CLINICAL EFFICACY OF VASANTKUSUMAKAR RASA IN DIABETIC PERIPHERAL NEUROPATHY: A RANDOMIZED SINGLE BLIND CLINICAL TRIAL

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Keywords:

Prameha Upadrava, diabetic peripheral neuropathy, Vasantkusumakar Rasa, Rasaushadhi.

ABSTRACT

Background: Diabetic peripheral neuropathy is the most important and under-treated microvascular complication of Diabetes Mellitus. The symptoms- tingling, numbness, pricking pain, allodynia- generally commence in the legs and show a stocking glove pattern. Few FDA- approved drugs like pregabalin, gabapentin, duloxetine are used as a part of management of diabetic peripheral neuropathy in the contemporary medicine. They are effective for symptomatic relief but are associated with significant adverse effects. Post-covid era has evolved as the most promising one for exploration of alternative medicine.
Rasaushadhis (herbo-mineral/ metallic compounds) are potent drugs that are thought to work at cellular level. Vasantkusumakar Rasa is a promising drug for diabetic complications as earlier studies have proven its protective effects on nerves via anti-oxidant, micronutrient and immune-modulatory effects. This study was intended to assess its efficacy and safety in diabetic peripheral neuropathy.
Methodology: A double-arm single blind randomized clinical trial was conducted on 30 subjects having diabetic peripheral neuropathy, randomized into two groups- 15 in each. Control group was treated with placebo drug (125mg twice daily with water) and trial group was treated with Vasantkusumakar Rasa (125mg twice daily with cow's ghee). A 30-day follow up (30^{th}, 60^{th} and 90^{th} day) was planned for this study. Conventional anti-diabetic medications were continued in both the groups. Reduction in signs and symptoms using Toronto Clinical Scoring System score and indifference between the serum creatinine and liver function tests were primary outcomes; reduction in Vibration perception threshold using biothesiometer, Visual Analogue Scale and HbA1c were secondary outcomes. Paired t-test and 2 sample t-test were used for statistical analysis.
Results: Vasantkusumakar Rasa posed a significant effect on diabetic peripheral neuropathy as p value is <0.05 for TCSS and VPT scores in trial group as compared to control group. Clinical safety of Vasantkusumakar Rasa was also evident as no adverse effects were observed on RFT and LFT parameters in trial group. (p value> 0.05)
Conclusion: Vasantkusumakar Rasa is a promising Rasaushadhi that may prove to be beneficial in reducing symptoms of DPN as an add-on drug along with the conventional modern medications.

Abbreviations:

VKR, Vasantkusumakar Rasa; DPN, Diabetic peripheral neuropathy; TCSS, Toronto Clinical Scoring System; VPT, Vibration perception threshold; VAS Visual Analogue Scale.

1. INTRODUCTION

Diabetic neuropathy (DN) is one of the most important microvascular complications of diabetes mellitus affecting 50% of diabetics.[1] Diabetic peripheral neuropathy (DPN) is the commonest form that affects sensory nerves of the lower extremities. Its prevalence in India ranges from 10.5% to 32.2% according to various studies.[2] It is poorly reported by patients and diagnosed late when irreversible nerve injury has occurred. This causes complications like diabetic foot ulcers, gangrene and may require amputation if left untreated. Current treatment protocol in the contemporary medicine focuses on relieving painful neuropathic symptoms using some FDA-approved drugs like pregabalin, gabapentin, duloxetine etc.[3] Currently there is paucity of treatment to address underlying nerve damage.[4] Today, Ayurveda is gaining popularity owing to its vast unexplored treasure of time-proven medical therapies, to address such challenging complications.

Ayurveda provides excellent methods for prevention and cure of infinite health disorders, based on certain principles like- Hetu (causative factors), Poorvaroopa (prodromal symptoms), Roopa (symptoms), Samprapti (etiopathogenesis), Dosha (Vata, Pitta, Kapha), Dhatu (body tissues), Mala (metabolic waste products), and Agni (digestive fire). An array of neuropathic symptoms is mentioned under Prameha Poorvaroopa (prodromal symptoms of diabetes) as well as its Upadrava (complications). Some typical neuropathic symptoms are also encountered in Vata Vyadhi prakaranam. These include daaha (burning sensation), chimchimayana (tingling sensation), toda (prickling sensation), supti (numbness), shoola (ache/pain), kampa (tremors), stambha (heaviness) etc.[5,6,7,8,9]

Rasaushadhis are compound drugs prepared from various Bhasmas (micro and nano particles of metals and minerals, processed in herbal decoctions) and possess sookshma (penetrating) qualities and high potency. Small dosing and good palatability are other benefits to their credit. They are thought to work at the cellular or tissue level and may affect various pathways that lead to diabetic neuropathy. Vasantkusumakar Rasa is one such Rasaushadhi that has been used by Ayurvedic physicians since a long time in the management of Prameha and its Upadravas. The safety of herbo-mineral drugs is questioned and challenged by the contemporary medical fraternity. There is a paucity of clinical studies using Rasaushadhis in diabetic neuropathy. This study aimed to re-establish the efficacy and safety of Vasantkusumakar Rasa in diabetic peripheral neuropathy.

