Research Article

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A STUDY ON KARYA-KARAN VADA WITH SPECIAL REFERENCE TO DIABETIC PERIPHERAL NEUROPATHY & ITS MANAGEMENT

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ABSTRACT

Diabetes and its complication have a significant global health issue. Peripheral neuropathy is one of leading complication of it. Nerve damage due to various cause like metabolic alteration, chronic hyperglycemia, mechanical injury, smoking and alcohol abuse also responsible for diabetic peripheral neuropathy (DPN). As per Ayurveda, aggravation of vata dosha (vyanvayu) and depletion of kapha dosha (tarpaka kapha) are vitiated rakta dhatu (vitiation of pitta dosha also). It produced padadaha (burning sensation of sole), padaharsha (tingling sensation of sole), padasuptata (numbness). All these features are alike with DPN. The purpose of study to establish the cause and effect theory (The karya karanavada) and evaluate as well as compare the efficacy of *Asparagus recemosus* Wild with bala tailamatra vasti in a patient with DPN. Materials and Method - The studies had been conducted for 90 days with individuals in DPN. 60 patients were randomly assigned into three groups. Group-A (n=10) served as placebo control group treated with old rice grain powder. Group-B(n=25) served as test drug treated with powder of shatavari (Asparagus racemosus wild) at the dose of 6gm.twice daily. Group-C(n=25) served as oral intake of powder. Shatavari at the doses 6gm. twice daily with balataila matra vasti 70ml after meal daily. Observation and Conclusion - The mean reduction of pain and numbness score during the entire phase of treatment were more with shatavari and bala taila matravasti rather than treated with shatavari alone. This finding suggested that matravasti of balataila is the major ingredient for management of pain and numbness in patient DPN.

Keywords: Diabetic peripheral neuropathy, Ayurveda, *Asparagus recemosus*, *Sida cordifolia*, Matra Vasti.

INTRODUCTION

It is well known that chikitsa in Ayurveda is based on karya-karanavada. Satkaryavada is an independent view of Sankhya darshanregardingkarya-karana[1]. According to the principle the karya is present in karan in a subtle form before its manifestation. All the karyas are possible due to existence of karan. On the basis of this ground, our present work would be carried out to establish karya-karana vada in patho-physiology of diabetic peripheral neuropathy.

Ama is formed due to impairment of function of agni[2]. Ama is predominantly associated with dhatukshaya which leads to vitiation of vayu. Dhatukshaya can also alter the function of vyan vayu which solely responsible for muscular activity of extremities. Due to avaran of vayu in srotamargo the function of vayu associated with rakta dhatu altered which leads to symptoms like padaharsha, padaprasupta and padadaha[3] in patient with diabetic neuropathy.

Tarpak kapha is responsible for smooth functioning of nervous system by virtue of its snehan qualities. Tarpak kapha is mainly responsible for the performance of neural function. It not only provides the nutritional supplement to the functioning neuron but also act as protective barriers against various injurious agents. The disarranged function of tarpak kapha by ama and vitiated vata leads to impair the function of nerve in general or nervous system as a whole.[4]

Diabetes is the most common cause of peripheral neuropathy. 60-70% of diabetic patient get neuropathy due to suffering of diabetes for over 10 -15 yrs. Risk increases with age and duration[5]. Nerve damage due to various causes like metabolic factors, chronic hyperglycemia and long duration of diabetes, mechanical injury, smoking and alcohol abuse also responsible for manifestation of diabetic neuropathy. Painful diabetic neuropathy affects approximately 30% of diabetic patient with neuropathy[6].

On the basis of extensive study in the filled of DPN the precise mechanism responsible is still unclear. The widely acceptable theory are metabolic hypothesis and vascular changes.[7]

Asparagus racemosus has been used in Ayurveda as a galactagogue, aphrodisiac, diuretic, antispasmodic and nervine tonic. The major active constituents of *Asparagus racemosus* are steroidal saponins (Shatavarins-iv) that are present in root.[8]Shatavari and matra vasti of Bala taila have been used in different clinical condition in Ayurveda. Vata and kapha dosha are thought to be responsible behind the development of diabetic neuropathy. Aggravated vata causes neuropathy as well as kapha aggravated responsible for diabetes. Therefore, Shatavari has been selected. Shatavari is having vatakaphagna activity[9] and antidiabetic effect and therefore definitely may be effective in diabetic neuropathy.

