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AN OVERVIEW OF POSTGRADUATE AND DOCTORAL LEVEL RESEARCH CONDUCTED IN AYURVEDA EDUCATION INSTITUTIONS DIABETIC NEUROPATHY :

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Abstract: Diabetes has become one of the major causes of premature illness and death in most countries. Vascular complications; both micro and macro vascular predominate the features of Indian diabetic patients due to delayed diagnosis and late presentation of the syndrome. Therefore many complications like Polyneuropathy are present at diagnosis. It is common, often severe but frequently unreported and inadequately treated. Lot of research on diabetic neuropathy is being done and reported but an considerable portion of it which is conducted by Ayurveda academic institutions go as part of PG & Doctoral thesis go unnoticed and unpublished. Hence an attempt is made to review the available academic clinical researches concerned with the management of diabetic polyneuropathy in the present article. A sudden surge of interest towards the complications of Diabetes can be noted by the number of works done after 2005 (out of 15, 12 were carried out after 2005). The works reviewed are based on obtained transcripts of the thesis or by personal communication or by acquaintances. Seven works/ abstracts (46.67%) were retrieved out of 15.

Keywords: Diabetic neuropathy, Ayurveda, Systematic review, PG and Ph.D.Thesis.

Introduction

At least 171 million people worldwide have diabetes; this figure is likely to be more than double by 2030.[1] At present India have 35 million diabetics (5.5% of population), which is likely to reach 80 million by 2030.

Overall, direct health care costs of diabetes range from 2.5% to 15% of annual health care budget, depending on local diabetes prevalence and the sophistication of the treatment available. In developed countries most people with diabetes are above the age of retirement whereas in developing countries those most frequently affected are in the middle, most productive years between 35 and 64 of age.[2]

Diabetes has become one of the major causes of premature illness and death in most countries. The number of deaths attributed annually to diabetes is around 3.2 million,[3] six deaths every minute. Vascular complications; both micro and macro vascular predominate the features of Indian diabetic due to delayed diagnosis and late presentation of the syndrome. Therefore many complications including polyneuropathy are present at diagnosis. Diabetic foot accounts for one of the largest in patients admissions in India. The neuropathies are among hospital the most common of the long-term complications of diabetes, affecting up to 50% of patients.[4,5] Long-standing peripheral neuropathic pain associated with peripheral neuropathy occurs in one of six diabetic subjects.[6]

These complications of diabetes have been recognized in modern science only since last two centuries. In the late 1800s, a series of papers appeared in which many of the subtypes of diabetic neuropathies were defined **(Althaus 1885, Leyden 1887, Auche 1890, Pryce 1893).** Included in these descriptions are patients not only with diabetic sensorimotor polyneuropathy but also others with proximal diabetic, truncal, median and ulnar neuropathies. Bruns focused further on the entity of proximal diabetic neuropathy (1890). Diabetic polyneuropathy was recognized as having various manifestations;

1. Asst. Professor 2. Director

Leyden identified 3 subtypes: painful, ataxic and paralytic. Autopsy studies on several patients showed peripheral nerve degeneration **(Leyden 1887, Auche 1890).**[7]

Major risk factors of this condition are the level and duration of elevated blood glucose. Neuropathy can lead to sensory loss and damage to the limbs. It is also a major cause of impotence in diabetic men. Diabetic foot disease, due to changes in blood vessels and nerves, often leads to ulceration and subsequent limb amputation. Diabetes is the most common cause of non-traumatic amputation of the lower limb. Simple measures like good glycaemic control and neuroadjuvants, visual inspection of feet and foot-care can save and salvage feet at risk.

With longstanding diabetes mellitus progressive damage to nerves is seen and the symptoms are most profound at the extremities of the limbs; this condition is known as Diabetic Polyneuropathy; the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes.[8]

The most common form of neuropathy is distal symmetrical sensory motor polyneuropathy. Early distal sensory motor neuropathy is usually asymptomatic, but sensory abnormalities may be detectable by neuro-physiological testing. Symptomatic distal sensory-motor neuropathy is manifested by sensory loss, and may be accompanied by paraesthesiae and/or pain. Peripheral neuropathy may be asymptomatic. When symptoms are present, they may be negative or positive. Negative symptoms include loss of sensation and loss of strength, while positive symptoms include pricking or pain.[9] One of the most distressing symptoms that people can suffer from is neuropathic pain and paraesthesia.[10] Chronic painful diabetic peripheral neuropathy can cause symptoms that last for years and severely impair quality of life.[11, 12] Severe distal sensory-motor neuropathy is manifested by motor involvement, and may be accompanied by disabling symptoms and the potential for ulceration, which can lead to infection, necrosis, gangrene, and loss of the limb.[13]

The recent study by **Daousi** *et al.*[14] investigated the prevalence, severity, and current treatment of chronic painful neuropathy was concluded that chronic painful peripheral neuropathy was "common, often severe but frequently unreported and inadequately treated."

Hyperglycemia associated with diabetes is thought to be central to the effect on nerve structure through a number of possible mechanisms, including increased activity in the polyol pathway, altered myo-inositol metabolism and non-enzymatic glycation. Other mechanisms may also be involved, e.g. alterations in nerve growth factor activity, blood viscosity, circulating platelets and the rate of synthesis and transport of intra-axonal protein. There may also be interactions between these pathways.

The loss of sensation in feet plays an important cause for the development of pressure sores which does not heal and ultimately terminating into diabetic gangrene. Hence in diabetics, prevention and management of Polyneuropathy is of utmost importance.

