Ayurved, Pune; Email: ritajavashishth@gmail.com

³Post Graduate Scholar, Department of Kayachikitsa, Bharati Vidyapeeth (Deemed to be University) Pune, College of Ayurved, Pune; Email: satyamkaushish28@icloud.com

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Abstract: Diabetic neuropathy (DN) is the most common and only microvascular complication of DM which lacks a specific disease modifying treatment. In Ayurveda, some typical neuropathic symptoms are mentioned under Poorvarooopa (prodrome) and Upadrava (complications) of Prameha (diabetes). It is also described under various Vata Vyadhi including Raktagata vata, twakgata vata and Avritta vata.

The American Diabetes Association (ADA) recommends diet and exercise as first-line prevention for Diabetic peripheral neuropathy. Various drugs, diet and lifestyle interventions mentioned under Prameha adhikara were from Ayurvedic classics and contemporary modern literature were explored with a thought that the same might be helpful in preventing diabetic neuropathy. It was found that most of the drugs and food products possess anti-diabetic, anti-oxidant, neuroprotective activities. Various exercises were also found to be beneficial in diabetic neuropathy. Thus, it could be concluded that the treatment regimen mentioned under Prameha adhikara may be implemented as a part of preventive medicine for patients suffering from diabetes.

Keywords: Diabetic neuropathy, preventive medicine, Ayurveda, Prameha, Ahara, Vihara, life style intervention.

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INTRODUCTION

Diabetic neuropathy (DN) affects 50% of diabetics, but quite under reported and inadequately treated. Most common type of DN is sensory peripheral neuropathy affecting both the legs and hands in a stocking-glove pattern. It is the strongest predictor of mortality in type 2 diabetes.¹ Its prevalence in India ranges from around 10.5% to 32.2% as reported in various studies across India.² Current treatment approach to DN in contemporary modern medicine focuses on glycemic control and pain relief using some FDA approved drugs, but disease modifying treatment is not yet established owing to the complex mechanisms and incomplete understanding of pathogenesis of DN. The American Diabetes Association (ADA) recommends diet and exercise as first-line prevention for Diabetic peripheral neuropathy.³

Studies suggest that oxidative stress possibly triggered by vascular abnormalities and associated microangiopathy in the nerve, is a key pathological process inducing nerve damage in diabetes in humans and experimental models.^{4,5,6}

In Ayurvedic classics, Prameha (Diabetes) has secured a position in the Ashta Maha-agadas due to chronicity and complexity. The symptoms of diabetic neuropathy are found scattered in the Poorvaroopas, Lakshanas and Upadrasvas of Prameha in the form of daaha, paridhoomayana, stambha, suptata, kampa, shoola, toda.^{7,8,9,10,11} The etiology of diabetic neuropathy as an Upadrava in Prameha is complex and occurs either due to Dhatukshayajanya Vaatprakopa i.e., vitiation of Vata due to destruction of body tissues or Margaavarodh janya Vaatprakopa i.e., vitiation of Vata due to obstructive causes. According to modern sciences Hence preventive measures

MATERIAL AND METHODS

This study was done with a motive to analyze the Ayurvedic treatment regimen mentioned under Prameha adhikara and to implement the same for prevention of diabetic neuropathy. The chapters on Prameha Nidana, Prameha Chikitsa, Vaata Vyadhi, mentioned in various Granthas like Charaka Samhita, Sushruta Samhita, Ashtang Hriday, Madhava Nidana, Bhaishajya Ratnavali were studied thoroughly. A list of about 40 Grathokta herbal drugs used in Prameha chikitsa was made. The drugs of animal, mineral origin as well as various life style interventions based on Ahara-Vihara (diet and exercise) in Prameha Vyadhi were also studied. Amongst these drugs, those which have a proven effect on either diabetic neuropathy directly or having anti-oxidant effects were thoroughly explored using the search engines like PubMed and Google Scholar by applying keywords like Latin names of certain herbs, for e.g., Curcuma longa and effect on diabetes/diabetic neuropathy/ nerves, exercise and diabetic neuropathy, foot bath and neuropathy etc. Various Peer reviewed international journals like Diabetes Care, The Lancet, American Academy of Neurology, International Diabetes Federation, Annals of Indian Academy of Neurology, Frontiers in Pharmacology, were surveyed to gain an in-depth knowledge pertaining to DN.