Vasti (enama) is considered as the best treatment to encounter vataja disorders[10]. Diabetic neuropathy is the result of the complication of diabetes mellitus (Madhumaha) and madhumeha is the absolute vataja disorder[11]. Therefore, matra vasti has been taken in diabetic peripheral neuropathy considering the antivatic activity[12] of bala taila (Both bala[13]& taila[14]). The plants Shatavari and matra vasti of bala taila have been taken into consideration in the present study.

MATERIALS AND METHODS

The present study was conducted in Institute of Post Graduate Ayurvedic Education & Research at S.V.S.P. Hospital, Kolkata in the Department of Ayurved Samhita & Siddhanta.

Sample Size[15] 60 patients.

Study Period 90 Days.

Drugs: Shatavari (*Asparagus racemosus* Willd), Bala taila. (*Sida cordifolia*).

Preparation of Bala Taila: Bala taila is medicated oil preparation made with Bala in murchita tila taila prepared as per classical text Sharangadhara Samhita.

Method of Preparation: Root of *Sida cordifolia* were taken as per API standardization and tila taila was used as murchita dravya then preparation of decoction of root of *Sida cordifolia* as prepare as per classical text. Then murchita tila taila was taken in a stainless steel vessel and heat it. Then added the kwath root of *Sida cordifolia* in murchita tila taila then allow heat for 3 hours with constant stirring maintaining the temperature between 50-90^{0}C during the first hour of heating. Then stop heating and allow standing overnight then storing it in glass containers and pack them air-tight to protect from light and moisture.
These two drugs are collected and properly identified from the department of Apothecary in I.P.G.A.E & R at S.V.S.P. hospital.

Chemicals: All the chemicals used in the present study were an analytical grade.

Criteria for Patient Selection: Individual with diabetic peripheral neuropathy who fulfills the inclusion criteria enrolled from the OPD & IPD in I.P.G.A.E &R at S.V.S.P Hospital, Kolkata for the present study. Collection of biological data, socio-demographical data, and presence of co-morbidity, relevant investigation and treatment received were recorded in case report form. Study was performed on 60 cases diagnosed as diabetic peripheral neuropathy. Patients were randomly selected from the OPD and IPD of I.P.G.A.E &R at S.V.S.P hospital.

Study Design: The studies have been conducted for 90 days with 60 individuals in diabetic peripheral neuropathy 60 patients were randomly assigned into three groups. Group -B &Group- C having 25 patients each and Group-A having 10 patients.
Group-A: Served as placebo control group treated with old rice grain powder.
Group-B: Served as test drug treated with powder of Shatavari *(Asparagus racemosus* Willd*)* at the dose of 6gm.twice daily.
Group-C: Served as oral intake of powder Shatavari at the doses 6gm. twice daily with matra vasti of bala taila 70ml after meal daily as per direction of classical text.

Inclusion Criteria

- Age – (16-70) years.
- Irrespectively of sex, religion and cast.
- Fasting blood sugar (FBS) -up to 180mg/dl &Post prandial blood sugar (PPBS)- up to 350 mg/dl.
- Glycosylated Hb (HbA1C)<10%.
- Duration of diabetic (5-10) years.

Exclusion Criteria

- Patient who has been treated with medicine due to diabetic neuropathy.
- Patient with severe cardiac, renal and hepatic disease and other organic diseases
- Patient who established neuropathy due to other causes.
- Pregnant women& lactating mother.
- Addiction to alcohol and drugs.

Parameters were Studied

For Diagnosis

- General history of the patient.
- Michigan neuropathy screening instrument[16]
- Visual analogue scale for pain[17].
- Biochemical parameter

Blood Sugar-FBS/PPBS
Glycosylated Hb (HbA_1C)
Blood for Urea and Creatinine.