Diabetic polyneuropathy is a sequel to *Madhumeha* which occurs due to further vitiation of the *Doshas* or due to *Vyadhi karshana*. The disease diabetic polyneuropathy is not directly mentioned in *Ayurvedic* texts. But the *lakshanas* of diabetic polyneuropathy i.e. burning sensation, tingling sensation, numbness etc. are explained under *purvaroopa* and *upadrava* of *Prameha*. When *Prameha* is neglected or ill-treated it will lead to *Madhumeha* by *dhatukshayajanya Vata prakopa* as a *Paratantra Vyadhi*.

Madhumeha is of two types according to *samprapti*; Due to *Shuddha Vata* & due to *Avarana*. In *Shuddha Vatajanya Madhumeha, Nidana* causes primary *Vataprakopa*. And in *Avaranjanya Madhumeha* aggravated *Kapha* and *Pitta* obstructs normal pathway of *Vata* and it leads to secondary *Vataprakopa*. The *prakopa* of *Vata* due to *marganirodha* leads in to diverse clinical scenarios of *Vataja nanatmaja vikara, karma kshaya* of *Vata* and increase of function of opposite factors i.e., *Pitta* and/or *Kapha.*

In both the types, this *prakupita Vata* along with *Kapha* and *Pitta* circulates all over the body and produces symptoms like *padadaha, pada supti, padaharsha*. In *Ayurveda, lakshanas* like *Pada supti, Padaharsha* are dealt under *Vataja nanatmaja vikaras*. These are correlated to diabetic polyneuropathy as told in modern system of medicine.

Management

The main objectives of therapy for diabetes mellitus are to reduce or eliminate microvascular and macrovascular complications of diabetes mellitus along with near normal glycaemic control, to treat associated disorders and to allow the patient to achieve as normal a lifestyle as possible.[15]

Management and prognosis of diabetic polyneuropathy depend largely on the underlying condition. The mechanisms of diabetic neuropathy are poorly understood since from 1864 Marchal de Calvi recognized the condition. At present, treatment alleviates pain and can control some associated symptoms, but the process is generally progressive. Treating the diabetes may halt progression and improve symptoms of neuropathy but recovery is slow. The painful symptoms of diabetic polyneuropathy may become severe enough to cause depression in some patients.

Despite advances in the understanding of the metabolic causes of neuropathy, treatments aimed at interrupting these pathological processes have been limited by side effects and lack of efficacy.[4] Thus, treatments are symptomatic and do not address the underlying problems.

The first line of treatment in diabetic polyneuropathy is the management of diabetes itself. *Vata dosha* is invariably involved as *Madhumeha* as it is of *Vataja* variety and the degeneration of nerves occurs due to *Vata kopa*. The morbid increase in the *Dhatus* prior to *Medas* and the resultant lack of *poshana* of *uttara dhatus* i.e, *Asthi*, *Majja* and *Shukra* causes various complications in *Madhumeha*. The present condition is nothing but a manifestation of *majja dushti* causing demyelination of nerve fibers due to microvasculopathy and hyperglycemic insult to nerves. The concept of *Avarana Vata* helps in understanding the condition better. The *roopavriddhi*, *roopahani* and *roopantara* of *Vata* are clearly observable in this condition. The *Avarana* may be due to primary *vriddha dosha* or *dushya* leading to *gatihanana* of *Vata* or primary *Vata prakopa* leading to the *dushti* of *ashrayee Dhatus*. Ultimately *Avarana* of *Vata* leads to *Vataprakopa*.

Objectives

To review the available academic research works (PG and PhD thesis) on the management of diabetic neuropathy through Ayurveda.

Methodology

The authors have consulted only Postgraduate and Doctoral level dissertations submitted in Ayurveda educational institutions for this study. Other academic researches that might have been submitted as dissertations in medical colleges, pharmacy colleges etc were not consulted. The published papers available on Google scholar or Pubmed were also not included in the study. The academic research works done were searched with key words on Diabetic Neuropathy and Diabetic Polyneuropathy yielded the following results;

1. **Dwivedi KN:** Effect of *Dashamoola* on Diabetic Polyneuropathy, Banaras Hindu University, Varanasi, **1986**.
2. **Dwivedi KN:** Role of *Jeevaneeya* and *Balya* drugs in Diabetic neuropathy. PhD thesis, Banaras Hindu University, Varanasi, **1996**.
3. **Vijaya K:** To evaluate the effect of *Takradhara* in the management of *Madhumeha upadravas* with special reference to Diabetic Peripheral Neuropathy- An observational study. Govt. Ayurvedic Medical College, Mysore, RGUHS, Bangalore, **2003**.
4. **Pravith N.K:** Clinical study on the efficacy of an Ayurvedic package in the management of Diabetic neuropathy with special reference to *Nadi Kwatha*, Govt. Ayurveda College, Trivandrum, **2005**

5. Nandeshwar Manisha: Clinical study of *Amritadi ghritam* as *anuvasana basti* in *Madhumehajanya Upadrava* w.s.r. ro Diabetic Neuropathy. KG Mittal Punarvasu Ayurveda College, Mumbai, **2006**.

6. Tiwari Priyaranjan: Clinical evaluation of *Dashamuladi Ghana Vati (Kalpita Yoga)* in the management of Diabetic Neuropathy, National Institute of Ayurveda, Jaipur, **2007**.

7. Nisha K: Comparative clinical trial to evaluate the efficacy of an Ayurvedic compound in Diabetic Neuropathy, Govt. Ayurveda College, Trivandrum, **2007**.