2. MATERIAL AND METHODS

2.1. MATERIAL

2.1.1. Subjects

Type-2 diabetic patients with neuropathic symptoms, fulfilling the inclusion criteria were selected for this trial. Inclusion criteria for this study was: 1) age between 30-80 years, 2) both genders, 3) controlled Type-II diabetes mellitus patients (glycated haemoglobin ≤ 7.5), 4) blood pressure ≤ 160/90mmHg at screening, 5) Diabetic neuropathy score (DNS)≥ 1, 6) Diabetic neuropathy examination (DNE) score≥ 3, 7) an abnormal Vibration perception threshold (VPT) and 8) patients willing for inclusion in the clinical trial. Exclusion criteria was: 1) Type-I diabetes mellitus, 2) pregnant and lactating women, 3) patients with deranged renal function (Serum creatinine ≥1.5mg/dl), 4) serious neurological conditions, 5) malignancies, 6) serious infections or those requiring long term steroid or hormonal treatment, 7) patients with any serious systemic illness within past three months and 8) those with history of renal transplant.

The study participants were recruited from the Kayachikitsa OPD/IPD of Bharati Ayurveda hospital (Bharati Vidyapeeth deemed to be University).

Sample size of 30 patients (15 in either group) was calculated according to the prevalence rate of this clinical condition in Bharati Ayurved Hospital.

A comprehensive case record form was prepared for documenting the clinical details of the patient and the disease.

2.1.2. Drugs

a) Vasantkusumakar Rasa
Vasantkusumakar Rasa was procured from a renowned GMP certified pharmacy.

b) Placebo drug
Placebo drug tablets were prepared from a local pharmacy using Jowar atta. Each tablet measured 125mg.

2.1.3. Standardization of drug
The Certificate of Analysis and No Objection Certificate were obtained from the GMP certified pharmacy.

2.2. Methodology
a) Screening and selection of patients
1. Screening of diabetic patients was done using Diabetic neuropathy symptom score[10] and Diabetic neuropathy examination score.[11]
2. Patients who passed the screening tests and fulfilled the inclusion criteria were then subjected to Toronto Clinical Scoring System (TCSS)[12] score and Vibration perception threshold (VPT) using a biothesiometer.

b) Randomization and blinding
The subjects were randomized into two groups to receive either the trial drug or placebo but were uninformed about their assigned treatment group. Both the drugs were identical in appearance.

c) Consent
Written informed consent was obtained from the participants prior to their enrolment.

d) Laboratory investigations
Blood investigations like HbA1c, Blood glucose levels- fasting/ post-prandial, serum creatinine, Liver function tests, and lipid profile were sent for analysis for both the groups, prior to treatment. The labs were repeated after 90 days of treatment.

e) Intervention (Table-1)

Specification	**Group A**	**Group B**
Number of patients	15	15
Medicine	Oral hypoglycemic agents and/or insulin + Vasantkusumakar Rasa	Oral hypoglycemic agents and/or insulin + Placebo drug
Dosage	125mg	125mg
Route of administration	Oral	Oral
Kaala	Vyaanodaan Kaala (after meals)	Vyaanodaan Kaala (after meals)
Anupana	Goghrita	Jala
Time period	3 months	3 months
Follow up	Day 30, 60 and 90	Day 30, 60 and 90

Table-1: Intervention

2.3. Study design
This study was a double-arm single blind placebo controlled randomized clinical trial. Participants were enrolled after approval from the Institutional Ethics Committee. (Ref. Project No.

BVDUCOA/EC/MD./KC/03/2020-21) The study was registered under the Clinical Trials Registry-India (CTRI/2022/03/040803)

2.4. Assessment parameters

Subjective parameters were assessed using the TCSS score while objective parameters were assessed using VPT measurements, VAS scale and HbA1c levels.

2.4.1. Primary study end-points

1. Reduction in signs and symptoms of diabetic peripheral neuropathy as evident from improvement in TCSS score.
2. No adverse effects on serum creatinine and liver function tests.

2.4.2. Secondary study end-points

1. Improvement in VPT measurements using biothesiometer.
2. Improvement in VAS scale.
3. Improvement in HbA1c levels.

2.5. Statistical analysis

The data obtained was subjected to statistical analysis using the SPSS software in terms of mean values, standard deviation (SD), standard error (SE). Paired t-test and two sample t-test were applied. Paired t-test was carried out at $p< 0.05\%$. The results were interpreted as: $P>0.05\%$ was insignificant while $P<0.05\%$ was significant.

3. Assessment of clinical safety of VKR

Pre- and post-treatment renal function tests (RFT) and liver function tests (LFT) were performed to rule out VKR toxicity.