For Assessment

- Blood Sugar- FBS/PPBS
- Glycosylated Hb (HbA_1C).
- Subjective Parameter

Pain
Tingling sensation
Burning sensation
Numbness
Patient global impression change[18]
Michigan neuropathy screening instrument[19].
Visual analogue scale for pain[20]

Michigan Neuropathy Screening Instrument (MNSI): For physical assessment in a case of diabetic peripheral neuropathy, the MNSI was used in the present study. The scale comprising five questions which indicated the appearance of feet, ulceration, and ankle reflexes vibration perception at great toe and monofilament. Ten points allotted for this scale.[21]

Verbal pain intensity Scale: The scale comprising 6 items and used for evaluating the pain intensity of the patient with the diabetic peripheral neuropathy.[22]

It ranging (0-5)		
No pain indicating	-	0
Mild pain indicating	-	1
Moderated pain indicating	-	2
Severe pain indicating	-	3
Very severe pain indicating	-	4
Worst possible pain indicating	-	5

Patients' Global Impression of Change (PGIC) Scale: The activity, limitations, symptoms, emotions and overall quality of life related to painful condition were measured by PGIC scale. The scale comprising 7 questions and data of before and after treatment were recorded by this scale.[23]

STATISTICAL ANALYSIS

Data was expressed as mean ± standard error. The student Paired 't' test was used in independent group for parametric variable.

Group mean was compared by ANOVA, $p<0.05$ will be consider as significant.

OBSERVATIONS AND RESULTS

Observation and result section consisting two divisions i.e. the demographical profile and results of the clinical trial of the present work.

Socio-Demographical Profile

Age Group Wise
Distribution of the patients was found that the maximum 20 (33.33%) individuals with diabetic peripheral neuropathy belong to (51-60) years of age. 3 individuals (5%) belongs to (20-30) years of age. Another important age group are (61-70) year, consisting 18 individuals (30%) with diabetic peripheral neuropathy and also another important age group (41-50) years, consisting 14 individuals (23.33%) with diabetic peripheral neuropathy.

Sex Wise
Distribution of the individuals as per Sex ratio of 60 individuals with diabetic peripheral neuropathy 32 (53.33%) were female and rest of the individuals i.e.28 (46.67%) were male.

In Religion Wise
Distribution of 60 individuals with diabetic peripheral neuropathy was found to be more prevalent in Hindu religion (53.33%) followed by it was found to be comparatively less in Muslim religion (41.67%).

The Frequency of Distribution
Individuals with diabetic peripheral neuropathy was found to be more prevalent in middle income group (53.33%), followed by lower income group (30%) and rest (16.67%) of the individuals belongs to higher income group.

The Educational Status
Out of 60 individuals maximum 30(50%) individuals appeared with primary education followed by 18 (30%) individuals had a graduate level education and 12 (20%) individuals had secondary education.

According to Occupational Distribution
Out of 60 individuals maximum 22 (36.66%) individuals housewife followed by 15 (25%) individuals came from businessman and labor class 10 (16.67%) service holder 8 (13.33%) and unemployed 05 (8.33%) respectively.

Habitat Wise Distribution
The prevalence of disease was found to be more in rural area i.e. 35 (58.33%) and disease was comparatively less found in urban area i.e. 25 (41.67%).

Marital Status Wise Distribution
It has been found that out of 60 individuals with diabetic peripheral neuropathy maximum 43 (71.67%) were married followed by only 10 (16.67%) individuals were having status of unmarried and rest 7 (11.67%) individuals were in widow status.

Addiction Wise Distribution
The majority of the individuals 30 (50%) were found having no addiction and only 10 (16.67%) individuals were found having addiction with alcohol and rest 20(33.33%) individuals were found to be addiction with tobacco.

The Frequency of Distribution as per Heredity
Out of 60 individuals 45 (75%) individuals were positive family history and rest of 15 (25%) were found no heredo-familial history.

CLINICAL TRIAL

Study was conducted on 60 individuals diagnosed as diabetic peripheral neuropathy. Finally results of the clinical trial of 60 patients summarized in 3 groups.