8. Karishma: Evaluation of the Efficacy of *Sapta-Avartita Guduchi Taila* in *Twak - Gata-Vata* (Diabetic Peripheral Neuritis) - A Comparative Clinical Study. Govt. Ayurveda Medical College, Bangalore, RGUHS, Bangalore, **2008**.

9. Kokane Deepti: Ayurvedic Management of Diabetic Polyneuropathy, Ayurveda Mahavidyalaya, Hubli, RGUHS, Bangalore, **2008**.

10. Sawant Manish: Clinical study of *Ardhamatrika basti* in *Madhumehajanya Upadrava* w.s.r. to *Vatanadi pratana shosha* (Diabetic Neuropathy), KG Mittal Punarvasu Ayurveda College, Mumbai, **2008**

11. Kumar Sanjay: A clinical study on *Naimittika Rasayana* effect of *Shilajatu* and *Mamajjaka* in patients of Diabetes mellitus with special reference to Diabetic Neuropathy, Banaras Hindu University, Varanasi, **2009**.

12. Jaideep: A clinical study to evaluate the effect of Ayurvedic formulation in patients of Diabetic Neuropathy, RGGPG Ayurveda College, Paprola, **2009**.

13. Manish Jain: A comparative clinical management of Diabetic neuropathy with *Nishoshiradi tailam* as external application, BNMR Ayurvedic Medical College, Bijapur, RGUHS, Bangalore, **2010**.

14. Vyasaraja Tantri A: A Comparative Study on the efficacy of *Shamanoushadhis* in the management of Peripheral & Proximal Diabetic Neuropathy, Govt. Ayurveda Medical College, Mysore, RGUHS, Bangalore, **2011**

15. Niranjan Y: A clinical study on the management of Diabetic Polyneuropathy with Dashamooladi Rasayana compound, PhD thesis, IPGT&RA, Gujarat Ayurveda University, Jamnagar, **2011**

Discussion

Research in medical sciences should be a process that converts data into information, information into knowledge and knowledge into wisdom of physician for usefull clinical application of the gained wisdom. It should be: Balanced and comprehensive with equal emphasis on literary, field, experimental and clinical research, able to impact the fields of education, pharmacy and practice in a profound way. Present day Ayurvedic Researches are failing in this respect as they are unable to disseminate the knowledge gained from the researches as research work becomes valid and accepted when it is published in peer reviewed journals. Documentation and publication of research findings is the main issue faced by Ayurveda in the global arena as the publications are scarce.

Lacunae in Ayurvedic Research:

⇒ Majority of the studies belongs to evidence levels 2nd to 4th. A few studies fall under level 1a to 1b.

⇒ Small sample size making them vulnerable for methodological error.

⇒ Rationale for selected study designs is not always properly described.

⇒ Understanding of Ayurvedic classical terminologies and their grading for objectivity and universalization

⇒ Dependency of researches on symptomatology alone.

⇒ Missing values complicate the calculation of probability and power.

⇒ There are no networks of competence or centers for excellence.

⇒ No publication on health services research (HSR) and health technology assessment (HTA)

⇒ The evidence of Ayurveda is difficult to survey. As there are no comprehensive electronic databases for Ayurvedic studies.

⇒ Many publications are only retrievable via hand - search of references and interviews of experts.

⇒ In common western databases and CAM databases, only a small number of Ayurvedic studies are listed.

⇒ Various studies are published in regional languages, many of them only as abstracts. A large number is not available at all.

Hence to make this overview more precise, the work is restricted to academic researches at various Ayurvedic institutes across the nation. The authors have restricted their study to Postgraduate and Doctoral level dissertations submitted in Ayurveda educational institutions due to the scarcity in obtaining reports on this regard. The authors of certain studies were reluctant to provide their findings for review.

A sudden surge of interest towards the complications of Diabetes can be noted by the number of works done after 2005 (out of 15, 12 were carried out after 2005). The works reviewed are based on obtained transcripts of the thesis by personal communication or by acquaintances. Seven works/ abstracts were retrieved out of 15 (46.67%).

The work of **Dwivedi KN**[16] **(1986)** is the first of its kind on Diabetic Neuropathy. Role of *Jeevaneeya* and *Balya* drugs in Diabetic neuropathy was also worked out by the same scholar in 1996. The abstract of the work was published[17] in Sachitra Ayurved entitled "Sushruta's *dashamula* and its application in diabetic neuropathy" in 2003. The efforts to retrieve the transcripts of the thesis/ article went unproductive.

In the work done by **Tiwari Priyaranjan**[18] *et al.* **(Table 1)** the trial drug was a combination of *Dashamula, Madhyama Panchamula (Bala, Punarnava, Eranda, Mudgaparni and Mashaparni)* and *Vanga Bhasma*. 25 subjects are included for this study among them 18 completed the schedule. The study had three groups; Methylcobalamin (500 mcg BD) as Control group, Trial group and Mixed therapy. Three groups of 6 patients are statistically tested after 2 months of trial. Among the three groups studied, mixed therapy yielded maximum results and Trial and control groups fared moderate and mild results. The authors concluded that *Dashamuladi Ghana vati* might have the property of myelin sheath repair which has resulted in improvement in nerve conduction studies.