Additionally, a list of Apakwa bhasma janit lakshanas (symptoms and signs of acute/chronic toxicity of various metals/minerals) was formulated based on classical references from classics of Rasashastra like Bhaishajya Ratnavali, Rasatarangini and Rasaratnasamuchhaya.[13,14,15,16] Each patient was assessed for presence of any of these symptoms at each follow-up and record was maintained.

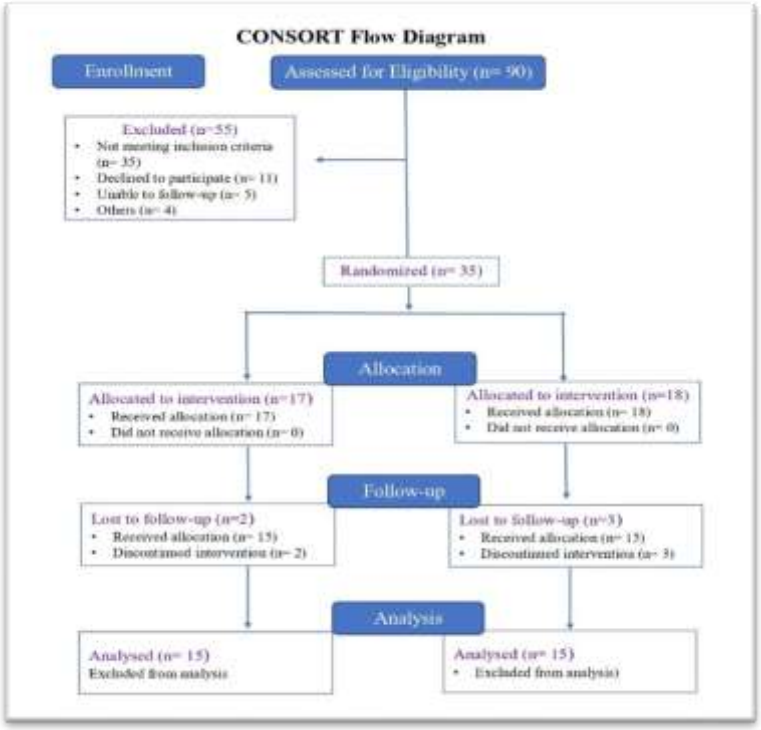

Figure-1: CONSORT Flow diagram

4. OBSERVATIONS

Maximum number of participants (68%) were found to be between the age group of 50-70 years. Most patients showed Pitta-Vata pradhana lakshanas like daaha (28.57%), chimchimayana (28%) and padashoola (20%). Most subjects (37%) had more than 10 years chronicity of diabetes. 57.14% patients consumed katu-rasa pradhan diet while 40% consumed Madhura-rasa pradhan diet. 42.85% participants had Atichintanam, 17.14% had Atishrama/ ativyayama/ atichankramana and 14.28% had prajagarana as Viharaja- hetu sevan (routine physical/ mental activities) history.

5. RESULTS

At the end of 3 months of treatment, the patients were subjected to TCSS score, VAS score and VPT measurement using the biothesiometer. Results demonstrated a statistically significant effect of Vasantkusumakar Rasa over placebo drug on diabetic peripheral neuropathy.

5.1. Effect on TCSS score

Parameter	Mean			x	% of improvement	t	p value
	GROUP	BT	AT				
TCSS	A	11.80	8.53	3.27	27.68%	7.789	0
	B	11.73	12.27	-0.53	-4.55%	-1.169	0.262

Table 2: Effect on TCSS score

Group A treated with VKR showed significant improvement (27.68%) in the TCSS score as P<0.05%. Conversely, Group B treated with placebo was found to be ineffective on TCSS score, as P>0.05%.