RESULTS AND DISCUSSION

The ancient Ayurveda Acharyas like Maharshi Charak, Sushrut and Vagbhat have very mindfully formulated the treatment regimen for diabetic patients in the form of drugs, diet and life style interventions. The drugs include those of plant, animal and mineral origin. Emphasis is laid on diet that must be followed by all diabetic patients. An array of exercises has been provided according to the strenuous physical activities that existed in that era.

Drugs

Audbhida (Plant Origin)

Sr.No.	Dravya	Latin Name	Action
1.	Triphala	Terminalia chebula, Terminalia bellirica, Emblica officinalis	Triphala treatment significantly increased the motor nerve conduction velocity and decreased the thermal and mechanical hyperalgesia, as well as mechanical allodynia. The treatment significantly inhibited levels of circulatory cytokines like TGF- β 1, TNF- α , and IL-1 β . ¹²
2.	Amalaki (Indian Gooseberry)	Emblica officinalis	E. officinalis extract attenuated diabetic induced axonal degeneration. It showed preventive and curative effect on nerve function and oxidative stress in animal model of diabetic neuropathy. ¹³ Another study found that insulin alone corrected the hyperglycemia and partially reversed the pain response in diabetic rats. However, combination with Emblica officinalis extract not only attenuated the diabetic condition but also reversed neuropathic pain through modulation of oxidative-nitrosative stress in diabetic rats. ¹⁴
3.	Daruharidra (Indian Barberry)	Berberis aristata	Berberine has a beneficial effect against diabetic neuropathy by improving micropathology and increasing neuritin expression via the mitogen-activated protein kinase signaling pathway. ¹⁵

4.	Maricha (Black pepper)	Piper nigrum	Viphyllin exerts antidiabetic effects and improves nerve conduction to mitigate neuropathic pain. ¹⁶
5.	Haridra (Turmeric)	Curcuma longa	Curcumin supplementation for 2 months improved and reduced the severity of DSPN in patients with T2DM. ¹⁷ Another study showed that curcumin can be considered as a new therapeutic potential for the treatment of diabetic neuropathic pain and the activation of opioid system may be involved in the antinociceptive effect of curcumin. ¹⁸
6.	Guduchi (Giloy)	Tinospora cordifolia	Tinospora cordifolia prevents the hyperalgesia in experimental diabetic neuropathy. It has an aldose reductase inhibitory activity in-vitro which may contribute to the beneficial effects. ¹⁹
7.	Nimba (Neem)	Azadirachta indica	The treatment of diabetic rats with aqueous leaf extract of Azadirachta indica reduced the levels of blood glucose, Lipid peroxidation and restored the activities of antioxidant enzyme. ²⁰ Another study revealed that Azadirachta indica exerts its neuroprotection against partial sciatic nerve ligation induced neuropathic pain via inhibition of oxidative-nitrosative stress, the release of pro-inflammatory cytokines and apoptosis to improve MNCV. ²¹
8.	Musta	Cyperus rotundus	Hydroalcoholic extract of cyperus rotundus ameliorates H ₂ O ₂ -induced human neuronal cell damage via its anti-oxidative and anti-apoptotic machinery. ²²
9.	Indrayana	Citrullus colocynthis	Histological evaluation of the sciatic nerve showed that C. colocynthis decreased the number of demyelinated and degenerated nerve fibers. C. colocynthis fruit, through its antioxidant and hypoglycemic activities, has a positive effect in the treatment of diabetic neuropathy. ²³ Another study showed that application of a topical formulation of C. colocynthis fruit extract can decrease pain in patients with PDPN. ²⁴
10.	Palasha	Butea monosperma	Pretreatment with B. monosperma significantly attenuated vincristine-induced development of painful behavioural, biochemical and histological changes in a dose-dependent manner, which is similar to that of pregabalin-pretreated group. B. monosperma ameliorated vincristine-induced painful neuropathy. It may be due to its potential of antioxidative, neuroprotective and calcium channel inactivation. ²⁵ another study showed significant antihyperglycemic and antioxidant potential of the crude extract of B. monosperma bark indicating its probable use in the management of diabetes and resultant oxidative stress. ²⁶