Nisha K *et al.*[19] **(Table 2)** opined that Diabetic neuropathy can be considered as *upadrava* of *madhumeha*. A definite clinical syndrome which simulates neuropathy is not seen in Ayurveda. The *prakupita kapha, pitta medas* and other *dhatus* cause the *avarana* to *vata,* thereby manifesting symptoms of neuropathy. *Dhatukshaya* and *ojokshaya* causes neuropathy with predominant motor symptoms. A comparative clinical trial was conducted to assess efficacy of *Bhoonimbadi choornam* (one *karsha* with *madhu* and *ghrita* for six months) comparing with conventional medicine i.e. gabapentin, methylcobalamin, alpha lipoic acid & gamma linoleic acid. Twenty patients participated in study, 10 each in study wherein clinical, electrophysiological and biochemical parameters were assessed and analyzed statistically. *Bhoonimbadi choornam* was found to be effective in reducing signs and symptoms of diabetic neuropathy especially in subjective sensory symptoms. The general status of peripheral nerves is improved as revealed by electrophysiological studies. NCV increase to normal or near normal velocity, so that it can be concluded that the trial drug promotes remyelination. The FBS, PPBS, S. Cholesterol was found to be decreased significantly.

Karishma *et al.*[20] **(Table 3)** considered the condition as *Madhumehajanya Twak gata Vata* and conducted an open clinical trial using *Sapta-avartita Guduchi taila* (10-20 drops B.D. with warm milk) with and without *Padabhyanga* for one month in 30 cases. The results were based on the improvement in Neuropathy Total Symptom Score, Quantitative Sensory Tests (Monofilament, Biothesiometer, HCP Sensitometer) and Quality of Life using Nottingham health profile (NHP). Significant

improvement was observed in the symptoms, no change was noticed in the findings of neurological assessment (Quantitative Sensory Testing). Both the groups showed statistically significant improvements in the Quality of life.

Kokane Deepti[21] **(Table 4)** tried to explore the unexplored field of *Swarna Bhasma* in the management, comparator agent was *Dashamoola Kwatha*. Conceptual framework was based on Diabetic Polyneuropathy as *Madhumeha Upadrava*. Emphasis was given on the role of *Vata* causing symptoms due to *dhatukshaya* or *avarana*. It was an open study on 24 subjects receiving either *Dashamoola Kwatha* 40 ml. BD or Tablets of *Vasantkusumakar Rasa* 125 mg BD for 3 weeks. The oral hypoglycemic agents were continued as per diabetologist's recommendation. Burning sensation, Tingling sensation, Pain and Paraesthesia were graded and assessed. No objective parameters were used. Both the trial drug and comparator showed statistically highly significant results on parameters, but, *Dashamoola Kwatha* yielded better result in terms of overall effects.

Jaideep[22] **(Table 5)** studied 23 patients of diabetic neuropathy with 500 mg *Dashmool* extract + 50 mg *Pushkarmool* extract and 25 mg Hingu orally twice in a day and local *abhyanga* with *Masha taila* for 6 weeks. The oral drugs were referred from *Jhinjhinivata chikitsa* of Bhaishajya Ratnavali[23]. Vibration perception, Pinprick and deep tendon reflexes were assessed along with subjective parameters. It was an observational study without any control and the type of diabetes studied is not described. The response of the trial drug was found highly significant ($p<0.001$) in criteria but there was no much improvement in feeling of gloves and stockings.

Tantri V. *et al.*[24] **(Table 6)** studied on 40 subjects of NIDDM with signs and symptoms of peripheral & proximal neuropathy with *Gokshuradi Guggulu* (2 Tablets of 500mg TID with hot water after food) and *Twak Choorna Lepa* in group A and *Sahacharadi Kashaya* (15 ml TID after food) with *Moorchita Tila Taila* (5 ml) and *Ela Choorna Lepa* in group B and patients of both groups were given with *kataka khadiradi kashaya* of 15 ml TID with hot water before food without disturbing hypoglycemic agents. Assessment was done based on clinical graded signs and symptoms, FBS and PPBS after one month. The Group B has shown a better result than that of the *Gokshuradi guggulu* and *twak lepa*.

Niranjan *et al.*[25] **(Table 7)** studied Diabetic Polyneuropathy as a complex multifactorial disorder with varied clinical features due to *Avarana* of *Vata*. The underlying pathological phenomenons are postulated as a result of intricate *Vata Dushti* including *uttara dhatu kshaya*, *margavarana*, *Rakta dushti*, *indriya pradosha* and *ojakshaya*. The work is described in a unique way explained as per **Charaka Samhita**.[26] The trial drug was a combination of *Gokshura*, *Guduchi*, *Amalaki* and *Ashwagandha* processed with *Dashamoola Kashaya*. It stands as the biggest study based on the sample size, on 69 subjects. It is also registered in Clinical trial registry of India vide CTRI/2011/07/001885. The assessment was done based on changes in Neuropathy Symptom Score (NSS) and Michigan Neuropathy Screening Instrument (MNSI). Quality of life was assessed in detail using both traditional and WHO parameters.

Among 15 academic works on Diabetic Polyneuropathy carried out across the nation, all were PG thesis except two; **Dwivedi KN (1996)** and **Niranjan Y (2011).** No concrete conceptual decision was made in any of the works regarding *Ayurvedic* term equivalent for the condition. However there was an effort to understand the *Samprapti* in the lines of Ayurveda. Majority of the works revolve around DPN as *Madhumeha Upadrava*. The role of Vata in the manifestation of the condition is recognized by almost all the scholars. *Avarana* and *dhatukshaya* are considered as major pathological process terminating in neuropathy.