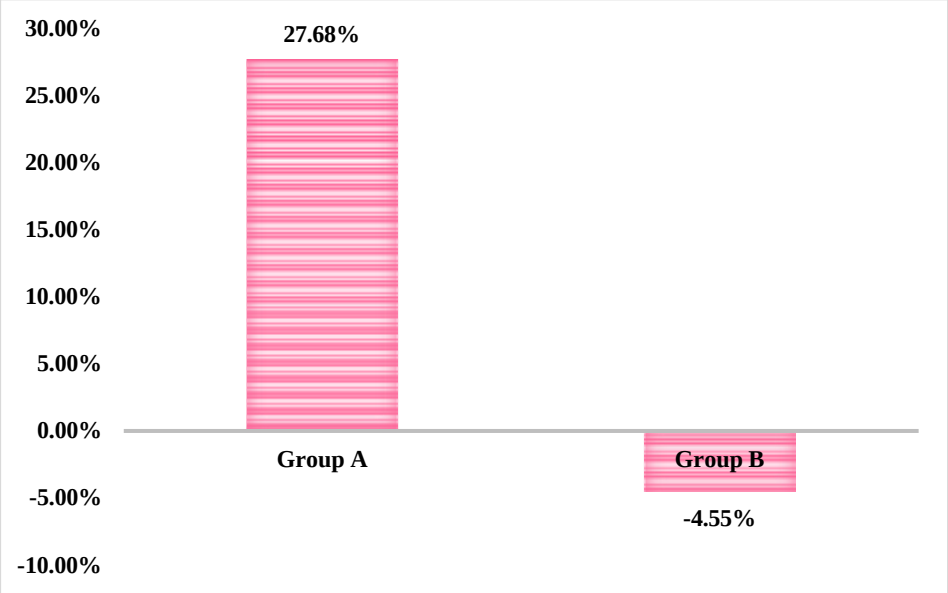

Figure 2: Effect on TCSS score

5.2. Effect on VPT of Right and Left foot

parameter		Mean	x		t	P value

	GROUP	BT	AT		% of improvement		
VPT OF RT. FOOT	A	29.13	25.93	3.20	10.98%	2.599	0.021
	B	32.93	34.27	-1.33	-4.05%	-1.173	0.26
VPT OF LT. FOOT	A	30.53	25.67	4.87	15.94%	5.445	0
	B	33.87	34.20	-0.33	-0.98%	-0.589	0.565

Table 3: Effect on VPT of Right and Left foot

Group A treated with VKR showed a significant improvement in the VPT of right and left feet (10.98% and 15.94% respectively), with P values 0.021% and 0 respectively. On the other hand, placebo treated group did not show any improvement in the vibration perception thresholds in right and left feet, as P values were 0.26% and 0.565% respectively.

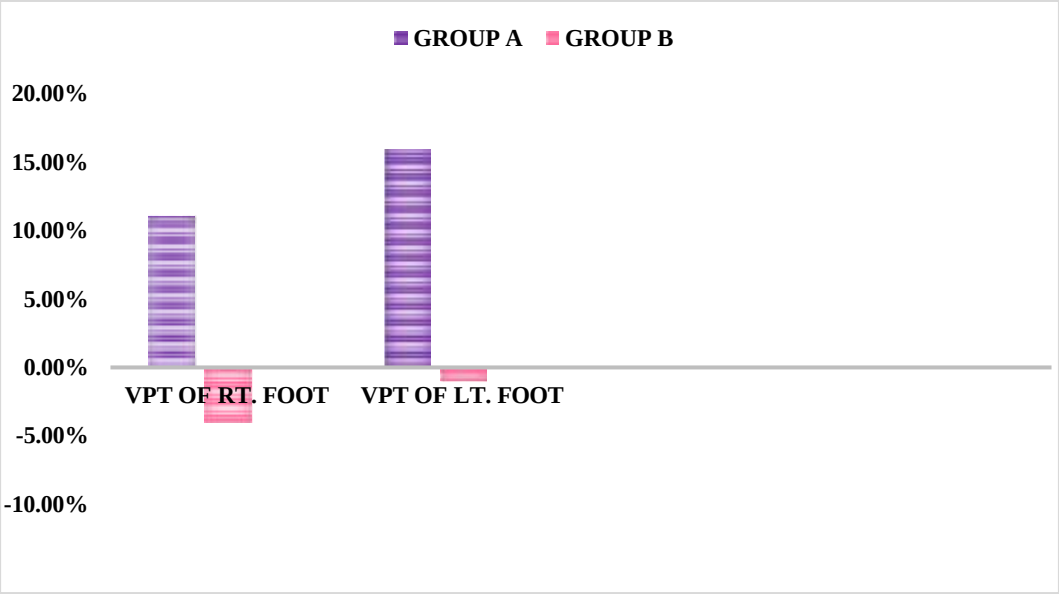

Figure 3: Effect on VPT of Right and Left foot

5.3. Effect on VAS score

Parameter	Mean		x	% of improvement	t	p value
	GROUP	BT	AT				
VAS	A	2.27	0.47	1.80	79.41%	4.583	0
	B	3.20	1.93	1.27	39.58%	5.551	0

Table 4: Effect on VAS scale

Using the two-sample t test, effect of both drugs on the VAS scale was studied. Both the groups showed a significant improvement in the VAS score as P value was 0 for both groups.
Comparison between the two groups revealed 79.41% improvement with VKR and 39.58% improvement with placebo effect.
Thus, comparison between the two groups demonstrated better efficacy of VKR over placebo.