11.	Saptaparna	Alstonia scholaris	Methanol extract (200 mg/kg) of A. scholaris showed the ameliorative effect in chronic constrictive injury of sciatica nerve induced neuropathic pain which may be due to the presence of kaempferol and attributed to its anti-oxidative and anti-inflammatory properties. ²⁷
12.	Singhada	Trapa Bispinosa	A study found that long-term administration of supplement with TBE and lutein improved the impaired regulation of retinal blood flow in response to systemic hyperoxia and flicker stimulation, suggesting that these supplements can prevent diabetic retinopathy by improving abnormal neurovascular coupling in type 2 diabetic mice. ²⁸
13.	Gokshura (Nerunjil)	Tribulus terrestris	Treatment with Nerunjil (100 and 300 mg/kg; p.o.) for 4 weeks significantly attenuated the nociception in behavioural models. Nerunjil also inhibited the tumour necrosis factor- α and interleukin-1 beta levels. Thus, in controlled diabetic states, Nerunjil attenuated the neuropathic pain through modulation of oxidative stress and inflammatory cytokine release. ²⁹
14.	Yavani	Trachyspermum ammi	Biomarker studies (SOD, NO, LPO, Na ⁺ K ⁺ ATPase, and TNF- α) confirmed thymol's diabetic neuropathy protective action. Isolated compound thymol was antidiabetic and neuroprotective as it has shown controlled glucose levels defensive nerve damage in STZ Wistar rats. ³⁰
15.	Sariva	Hemidesmus indicus	H. indicus root extract normalized the levels of antioxidant markers like SOD, CAT, GSH. It was able to prevent cataract by prevention of opacification and formation of polyols that underlines its potential as a possible therapeutic agent against diabetic complications. ³¹
16.	Vijayasara	Pterocarpus marsupium	A study suggested that Pterocarpus marsupium extract (200 mg/kg body weight) has the ability to reduce oxidative stress and inflammatory cytokines, such as tumor necrosis factor- α (TNF- α) Interleukin-6 (IL-6) messenger ribonucleic acid (mRNA), as well as protein expression and it could effectively reduce the inflammation and hyperglycemic condition in diabetic rat. ³² Another study suggested that the phytoextract showed prominent antioxidant, antiglycation property and, inhibited accumulation of sorbitol and ALR enzyme, thus promising a beneficial role in reducing/delaying diabetic complications. ³³

17.	Amra	Mangifera indica	Mangiferin obtained from leaves of mango tree has the potential to treat diabetes and it can be developed as a therapeutic agent for diabetes and the complications caused by diabetes. ³⁴
18.	Dadima	Punica granatum	The results proved that the highest dose levels of Pg extract, F1, F2 exerted remarkable hypoglycemic activity with 48, 52, and 40% drop in the mice glucose levels after 6 hours, respectively. The tested compounds also improved peripheral nerve function as observed from the latency tests. ³⁵
19.	Manjishtha	Rubia cordifolia	A case study showed that a combination of Ashwagandha, Haridra and Manjistha Churna was very effective in patients of Diabetic Neuropathy. ³⁶
20.	Arjuna	Terminalia arjuna	A study showed that Terminalia arjuna improves cardiovascular autonomic neuropathy in streptozotocin-induced diabetic rats. The study suggested that T. arjuna bark extract improves the altered baroreflex sensitivity in diabetic rats possibly through maintaining endogenous antioxidant enzyme activities and decreasing cytokine levels. ³⁷
21.	Rala	Shorea robusta	An animal study suggested that S. robusta resin can limit neurodegenerative changes in sciatic nerve by suppression of STZ-induced hyperglycemia associated oxidative stress may represent promising agents to improve peripheral nervous system functioning. ³⁸

From the above data, it is evident that these herbs contain such active principles which exert an antidiabetic effect as well as they possess potent anti-oxidant and anti-inflammatory properties. This has a protective effect on peripheral nerves and hence many studies have shown reversal of neuropathy in experimental models.