Regarding the interventions, four studies (Maximum) use *dashamoola* as sole or part of treatment strategy. New approach in the selection

of drug can be seen in the works of **Jaideep**[22] wherein the formulation was derived from *Jhinjhinivata chikitsa* of Bhaishajya Ratnavali. **Karishma (Bangalore, 2008)**[20] proposed a new understanding of the condition under *Twakgata Vata* and treated with *Guduchi*. **Sawant M. (2008)** considered DPN as *Vatanadi pratana shotha*. Jaideep, Tantri V and Jain Manish included local treatment (*Abhyanga*) along with systemic interventions. Nisha and Tiwari P. used modern drugs as control; methylcobalamin was the common drug in both the works. The criteria of inclusion were not quite rigid as the autonomic and proximal neuropathies are also included in certain trials.

Regarding the methodology, the works of Karishma and Nisha stands apart due to detailed account of methodical precision. The outcome measures were clinical in majority of works relying on graded symptoms and their assessment. Quality of Life (QoL) parameters were assessed in only one (Karishma) trial. Nerve Conduction Studies (NCS) were used to give objectivity in two trials. Majority of them had sample size < 40. All were randomized trials, but none mentioned method used for the same. No blinding/ masking were reported in any of the trials conducted so far.

Emerging trends

There has been an improvement in the quality of research over the years in terms of methodology. Majority of the works carried out are in the department of Kayachikitsa. The common method followed to avoid bias and to bring objectivity in such studies were randomization of sampling; however majority of them fail to report the methods followed for the same. The quality of theoretical discussions is constantly being upgraded and many hypotheses regarding the understanding of the condition are put forth looking the research question at different angles.

We could identify certain trends in the development of research methodology in the field of diabetic neuropathy research in Ayurveda.

· Inclusion of QoL parameters in assessing the response.

· An increasing effort to quantify and objectivism the parameters of assessment.

· Better application of fundamental doctrines of Ayurveda in understanding Diabetic neuropathy

· Better methodological rigors

· Adaptation of more validated and reproducible assessment scales instead of symptom scoring in assessing the efficacy.

Randomized controlled trials are considered gold standard when appropriately designed, conducted and reported. To assess a trial accurately readers require complete, clear and transparent information on its methodology and findings. One can notice a sustained improvemet in the quality of research being carried out in this regard. Application of CONSORT model[27] in describing the methodology will make the report widely acceptable and transparent.

Future Prospects

A long term prospective study to evaluate the prophylactic efficacy of *Dashamoola* may be taken up with a larger sample. More sensitive and precise quantification using Biothesiometer, Nerve Conduction Velocity, and Nerve biopsy may be used for better assessment. Pharmacological models to understand pathophysiological, pathobiochemical and structural abnormalities of diabetic polyneuropathy and the role of *Dashamoola* in preventing the development of these alterations, to halt their progression, or to induce their regression, despite concomitant hyperglycemia may be taken up.

Table 1. Tewari Priyaranjan

Study ID: Tiwari P *et al.*
Title: Clinical evaluation of *Dashamooladi Ghana Vati* (*Kalpita yoga*) in the management of Diabetic neuropathy
Authors: Tiwari P et.al.
Settings: Dept. of Kayachikitsa, National Institute of Ayurveda, Jaipur, India
Year: 2007 **Study Design:** Clinical study
Methods
Objectives: To assess the efficacy of compound drug- *Dashamooladi Ghana Vati* (*Kalpita yoga*) in the management of Diabetic neuropathy

Sample Size: Male 13; Female 12; Total 25

Eligibility Criteria: Symptomatic Diabetic polyneuropathy above the age of 12 years with evidence of diminished/ absent muscle jerks, pain, touch, vibration sense, orthostatic hypotension

Randomization: Done, method not specified

Adverse Effects: No adverse effects reported

Intervention

Sample size and Drug

Group I. 8 Patients : Tab. Methylcobalamin 500 mcg twice daily with lukewarm water after meals for two months.

Group II. 9 Patients : Tab. *Dashamooladi Ghana Vati* 500mg twice daily with lukewarm water after meals for two months.

Group III. 8 Patients : Tab. Methylcobalamin 500 mcg twice daily with lukewarm water after meals for two months along with Tab. *Dashamooladi Ghana Vati* 500 mg twice daily with lukewarm water after meals for two months.

Drop Outs: 7

Statistical Test Used: Subjective symptom rating scale developed by Prof. AK Sharma, BP, weight, pulse rate, respiratory rate, urine routine, GHb, FBS, PPBS, Lipid profile, Nerve conduction studies were assessed using students t test.

Overall Result: The clinical studies carried out on subjective and objective parameters revealed an overall mild improvement in I (Allopathic) group, moderate improvement in II (Ayurvedic) group and maximum improvement in third group. Group II was better than group I. Group II showed significant improvement in most of the symptoms and in nerve conduction studies in shorter duration of time. Mixed therapy proved to be most effective.

Conclusion and Remarks: *Dashamooladi Ghana Vati* has shown highly significant clinical and electrophysiological recovery in shorter duration of time without any complications. Physiological and haematological recovery noticed after the therapy was statistically insignificant.

Mixed therapy has shown highly significant results by producing marked symptomatic improvement and electrophysiological improvement in a very short span of time, without any complications, with early normalization of neurological abnormalities.

Dashamooladi Ghana Vati might be having the property of myelin sheath repair which ultimately increases the nerve conduction velocity. It may stimulate the property to induce the nerve growth factor naturally found in the body.