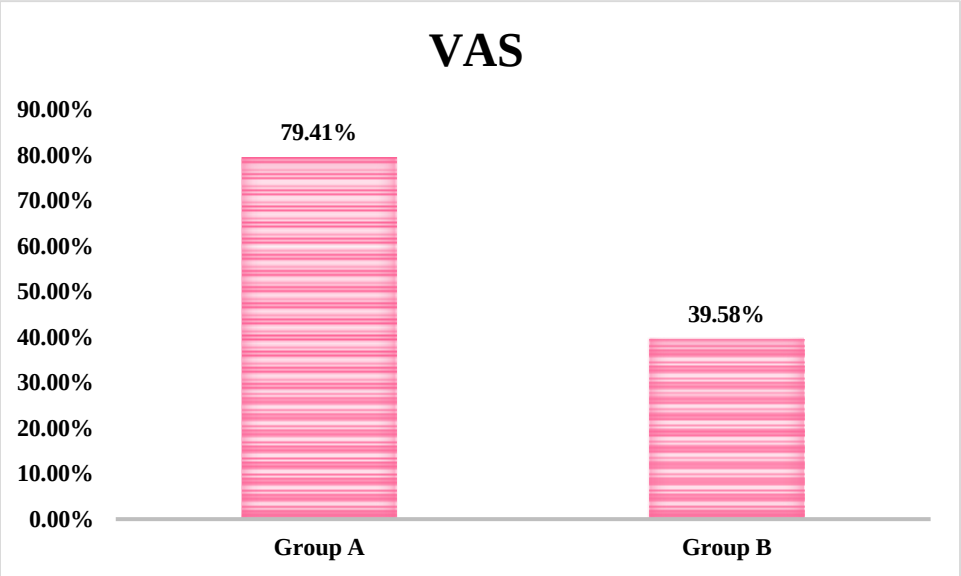

Figure 4: Effect on VAS scale

5.4. Effect on HbA1c levels

Parameter	Mean			x	% of improvement	t	p value
	GROUP	BT	AT				
HBA1C	A	6.77	7.00	-0.22	-3.31%	-1.103	0.289
	B	6.98	7.51	-0.53	-7.65%	-3.085	0.008

Table 5: Effect on HbA1c levels

From above table, it is evident that treatment with VKR did not improve the HbA1c levels significantly in the trial group subjects, as P value= 0.289. In control group, placebo drug did not improve the HbA1c levels either. However, P value of 0.008 shows significant worsening of HbA1c levels as percentage of improvement is -7.65%.

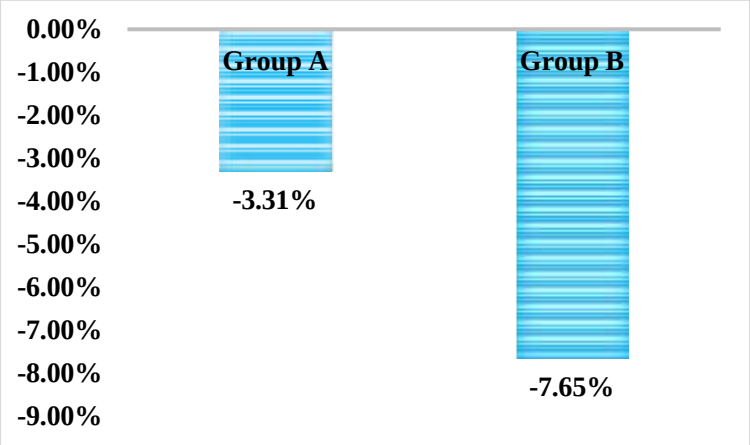

Figure 5: Effect on HbA1c levels

5.5. Effect on various laboratory parameters

parameter	Mean		x	% of improvement	t	P VALUE
	BT	AT				
SERUM CREATININE						
Group A	0.81	0.80	0.01	1.72%	0.317	0.756
Group B	0.80	0.91	-0.11	-13.67%	-3.554	0.003
SERUM BILIRUBIN (TOTAL)						
Group A	0.56	0.58	-0.02	-3.72%	-0.322	0.752
Group B	0.56	0.51	0.05	9.10%	0.651	0.525
SGOT						
Group A	23.18	23.63	-0.45	-1.94%	-0.303	0.767
Group B	23.73	22.73	1.00	4.21%	0.815	0.429
SGPT						
Group A	24.34	25.05	-0.71	-2.94%	-0.393	0.701
Group B	22.53	22.98	-0.45	-1.98%	-0.256	0.802
ALKALINE PHOPHATASE						
Group A	122.58	96.87	25.71	20.98%	0.929	0.369
Group B	92.60	88.73	3.87	4.18%	0.906	0.38
BSL-F						
Group A	125.80	118.13	7.67	6.09%	1.187	0.255
Group B	138.47	140.00	-1.53	-1.11%	-0.247	0.808
BSL-PP						
Group A	181.93	164.88	17.05	9.37%	1.364	0.194
Group B	210.87	215.87	-5.00	-2.37%	-0.396	0.698
SERUM CHOLESTEROL (TOTAL)						
Group A	174.80	170.20	4.60	2.63%	0.98	0.344

Group B	178.07	177.69	0.38	0.21%	0.058	0.955
SERUM TRIGLYCERIDES						
Group A	126.04	122.03	4.01	3.18%	0.616	0.548
Group B	122.53	151.11	-28.57	-23.32%	-2.667	0.018
HIGH DENSITY LIPOPROTEINS (HDL)						
Group A	45.62	47.64	-2.02	-4.42%	-0.89	0.388
Group B	46.96	45.31	1.66	3.52%	1.83	0.089
LOW DENSITY LIPOPROTEINS (LDL)						
Group A	104.75	97.48	7.27	6.94%	0.804	0.435
Group B	112.91	110.11	2.79	2.47%	0.378	0.711