Group-A (n=10) serve as control group treated with old rice grain powder at a dose of 6gms twice daily. Group B (n=25) treated with powder of Shatavari *root* at a dose of 6 gms twice daily. Group-C (n=25) treated with matra vasti of bala taila at a dose of 70ml per day after meal for 16days associated with orally intake of powder Shatavari 6 gms twice daily.

Effect of Drugs on Plasma Fasting Blood Sugar (FBS)
Plasma FBS significantly reduced in Group-B ($P<0.001$) treated with Shatavari and Group-C ($P<0.001$) treated with matra vasti of bala taila with orally Shatavari whereas no significant reduction in plasma FBS concentration was observed in placebo control Group-A ($P>0.05$).

Effect of Drugs on Post Prandial Blood Sugar (PPBS)
Plasma PPBS level was significantly reduced in Group-B ($P<0.001$) and Group C ($P<0.001$) whereas no significant changes in Plasma PPBS concentration was observed in Group-A ($P>0.05$).

Effect of Drugs on Glycosylated Haemoglobin (HbA_1C)
The HbA_1Csignificantly decreased in Group-B ($P<0.001$) and Group-C ($P<0.001$). Whereas no significant reduction of HbA_1C level found in Group-A ($P>0.05$), treated as placebo control.

Effect of Drugs on Verbal Pain Intensity Scale in Patient with Diabetic Peripheral Neuropathy
A significant Score reduction was found in Group- C ($P<0.0001$) followed by Group-B ($P<0.05$) whereas no significant changes were found in placebo control Group-A ($P>0.05$).

Effect of Drugs on Michigan Neuropathy Screening Instrument (MNSI) in Patient with Diabetic Peripheral Neuropathy
A Significant score reduction was found in Group-B ($P<0.001$) treated with *Asperagus racemosus* and Group-C ($P<0.001$) treated with matra vasti with bala taila and orally *Asperagus recemosus* whereas no significant changes were found in placebo control Group-A ($P>0.05$).

Efficacy of Different Drugs on Patient Global Impression Change (PGIC) Scale for Pain with Diabetic Peripheral neuropathy
A significant reduction of pain scoring was found in Group-B ($P<0.01$), Group-C ($P<0.01$) Whereas no significant reduction was found in Placebo control Group-A ($P>0.05$) which was statistically insignificant.

Efficacy of Different Drugs on PGIC Scale for Tingling Sensation in Diabetic Peripheral Neuropathy
A significant changes of scoring on tingling sensation was found in Group-B ($P<0.01$) and Group-C ($P<0.001$) whereas no significant changes were observed in Placebo control Group-A ($P>0.05$).

The Efficacy of Different Drugs on Patients Global Impression of Change (PGIC) Scale for Burning Sensation in Patient with Diabetic Peripheral Neuropathy

A significant score reduction was found in Group-B (P<0.001) followed by Group-C (P<0.001). No significant changes were found in Placebo control Group-A (P>0.05).

The Efficacy of Different Drugs on Scoring of Patients Global Impression of Change (PGIC) Scale for Numbness with Diabetic peripheral Neuropathy

A significant Score reduction was found in Group-B (P<0.001) followed by Group-C (P<0.05) whereas no significant changes were found in Group-A (P>0.05).

Table 1: Effect of drugs on various biochemical parameters in patient with diabetic peripheral neuropathy

Groups	FBS		PPBS		HbA1C	
Group- A (n=10)	BT	AT	BT	AT	BT	AT
	140 ± 5.67	140.30* ± 5.62	148.30 ± 5.79	147.70* ± 5.85	6.08 ± 0.13	5.98* ± 0.19
Group-B (n=25)	240.40 ± 14.23	217.40** ± 14.47	295.72 ± 10.40	251.92** ± 11.52	7.77 ± 0.15	6.93** ± 0.14
Group-C (n=25)	239.56 ± 11.04	215.52** ± 14.53	283.88 ± 8.23	257.44** ± 9.79	7.85 ± 0.13	7.32** ± 0.13
One-Way ANOVA Test	F	5.34	19.42		14.32	
	df	(2,57)	(2,57)		(2,57)	
	Significant	P < 0.01	P<0.001		P<0.001	

BT = Before treatment, AT= After treatment, n= Number of patient, * = P > 0.05, ** =P < 0.001, P< 0.05 consider as significant