Trial dug was potent in the management of diabetic neuropathy

Table 2. Nisha K

Study ID: Nisha K *et al.*

Title: A comparative clinical trial to evaluate the efficacy of an Ayurvedic compound in Diabetic Neuropathy

Authors: Nisha K, Radhakrishnan VN, Lila AS, Chandra SR

Settings: Dept. of Kayachikitsa and Panchakarma, Govt. Ayurveda Medical College. Thiruvananthapuram, Kerala, India

Year: 2007 **Study Design:** Comparative clinical trial

Methods

Objectives: To evaluate the efficacy of *Bhoonimbadi choornam* in reducing signs and symptoms of diabetic neuropathy and to evaluate the changes in blood biochemical parameters

Sample Size 20 (Group A-10, Group B-10)

Eligibility Criteria Patients with clinical and laboratory evidence of diabetic neuropathy

History of diabetes mellitus of more than 5 years

Age group: 40-70 years of both sex

Randomization: Not mentioned

Adverse Effects: The drug administered with hot water produced gastric irritation

The drug was not patient friendly in terms of disagreeable taste.

Intervention

Sample size and Drug

Group A. 10 patients were given *Bhoonimbadi choornam* (*A.Hr. Kushta Chikitsa*) 6g with *madhu* and *sarpi* before food twice daily as *leha* for 6 months with oral hypoglycaemic drugs.

Group B. 10 patients were given Gabapentin 300mg, Methylcobalamin 500mcg, Alphalipoic acid 50m, Gammalinolenic acid 50mcg with oral hypoglycaemic drugs.

Drop Outs: Not reported

Statistical Test Used: Quantitative sensory testing, vibration sense test, pin prick, monofilament sensory test, temperature discrimination, motor system examination and autonomic system examination were done.

Nerve conduction study (NCV) was done to assess the condition of nerves and to differentiate axonal degeneration or demyelination type of neuropathy. Motor nerve conduction velocity was done in median, ulnar, common peroneal and posterior tibial nerve. Sensory NCV was done in median, ulnar and sural nerves. Amplitude of impulse was also assessed to know the effect on axonal degeneration.

Overall Result: Statistical significance at $P < 0.05$ level were noted within study group in SNCV velocity of median nerve and symptoms like tingling sensation, burning sensation, numbness, feeling of walking on cotton / wool, pain which worsens at night inducing sleeplessness, muscle weakness ,stumble while walking, indigestion, constipation, dizziness, wasting and signs like impaired pain and touch sensation. The biochemical parameters like FBS, PPBS and Serum cholesterol also have statistical significance at $P < .05$ level. Comparing both groups the study group had improvement in the clinical responses within group than that of control group. In other criteria, it can be concluded that, the intervention in both groups are equally effective.

Conclusion and Remarks: A definite clinical syndrome which simulates neuropathy is not seen in Ayurveda.

Diabetic neuropathy can be considered as *upadrava* of *madhumeha*. The *prakupita kapha*, *pitta*, *medas* and other *dhatus* cause the *Avarana* to *Vata*, thereby manifesting symptoms. *Dhatukshaya* and *ojokshaya* causes neuropathy with predominant motor symptoms.

The treatment with *Bhoonimbadi choornam* was found to be effective in reducing signs and symptoms.

The general status of peripheral nerves was improved as revealed by electrophysiological studies. NCV increase to normal or near normal velocity, so that it can be concluded that the trial drug promotes remyelination.

The FBS, PPBS, S. Cholesterol was found to be decreased significantly. So drug is effective in improving the blood biochemical parameters i.e., on blood sugar and lipid levels. The drug was found more effective in subjective sensory symptoms.

Table 3. Karishma

Study ID: Karishma *et al.*

Title: Evaluation of the efficacy of *sapta-avartita Guduchi taila* in *twakgata vata* (Diabetic peripheral neuritis)- A comparative clinical study

Authors: Karishma *et al.*

Settings: Dept. of PG studies in Dravyaguna, Govt. ayurveda Medical College, Bangalore and SJIM Hospital, Bangalore

Year: 2008

Study Design: Comparative clinical trial

Methods

Objectives: To compare and evaluate the efficacy of *Sapta avartita Guduchi taila* in the form of oral administration and *Padabhyanga* in *madhumehajanya twakgata Vata* (Diabetic peripheral neuritis)

Sample Size: Male 15; Female 15; Total 30

Eligibility Criteria: Diabetic patients (NIDDM) type, presenting with classical features of peripheral neuropathy within the age group of 35-55 years of either sex, who are on a standard anti diabetic medicine.

Randomization: Open clinical trial

Adverse Effects: None mentioned

Intervention

Sample size and Drug

Group A. 15 Patients : *Sapta avartita Guduchi taila* orally 10-20 drops twice daily with warm milk for one month

Group B. 15 Patients : *Sapta avartita Guduchi taila* orally 10-20 drops twice daily with warm milk for one month and *Padabhyanga* with the same at night for one month

Drop Outs: Nil

Statistical Test Used: Neuropathy total symptom score scale, Quantitative sensory tests including Monofilament, Biothesiometer, HCP sensitometer, Quality of life (Nottingham health profile) were used as parameters of assessment of response.

Symptoms were analysed by non-parametric Friedman test, Wilcoxon signed rank test (Paired t test), and between the groups assessment was done using non-parametric Mann-Whitney test.

Overall Result: Statistically significant results were observed in Hyperalgesia, *daha*, shooting pain.

Statistically non-significant results were seen in *Twak bheda* (aching pain), numbness, tingling.

No change observed in neurological assessment even though it was statistically significant. Statistically significant changes were brought in Quality of life parameters, however on comparison it was non-significant.

Conclusion Remarks: Patients receiving *Sapta avartita Guduchi taila* both orally and in the form of external application exhibited a significant improvement in the symptoms of diabetic peripheral neuropathy when compared to the other group.