Table 6: Effect on various laboratory parameters

It can be inferred from the above table that VKR did not cause any significant changes in serum creatinine levels, as P value> 0.05%. Group A showed 1.72% improvement in serum creatinine while Group B showed mild worsening as evident from above table. This may suggest nephro-protective effect of Vasantkusumakar Rasa.
Similarly, VKR did not pose any adverse effects on the liver function parameters as P value>0.05%. We did not observe any improvement in the LFT, neither any derangement in the liver enzymes.
Thus, clinical safety of VKR was proven in Group A treated with VKR as p value >0.05 for all lab parameters.
There was some degree of improvement in the fasting and post-prandial glucose levels, but it was statistically insignificant as P>0.05%.
Trivial improvements were seen in serum total cholesterol, serum triglycerides and serum low density lipoproteins, but they too were insignificant as P value>0.05%.

6. DISCUSSION

Diabetic peripheral neuropathy is peripheral nerve dysfunction due to long standing hyperglycemia. This results in increased oxidative stress. Pathogenesis involves activation of multiple metabolic pathways due to formation of advanced glycation end-products (AGEs). Other factors include vascular ischemia, nerve hypoxia, and microangiopathy. Specific treatment for correction of underlying nerve dysfunction is not available at present.[17]
From Ayurveda point of view, Vata vriddhi is responsible for diabetic neuropathic symptoms like ruja or shoola, (pain), supti (numbness), romaharsha/ angaharsha (parasthesias), chimchimayana (tingling sensation), whereas, Pitta vriddhi will show symptoms like daaha (burning sensation), osha (localized burning sensation), paridaha (burning sensation all over the body), and dhoomayana (feeling of hot gas coming out of body). Kapha vriddhi will cause symptoms like gaurava (heaviness), shaitya (coldness), and mandakriya (slow perception). Vyana and Apana Vayu are predominantly involved in the pathophysiology of DPN. Ashayapakarsha of Pitta by Vyana Vayu causes daaha[18], while that of Kapha will cause shaitya, gaurava etc. Rasa, rakta, mamsa, meda and majja dhatu are predominantly involved in the pathogenesis of diabetic peripheral neuropathy.
Ayurvedic management of diabetic peripheral neuropathy is multifocal and should involve-[19] 1) nidana parivarjan (cessation of causative factors); 2) santarpanam (maintaining anabolic state), prevention and treatment of Agnimandya at all three levels i.e., Jatharagni, Dhatwagni and Bhootagni; 3) Amapachana (removal of waste metabolic products) at all three levels; 4) Treatment of Avarana: specific treatment of Avaraka dosha, e.g. pittanashak in case of Pittavrita Vayu followed by vatanulomana, vatashamana, shodhan using Basti; 5) Dhatuposhana, i.e. to impart strength to the tissues, decrease their laxity and remove kleda; 6) Ojovardhan: to increase Oja- the supreme essence of Dhatus, which helps to maintain integrity and immunity of the body. This helps to combat the oxidative stress; and 7) Rasayana therapy- aimed at nourishing all seven dhatus, Oja and would help in preventing recurrence or progression of neuropathy.

In the current study, most subjects showed Madhyama-Vriddhawastha, a Pitta- Vata predominant stage of life. Thus, pitta-vata pradhana lakshanas like daaha, chimchimayana and padashoola were seen predominantly. Dhatukshaya and Ojokshaya in Vriddhavastha lead to Vata prakopa naturally. Chronicity implies a state of Dhatukshayawastha. This is attributed to loss of important dhatus like Ojus and other dhatus through urine (as in Madhumeha) resulting in Prameha Upadrava- diabetic neuropathy. It is observed that diabetic patients tend to avoid madhura rasa completely; this might be the reason why most participants in this study, were seen to prefer katu- pradhan ahara. Excessive intake of katu rasa leads to catabolic state of Rasadi dhatu. Vayu and Agni mahabhoota predominance in Katu rasa cause davathu (burning sensation), toda (prickling sensation), bheda (severe ache) in lower limbs, upper limbs, flanks, back etc.[20] The Viharaja hetu clearly favoured vata prakopa. To summarize, following etiopathogenetic factors were found to cause diabetic peripheral neuropathy in the trial subjects- 1) vata-pitta prakopak ahara (diet causing vitiation of Vata and Pitta doshas), 2) Vata-prakopak Vihara (life-style or activities causing vitiation of vata), 3) Vriddhawastha (catabolic state of life) and dhatukshayawastha (chronicity of diabetes).
Primary end-points were achieved in Group A patients, treated with Vasantkusumakar Rasa as there was improvement in signs and symptoms of DPN, shown by an improved TCSS score. there was no worsening of serum creatinine and LFT.

VKR also improved the VPT and VAS scores in both feet. Thus, VKR was effective to achieve secondary end-points of the study as well.
Optimized glucose control is thought to be crucial in preventing or delaying the development of diabetic peripheral neuropathy.[21] HbA1c levels did not show much improvement in this study. Despite this fact, remarkable improvements were seen in TCSS, VAS and VPT scores. This may be attributed to the powerful Rasabhasmas in VKR and their antioxidant, neuroprotective effects, rather than glycemic control.
On the other hand, Group B patients treated with placebo drug showed no significant improvement in TCSS and VPT scores. Improvement in VAS score may be attributed to its placebo effect.