Table 2: Effect of drugs on various scale parameters

Groups	Verbal pain Intensity Scale		MNSI	
	BT	AT	BT	AT
Group-A (n=10)	2.30±0.30	2.20±0.20$^{N.S.}$	3.29±0.23	3.20±0.20$^{N.S.}$
Group-B (n=25)	2.76±0.24	2.28±0.21**	4.16±0.24	3.68±0.21***
Group-C (n=25)	2.64±0.17	1.72±0.16***	5.10±0.25	4.40±0.23***
One-Way ANOVA TEST	F	2.54	5.50	
	df	(2,57)	(2,57)	
	Significant	P>0.05	P<0.01	

N.S=Not significant, BT= Before treatment=P<0.05, AT=After treatment** **= P<0.01, *** =P<0.001, *=p<0.05, p<0.05 is consider as significant.

Table 3: Effect of drugs on various neuropathic scale parameters

Groups	PGIC (Pain)		PGIC (Tingling sensation)		PGIC (Burning sensation)		PGIC (Numbness)	
	BT	AT	BT	AT	BT	AT	BT	AT
Group-A (n=10)	2.20 ± 0.24	2.10$^{N.S}$ ± 0.31	1.70 ± 0.30	1.90$^{N.S.}$ ± 0.10	2.00 ± 0.36	2.30$^{N.S}$ ± 0.39	1.70 ± 0.42	1.90$^{N.S}$ ± 0.37
Group-B (n=25)	1.60 ± 0.16	1.20** ± 0.17	1.88 ± 0.13	1.40** ± 0.14	1.68 ± 0.12	1.04*** ± 0.12	2.12 ± 0.12	1.60*** ± 0.12
Group-C (n=25)	2.52 ± 0.13	2.00*** ± 0.15	2.48 ± 0.14	1.64*** ± 0.12	2.48 ± 0.12	2.00** ± 0.14	2.40 ± 0.15	2.08* ± 0.12
One-Way ANOVA TEST	F	7.02	F	2.94	F	13.48	F	2.53
	df	(2,57)	df	(2,57)	df	(2,57)	df	(2,57)
	Significant P<0.01		P> 0.05		P<0.001		P>0.05	

N.S= P>0.05; *= P<0.05; **= P<0.01 ; *** = P<0.001

DISCUSSION

The review of literature on diabetic peripheral neuropathy in patients with diabetes mellitus, suggested that the concepts of diabetic peripheral neuropathy in patients with diabetes mellitus. The patho-physiology, clinical features and its managements were vividly described in different Ayurvedic classical texts. Many references have been given in the literary part of the work in order to elucidate the fact that ancient Ayurvedic scholars, have had a fundamental knowledge on diabetic peripheral neuropathy in patients with diabetes mellitus.

The Socio-economical data of patients with diabetic peripheral neuropathy in case of diabetes mellitus showed that maximum 33% individuals with diabetic peripheral neuropathy belongs to 51-60yrs of age group and 53% were female and mean duration of diabetes was more than 8yrs.It is very much consistent with findings of others recent research work on DPN.

Diabetes mellitus is the most common cause of diabetic peripheral neuropathy. It was reported by a research worker that 60-70% of the diabetic patients get neuropathy due to suffering of diabetes over 10-15yrs[24].Our present study showed that 30-33% of diabetic patients gets neuropathy was suffering over 5-

10yrs. Though the prevalence of neuropathy in patients with diabetic mellitus was only 30-35%which is different from the above study may be due to allocation of small amount of patients with diabetes mellitus in the present study. Diabetic peripheral neuropathy (DPN) is one of the most common complications of chronic Diabetes mellitus.

Neurotrophic factors are essential for the maintenances and survival of the neurons. When peripheral nerves are injured, neurotrophic factors can bond to specific tyrosine kinase receptors on the surface of the target cells, promotes neurol and axon regeneration. Hyper glycaemia leads to excessive formation of sorbitol and fructose in Schwann cells and excessive accumulation of such sugar disrupt the function and structure of peripheral nerves[25]. Vascular hypothesis stresses the early development of reduced endo-neural blood flow, increase endo-neurial vascular resistance and decreased oxygen tension[26].