Though significant improvement was observed in the symptoms, no changes were noticed in neurological assessment (Quantitative sensory testing).

Table 4. Kokane Deepti

Study ID: Kokane D *et al.*

Title: Ayurvedic management of Diabetic Polyneuropathy

Authors: Kokane DG, Subbanagowda PG, Joshi H

Settings: Dept. of Kayachikitsa, Ayurveda Mahavidyalaya, Hubli, Karnataka India

Year: 2008

Study Design: Clinical Trial

Methods

Objectives: To assess the efficacy of Ayurvedic formulations in the management of Diabetic Polyneuropathy

Sample Size: Male 14; Female 10; Total 24

Eligibility Criteria: Type II Diabetes with Diabetic Polyneuropathy

History of Diabetes type II less than 10 years

Good blood sugar maintenance

Preserved tendon reflexes in lower limbs

Randomization: Done, method not described

Adverse Effects: None described

Intervention

Sample size and Drug

Group A. 12 Patients : *Dashamoola Kwatha* 40 ml twice daily with Oral Hypoglycemic agents, *Sukhoshna jala anupana* for 21 days

Group B. 12 Patients : *Vasantakusumakara Rasa* 125 mg twice daily with Oral Hypoglycemic agents, *Godugdha anupana* for 21 days

Drop Outs: Nil

Statistical Test Used: Symmetrical burning sensation, tingling, pricking pain (pins & needles), pain and parasthesiae in lower limbs were graded and assessed using Students t test

Overall Result: 100% of group A showed good improvements. 58.3% , 33.3%, 8.33% in group B showed good, marked and moderate improvements Group A showed better results than group B

Conclusion Remarks: *Madhumeha* resembles and coincides with the disease Diabetes mellitus

Most of the symptoms mentioned under *Poorvarupa* and *Upadrava* of *Prameha* such as *Pada daha, pada suptata* and *shoola* are similar to diabetic polyneuropathy symptoms.

Diabetic polyneuropathy can be studied under *Madhumeha Upadrava*

Dashamoola Kwatha is very effective for diabetic polyneuropathy, it can also be managed with *Vasantakusumakara Rasa*

Good sugar control plays important role in diabetic polyneuropathy Diabetic polyneuropathy can be managed with Ayurvedic preparations

Table 5. Jaideep

Study ID: Jaideep *et al.*

Title: A clinical study to evaluate the effect of Ayurvedic formulation in patients of Diabetic Neuropathy

Authors: Jaideep, Mishra A, Mehra BL

Settings: Dept. of Kayachikitsa, RGG PG Ayurveda College, Paprola, Himachal Pradesh, India

Year: 2009 **Study Design:** Observational clinical study

Methods Objectives: To evaluate the efficacy of trial drug in the management of Diabetic Neuropathy.

To study its adverse effect (if any).

Sample size: Male 08; Female 15; Total 23

Eligibility Criteria: Patients who are already diagnosed as Diabetics.

Patients whose blood sugar level >120mg/dl for more than 3 weeks. Patients with symptoms of peripheral neuropathy such as Tingling sensation, Burning Sensation, Numbness, Pain.

Randomization: Not applicable

Adverse Effects: No side effects were seen

Intervention

Sample size and Drug

23 Patients : Each capsule (wt-575mg) containing *Dashmool* extract 500mg, *Pushkarmool* extract 50mg, *Hingu* 25mg (*Chakradatta, Vatavyadhi Chikitsa*).

Dose- One capsule twice a day for 6 weeks

Abhyanga with *Masha taila* for 15-20 min once daily

Drop Outs: 01

Statistical Test Used: Neuropathy signs were assessed with the help of Neuropathy kit- containing Buck reflex hammer to elicit deep tendon jerks, sterilised needle to check for pin sensitivity, tip therm to check for perception of cold sensation, test tube for adding hot water to check for perception of hot sensation and a vibration tuning fork of 128Hz to assess the vibration perception of the patients.

Assessment was done on graded symptoms and signs- *karapada daha*, tingling, numbness, *shoola*, gloves and stockings, thermal perception, vibration perception, pin sensitivity, deep tendon reflexes.

The results were analyzed using Students t test.

Overall Result: Highly significant ($p<0.001$) improvements in maximum assessment criteria except gloves and stockings, statistically highly significant results on blood sugar.

Conclusion Remarks: The response of the trial drug was found highly significant ($p<0.001$) in maximum of assessment criteria but there was no much improvement in feeling of gloves and stockings.

As the patients were taking Oral hypoglycaemic drugs so the effect on fasting blood sugar was found highly significant. The other routine baseline haematological and biochemical investigations were normal before the therapy and remained, normal after the treatment also, so they were not altered by therapy on these profiles.

Table 6. Vyasaraja Tantri A

Study ID: Tantri VA *et al.*

Title: A comparative study on the efficacy of *shamanaoushadhis* in the management of Peripheral and Proximal Diabetic Neuropathy

Authors: Tantri VA *et al.*

Settings: Dept. of Kayachikitsa, Govt. Ayurveda Medical College, Mysore, Karnataka, India

Year: 2011 **Study Design:** Pre & post test clinical study

Methods

Objectives: To evaluate the efficacy of *Kataka Khadiradi Kashaya* and *Gokshuradi Guggulu* internally & *Twak Lepa* externally in group A.To evaluate the efficacy of *Kataka Khadiradi Kashaya* and *Sahacharadi Kashaya* internally with *Moorchita Tila Taila* & *Ela Lepa* externally in group B

To compare and assess the efficacy of combined treatment in group A & B.