Vasantkusumakar Rasa is a compound drug formed by mixing various bhasmas like Suvarna, Rajata, Vanga, Naga, Loha, Abhraka, Rasasindoora, Mukta and Prawal. It is triturated with various herbal decoctions/juices including - Godugdha (cow's milk), Ikshurasa (sugarcane juice), Vasa (Adhatoda vasica), Shweta Chandan (Santalum album), Usheera (Vetiveria zizanioides), Hreebera (Pavonia odorata), Haridra (Curcuma longa), Mochakanda (Musa paradisiaca), Kamalapushpa (Nelumbo nucifer), Malatipushpa (Jasminum officinale) and Kasturi (musk). The process of trituration helps to get rid of the unwanted impurities and toxicities of bhasma as well as enhances the potency of bhasma. These bhasmas are known to possess numerous beneficial qualities.
"Meheshu santarpanameva kaaryam…" Treatment principles of Prameha have laid importance on Santarpan chikitsa in Prameha, despite the fact that it is a Santarpanothha disease. Santarpan indicates anabolism. Anabolism results in good tissue strength and quality, i.e., dhatu shaithilya reduces, dhatu bala (strength) improves and kleda formation reduces. Vasantkusumakar Rasa is one such drug that is capable of providing anabolism to the body.
Suvarna bhasma is known to possess madhura vipaka, snigdha, guru and pichhila gunas. Thus, it has an anabolic effect on the body tissues and helps to alleviate Vata dosha. Recent research showed that gold nanoparticles could exert cytoprotective effects on the diabetic mice by stimulating glutathione levels, which is an endogenous anti-oxidant.[22]
Rajata bhasma possesses Vata-Kapha nashak qualities as well as prameha nashak, agnideepana, rasayana, dhatuposhak qualities. It is known to boost the Ojus. An experimental study showed that Rajata Bhasma exerted significant antidiabetic action in streptozotocin-induced diabetic rats.[23] An in-vitro study demonstrated the anti-oxidant activity of Rajat bhasma.[24] Vanga due to its ushna veerya, laghu-rooksha gunas, is indicated for use in Prameha, polyuria etc. A clinical trial showed the efficacy of Vanga bhasma in relieving Prameha symptoms like hasta-pada daaha, shithilangata, pindikodweshtan. It also improved blood sugar levels.[25] Naga having ushna veerya, madhura vipaka, agni-deepana, amanashak, balya, Rasayana and tridosha nashak qualities is considered as a best drug in treating Prameha. A clinical trial showed significant lowering of blood sugar levels in diabetic patients

treated with a single dose of 120mg of Naga Bhasma once daily for 6 months.[26] An experimental trial using Naga bhasma demonstrated a remarkable reduction in the blood sugar levels in glucose overloaded Wistar albino mice.[27]

Loha having madhura vipaka, sheeta veerya, guru,rooksha, tridosha nashak qualities is Prameha nashak. It shows a unique characteristic of alleviating Pitta related disorders of upper and lower extremities.[28] An in-vitro study demonstrated the anti-oxidant effect of Loha bhasma.[29] Rasasindoora is a potent drug having deepana, amapachan, vata niyamana, pitta-nissaraka, Rasayana, balya qualities. It is a yogavahi i.e. catalyst like action. It enhances actions of the drugs that it is used with. It importantly converts the saama kapha into nirama one by digesting the associated Ama. It works on Rasa and Mamsa Dhatu. [30] An experimental study using Rasasindoora as a dietary supplement in the Drosophilia larvae considerably suppressed neuro- degeneration in fly models.[31] Another study in Drosophilia flies showed that Rasasindoora reduced the levels of pro-apoptotic proteins and increased the levels of anti-apoptotic proteins like DIAP-1 and DIAP-2, thus indicating suppression of induced apoptosis which is concerned with neurodegeneration.[32] Abhraka possesses madhura ras and vipaka, sheeta veerya, snigdha, deepana, pachana, balavardhaka, Prameha nashak qualities. An animal study showed increased activity of catalase and SOD enzymes with the use of Abhraka

Bhasma, suggesting its anti-oxidant properties. It also showed potentiation of DNA-repairing properties of Abhraka Bhasma.[33] Prawal has madhura vipak, sheeta veerya, tridoshanashak qualities. Mukta has madhura vipaka, sheeta veerya, kapha-pitta nashak qualities. It is prameha-hara, balya and hridya. Thus Mukta-Prawal may help in alleviating daaha.

The bhavana dravyas that are used while preparing Vasantkusumakar Rasa possess sheeta veerya, tarpana qualities and thus help in alleviating daaha.