Jangama (Animal Origin)

Sr.No.	Dravya	Action
1.	Madhu (Honey)	Three months honey supplementation reduced participants' subjective pain scores and symptoms from diabetic neuropathy and improved their QOL. ³⁹
2.	Gomutra arka (Cow urine aqueous extract)	A study showed that GoA significantly lowered blood glucose in diabetic rats although the observed effect was found to be less than glibenclamide. It also significantly lowered the level of malondialdehyde. ⁴⁰

Honey can be used as an Anupana Dravya, i.e., a vehicle that can enhance the properties of certain drugs and may improve their transportation to certain target sites. It can be given along with different

combinations of above mentioned herbs so as to prevent diabetic neuropathy. Gomutra arka can also be used to prevent diabetic neuropathy by reducing oxidative stress

Khanija (Mineral Origin)

Sr.No.	Name	Scientific Name	Effects Observed
1.	Suvarna (Gold)	Aurum	An animal study revealed that topically applied nanoparticles with neurotropic targeting ligands can be utilized for delivering nanoparticles to neuronal cell bodies via axonal transport mechanisms. ⁴¹
2.	Rajat (Silver)	Argentum	Green synthesis of silver nanoparticles in combination with Nigella sativa extract could be a newly neuroprotective agent against inflammation and oxidative stress characterizing diabetic neuropathy through their antidiabetic, anti-inflammatory and anti-oxidants effects. ⁴²
3.	Abhrak (Mica)	Muscovite	An animal study showed a noteworthy reduction in blood glucose, total cholesterol, and triglycerides levels in AB-treated diabetic rats. ⁴³ Dose-dependent increased immunomodulatory effects of Abhraka Bhasma were seen in a study. ⁴⁴
4.	Jasada bhasma	Zinc oxide	An experimental study on Jasada bhasma showed blood glucose lowering effects of Jasada bhasma in STZ induced diabetic rats. ⁴⁵
5.	Vanga bhasma	Tin oxide	A review on therapeutic uses of Vanga bhasma concluded that Vanga bhasma is choice of drug in prameha, Shukravaha strotas dushti. ⁴⁶

Rasaushadhis prepared from various Bhasmas (nano particles of metals and minerals) possess sookshma (penetrating) quality and can probably work at the cellular/tissue level to affect various pathways that lead to neuropathy. As suggested by above studies, these can help in correcting hyperglycemia as well as to relieve oxidative stress. In Ayurvedic literature, these potent medicines are known to impart strength to nerve tissue and improve its functions. Thus these can be incorporated as a part of preventive medicine in diabetic neuropathy.

Diet

Ayurveda has put forth certain dietary principles to be followed in diabetic patients in the form of Pathya (beneficial) and Apathya (harmful).

Pathyaahaar

Acharya Sushruta and Charaka have included the following food products in the diabetic diet: Purana shali (one year old rice), Shashti shali (Brown rice), Kodo millet, Godhuma (wheat), Yava (barley), Chanak (chickpeas), Adhaki (Pigeon pea), Mudga, oils of Danti, Ingudi, Atasi, Mustard etc, bitter vegetables including patola (Luffa acutangula), chakwad etc. Of these, the following table represents the anti-diabetic, anti-oxidant activities of these food products that have been proven in various research studies.