Sample Size: Male 31; Female 09; Total 40

Eligibility Criteria: NIDDM patients with signs and symptoms of peripheral & proximal neuropathy

Patients of either sex of age group : 25 – 75 years

Randomization: Done, method not described

Adverse Effects: Palatability of *Kataka Khadiradi Kashaya* was a reason for dropouts

Intervention

Sample size and Drug

Group A: 20 : Patients of both groups were given *kataka khadiradi kashaya* of 15 ml t.i.d. with hot water before food without disturbing hypoglycemic agents.

Two tablets of *gokshuradi guggulu* t.i.d. (each tab. of 500mg) with hot water internally after food and *Twak lepa* externally to the affected area

Duration- One month

Group B: 20 : Patients of both groups were given *kataka khadiradi kashaya* of 15 ml t.i.d. with hot water before food without disturbing hypoglycemic agents.

15 ml *sahacharadi* kashaya t.i.d with 5ml *moorchita tila taila* internally after food and *Ela lepa* externally to the affected area

Duration: One month **Drop Outs:** 13

Statistical Test Used: Graded signs and symptoms like pain and burning sensation, altered sensation, muscle weakness, sensory loss, FBS, PPBS. Physical examinations like muscle strength, reflexes, touch, vibration, temperature, position and pain sensation were assessed pre and post test. t test, Chi square test, repeated measure ANOVA were used for statistical analysis.

Overall Result: Group B was better than group A. Burning sensation is the only parameter which was reduced to highly significant level in group A

Conclusion Remarks: The specific references for the detailed concept of the Diabetic Peripheral and Proximal Neuropathy are not found in the Ayurvedic treatises.

The *Karapada Daha* and *Suptata* even though found in the *poorvaroopa* of *Madhumeha*, explanation of manifestation of *Vatavyadhi* in the improper treatment of *Vataja Prameha* by Acharya Vagbhata holds good to explain Diabetic neuropathy as a complication.

Diabetic Peripheral & proximal Neuropathy can be explained as *Madhumeha Vyadhi Karshana Janya Vatavyadhi*

The study was conducted to compare the effect of *Prameha chikitsa* and the *Prameha chikitsa* with *Vatavyadhi chikitsa*.

Both the groups have shown the highly significant result in the reduction of FBS and PPBS. But there was a comparatively more decrease in Group B.

The neuropathic symptoms were better cured by *Prameha Chikitsa* Added with the *Vatavyadhi chikitsa* (*Sahacharadi Kashaya* with *Moorchita tila taila*) than only *Prameha chikitsa*.

Table 7. Niranjan Y

Study ID: Niranjan Y *et al.*

Title: A clinical study on the management of Diabetic Polyneuropathy with *Dashamooladi Rasayana* Compound

Authors: Niranjan Y, Santwani MA, Baghel MS

Settings: Dept. of Kayachikitsa, Institute for Post Graduate Teaching and Research in Ayurveda, Gujarat Ayurved University, Jamnagar

Year: 2011

Study Design: Open ended randomized controlled clinical study

Methods

Objectives: To review the etiopathogenesis of Diabetic Polyneuropathy in light of available classical literatures of Ayurveda

To assess the efficacy of Ayurvedic formulation-*Dashamooladi Rasayana* Compound in Diabetic Polyneuropathy.

Sample size: Male 36; Female 35; Total 69

Eligibility Criteria: Metabolically stable diabetic patients with symptomatic diabetic sensorimotor polyneuropathy

Patients of either sex between the age group of 35-70 years.

Patients with Diabetic Polyneuropathy in stage N3 of Dyck's staging[1]

Randomization: Computer generated randomization

Adverse Effects: No Adverse effects reported

Intervention

Sample size and Drug

Group A. 38 Patients : Tab. *Dashamooladi Rasayana* Compound- 3 tablets of 500mg twice daily after food with *Sukhoshna Jala*

Group B. 33 Patients : Cap. Pregabalin75mg + Methylcobalamin 750 mcg One capsule OD

Duration-8 weeks **Drop Outs:** 6

Statistical Test Used: Primary outcome measures: Changes in Neuropathy Symptom Score (NSS) and Michigan Neuropathy Screening Instrument (MNSI).

Secondary outcome measures: Changes in *Agni Bala*, *Deha Bala*, *Chetas Bala* , WHO Quality of Life (WHO QoL) BREF

The data generated in the clinical study was analyzed by applying student't' test using Statistical software-Sigmastat 3.5.

Overall Result: In Group A 33 (94.29%) subjects responded with Moderate positive response and 2 (5.71%) showed mild positive response. In Group B, 27 (90%) responded with moderate positive results and 3 (10%) showed mild positive response to the allocated treatment. Out of sample size of 65, 60 (92.31%) showed moderate positive response and 5 (7.69%) showed mild positive response.

Conclusion Remarks: Diabetic polyneuropathy is a complex multifactorial disorder with varied clinical features due to *Avarana* of *Vata*. It cannot be directly correlated to any predefined condition in Ayurveda as the nature of *Avarana* of *Vata* decides clinical presentation.

The alternate hypothesis is accepted as *Dashamooladi Rasayana* Compound radically improved both primary and secondary outcome measures.

Based on the results on diabetes profile; *Dashamooladi Rasayana* compound cannot be a standalone drug in diabetes with neuropathy, but an excellent adjuvant with anti diabetic drugs in the management of Diabetic Polyneuropathy. However it has some positive role on Diabetes as evident by the results on biochemical parameters. The hematological and biochemical investigations generate evidence that the trial drug is well tolerated and safe for long term use.

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