Thus, the cumulative effect of the individual drugs in the compound drug Vasantkusumakar Rasa will be- Rasa- madhura, tikta; Vipaka- Madhura; Veerya- sheeta; Guna- snigdha, guru, brimhana, dhatupoushtik, balya, Rasayana, vajikarana, ojovardhak, Prameha-nashak.

VKR chiefly acts on and imparts strength to Vatavaha mandal (nervous system), Manodesha (psyche), Phuphusa (lungs), Hridaya (heart), Pachanendriya (digestive system) and Jananendriya (reproductive system).[34]

'Chala' and 'rooksha' attributes of Vata Dosha are regulated by VKR leading to its pacification. It also attenuates the 'ushna' and 'teekshna' attributes of Pitta Dosha. It acts primarily on Rasa, Rakta, Mamsa, Meda, Shukra dhatus as well as the Dhatwagnis.

An animal trial showed that treatment with VKR had a protective effect and prevented the development of retinopathy in streptozotocin induced diabetic rats. VKR significantly reduced the aldose reductase (AR) and vascular endothelial growth factor (VEGF) levels in eye tissue, thus indicating reduced oxidative stress. It increased the endogenous anti-oxidant levels. It restored the serum lipid profile.[35] VKR helps to improve microcirculation in the endoneurial blood vessels. It thus reduces endoneurial hypoxia which is one of the causes of diabetic neuropathy. The microvascular complications like retinopathy and neuropathy share common pathophysiological mechanisms, thus VKR can aid the management of diabetic peripheral neuropathy in similar fashion.

Most of the Bhasmas have demonstrated an inhibitory effect on oxidative stress as well as enhanced endogenous anti-oxidation. Bhasmas like Abhraka, Naga, Vanga etc. have also been proved to have anti-hyperglycemic activity in various studies.

Thus, Vasantkusumakar-Rasa offers a wide range of effects which may help to protect against diabetic neuropathy (Figure-6). This study also showed that VKR is most useful in Vata-pitta predominant symptoms like daaha and chimchimayana.

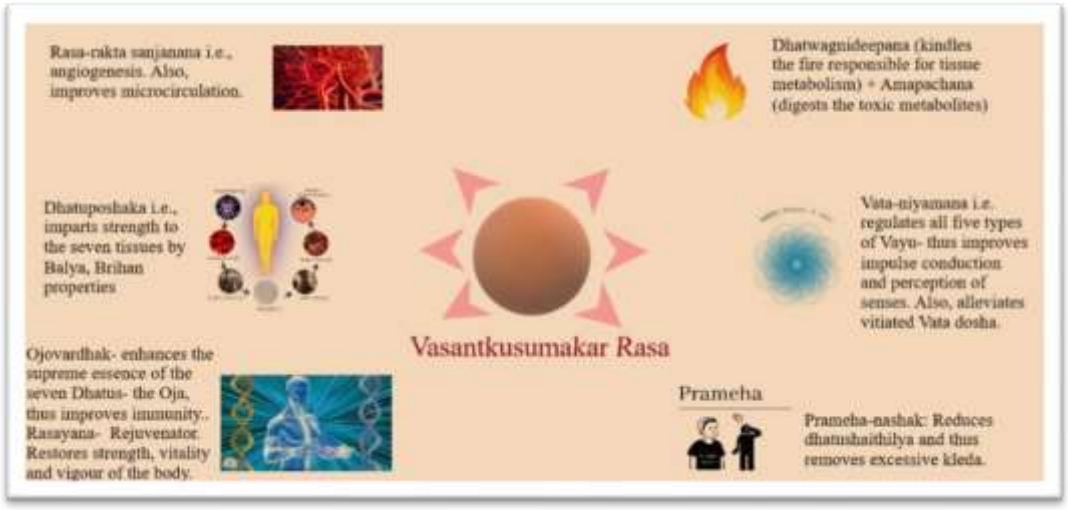

Figure 6: Diagrammatic representation of probable mode of action of Vasantkusumakar Rasa in diabetic peripheral neuropathy

Contents like mercury (in Rasasindoora) and lead (Naga) are known to cause harmful effects on the human body. Our study observations suggest a probable nephroprotective effect of VKR. An experimental study showed that treatment with VKR in diabetic rats improved the creatinine clearance and erythropoietin levels, thereby suggesting delay of progression to renal complications.[36]
Each patient was assessed for Apakwa bhasma janit lakshana at every visit. None of the patient showed any symptoms of toxicity. Thus, clinical safety of the drug was proven.

7. CONCLUSION

It was thus concluded that Vasantkusumakar Rasa is helpful to relieve diabetic neuropathic symptoms and can be safely used in clinical practice.

8. FURTHER SCOPE OF STUDY:

Future studies should be carried out using a combination therapy of Shodhana therapy along with VKR which may improve patient outcomes. Comparative studies using a polyherbal medication and VKR should be done to find out better efficacy, as VKR may not be a convenient option for many patients, owing to its cost. Further studies should be done to warrant the non-toxic effects of Vasantkusumakar Rasa by incorporating heavy metal analysis.

9. Conflicts of interest: None

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