Type of food	Name	English Name	Observed effects
Whole grains	Yava	Barley	The incorporation of barley microgreen in the diet was able to control type 2 diabetes mellitus and the improved outcomes observed with barley microgreen treatments involved or occurred in conjunction with improved biomarkers of oxidative stress. ⁴⁷
Lentils	Chanak	Bengal gram	Chickpea protein hydrolyzates are good sources of peptides with antidiabetic potential, showing high antioxidant activity and inhibition of enzymes related to carbohydrate metabolism and type 2 diabetes. ⁴⁸
	Mudga	Green gram/ Moong dal	Study showed reduced reactive oxygen species and increased glucose uptake in insulin-resistant HepG2 cells dose-dependently with Mung bean seed coat extract. The anti-inflammatory activity of MSE was also observed. ⁴⁹
Oils	Ingudi	Egyptian balsam	BA exerted hypoglycemic, hypolipidemic, insulinotropic and antioxidant effects. Additionally, it reduced apoptosis in pancreatic β -cells and increased glucose uptake in muscle. These results suggest that the hypoglycemic effect of BA is due to the inhibition of the SAPK-JNK pathway. ⁵⁰
	Sarshapa	Mustard seeds	Mustard oil elicits hypoglycemic effect by increased insulin activity and up-regulation of Glut 4 gene expression in muscle tissue of STZ-induced diabetic rats. ⁵¹
	Atasi	Flax seeds	Flaxseed in the pre-and postnatal period displays favourable influence on the development of rat optic nerve and retina, probably leading to myelination. ⁵² Another study revealed that Flax and Pumpkin seeds mixture supplemented in diet of diabetic rats may be helpful to prevent diabetes and its complications. ⁵³

Exercise And Other Lifestyle Changes

Ayurved has proposed a variety of exercises for diabetic patients. Contemporary modern medicine also focuses on use of different exercise regimen to be followed by diabetic patients.

Sr.No.	Type Of Exercise	Observed Effects
1.	Cycling	The effect of exercise training on the measures of superficial femoral artery (SFA) and neuropathic symptoms in patients with DPN was seen. Significant improvement in fasting glucose, HbA1c and Michigan Diabetic Neuropathy Score (MDNS) following exercise intervention (all $P < 0.05$) was observed. ⁵⁴
2.	Walking	Effects of long-term exercise training on the development of DPN in both Types 1 and 2 diabetic patients without signs and symptoms of DPN was studied. Long-term aerobic exercise training (in the form of brisk walking) can prevent the onset or modify the natural history of DPN. ⁵⁵
3.	Swimming	Swimming Exercise Induced Reversed Expression of mir-96 and Its Target Gene nav1.3 in Diabetic Peripheral Neuropathy in Rats. This study introduced a new and

		potential miRNA-dependent mechanism for exercise induced protective effects against diabetic thermal hyperalgesia. ⁵⁶ Another study suggests that swimming exercise training has protective and therapeutic effects on DPN of STZ-induced diabetic rats. ⁵⁷
4.	Yogasana and Pranayama	Yogasanas included in this study were Suryanamskar, Tadasan, Konasan, Padmasan, Paschimottansan, Ardhamatsyendrasan, Shavasan, Pavanmukthasan, Sarpasan, Shavasan and Paranayama. This study showed that Yoga asanas have a beneficial effect on glycaemic control and improve nerve function in mild to moderate Type 2 diabetes with sub-clinical neuropathy. ⁵⁸
5.	Udvardana (herbal body scrubs)	A case study showed that Udvardana can help in normalizing lipid profile also in reduction of weight; BMI, body circumference and skin fold thickness in case of dyslipidemia. ⁵⁹

Ayurveda has mentioned ‘Avyayama’ and sedentary lifestyle as important etiological factors along with other dietary factors which contribute to the pathogenesis of Prameha(diabetes). ‘Vyayama’ is an essential component of the daily routine. Vyayama leads to lightness in the body, it enhances one’s stamina, it kindles the digestive fire, destroys fat and imparts a good muscular tone to the body. All these factors play important role in combating diabetes and its related complications. Thus, various forms of exercises can be incorporated into a diabetic patient’s daily regimen as preventive measures against diabetic neuropathy. Similarly, ‘Udvardana’ i.e., herbal body scrubs forms an important part of the ‘Dinacharya’- the daily routine that has been advocated by all the Ayurvedic scholars for maintaining good health. Daily Udvardana helps to pacify the vitiated Kapha dosha, liquefies the Meda (affects fat metabolism), imparts strength and stability to the body and helps to maintain the skin lustre. This can be easily included as a daily routine in diabetic patients.

CONCLUSION

From the above data, it can thus be concluded, that various types of herbs, diet and life style interventions mentioned under the Prameha Adhikara may be effectively implemented in clinical practice. Early institution of such preventive measures in diabetic patients may help in preventing diabetic neuropathy and its disastrous sequel.

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