The important causes the formation of advanced glycated product i.e. increased oxygen free radical (OFR)activity and reduced endothelial NO_2 activity. Which farther leads to irreversible structural changes of concerned blood vessels wall and peripheral nerve and more and more AGE accumulation leads to early atherogenesis?

Increased generation of oxidative free radicals or impaired antioxidant defense mechanism have been implicated in chronic diseases includes diabetes mellitus. Ayurveda also believes that madhumeha and its complication is a set of complex etiopathological events. Apart from various etiological factors agni, ama (Oxidative free radicals), oja and medas are considered as the major morbid factors for the causation of madhumeha and its complications. Dhatukshaya due to vyadhi swabhav itself can lead to provoked vata in the systems, which in turn exacerbates the existing vitiated in vata dosa in madhumeha (diabetes mellitus).

A vicious cycle is setup resulting in ojakshaya and dhatukshaya. This may lead to neuro-degeneration in patients with diabetes mellitus. Various clinical trial for the symptomatic relief of diabetic peripheral neuropathy have demonstrated that a details history and physical examination are adequate for diagnosis of neuropathy in patients with diabetes mellitus using MNSI(Michigan Neuropathy Screening Instruments). In our present study, diagnosis was more dependent of symptoms and clinical finding rather than electrophysiological data. Diabetic neuropathy is a major microvascular complication of uncontrol diabetes. This may result from increased oxidative stress that accompanied diabetes. Hence plants with antioxidant action play an important role in management of diabetes and its complication. Indigenous plants like *Asparagus racemosus* and *Sida cordifolia* contains such as phenolic compound, carotenoids, thiols etc., have shown antioxidant activity that induced scavenging free radical species and inhibiting the production of reactive species resulting from normal cell metabolism[27].Several research studies has shown that serum Nitrite level was significantly enhance in patients suffering from DPN .Biswas P and Saha A, (2006) reported that water extract of *A.recemosus* (500mg/kg/B.Wt) produced a significant decreases in serous Nitrate level in experimental animals[28].

Application of matra vasti with oil of *Sida cordifolia* and powder of *Asparagus racemosus* per orally had significant effect on the improvement on overall status rated by patients ($P<0.001$); as a indicated by PGIC (Patients' Global Impression of Change Scale) in our present study. The present study showed a significant reduction score as accessed on MNSI in both drugs treated groups indicating similar therapeutic benefits ($P<0.001$).

A significant score in PGIC scale for pain reduction were found in group- B ($P<0.01$) and group-C ($P<0.001$) treated with *Shatavari* alone and application of *matra vasti* with *Bala taila* associated with *Shatavari* for orally respectively.

This finding suggested that treatment with *matra vasti* of *bala taila* associated with *Shatavari* powder per orally could be ideal for patient with diabetic peripheral neuropathy in whom a faster reduction of intensity is necessary. The mean reduction of pain and numbness score during the entire phase of treatment were more with *matra vasti* with *bala taila* rather than treated with *Shatavari* alone. This finding suggested that *matra vasti* of *bala taila* is the major ingredient for management of pain and Numbness in patient DPN in DM.

Sida cordifolia and *Asparagus racemosus* may have a neuroprotective effect on Schwann cells and neurotrophic factors and its possible mechanism of promoting nerve repair and regeneration in DPN.

CONCLUSION

According to *Ayurvedic* principle, the symptoms of diabetic peripheral neuropathy like paranesthesia, pain and tingling sensation indicates the involvement of *vata dosa* whereas burning sensation is thought to cause by vitiation of *pitta dosha*. Hence, *vata* and *pitta* pacifying drugs are useful in the treatment of diabetic peripheral neuropathy.

The drug *Shatavari* and *matravasti* of *bala taila* were very much effective to mitigate the signs and symptoms of diabetic peripheral neuropathy. However, further a large scale and long duration study is essential to confirm the therapeutic effects of *bala taila matra vasti* alongs with *Shatavari.* The follow up of patients was continued for only 12 weeks, therefore long-term efficacy of the studied drugs could not access.

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