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RESEARCH ARTICLE

CLINICAL STUDY TO EVALUATE THE EFFICACY OF BODHI VRIKSHA KASHAYA PAAN IN THE MANAGEMENT OF HYPERURICEMIA

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ABSTRACT

30 clinically diagnosed patients were randomly categorized into two equal groups. In Group A, *Bodhi Vriksha Kashaya* was administered orally in a dose of 40 ml twice a day. In Control Group i.e. Group B (Allopurinol) was given in the dose of 100 - 200 mg twice a day after breakfast/meal. Period of study was for 60 days along with a follow up at the interval of 15 days for one month. Assessment was done on symptoms of Hyperuricemia/*Vatarakta* as subjective parameter and serum uric acid as objective parameter. Obtained results were analysed statistically and significance of results were evaluated. Interventions were found to be significantly effective in reducing serum uric acid and in *Kandu*, *Daha*, *Ruja*, *Toda*, *Sandhi Sotha* and *Stabdhata* with p value < 0.001, more percentage relief was found in *Daha*, *Ruja*, *Toda* in patients treated with standard drug. After one month of treatment more sustained response was observed in patients treated with *Bodhi Vriksha Kashaya.* In Group A, only 23.07% show relapse to mild improvement after having moderate improvement. *Bodhi Vriksha Kashaya Paan* is quite promising, efficacious and safe treatment; its efficacy can be better interpreted by conducting a clinical trial on large sample size.

INTRODUCTION

Hyperuricemia is defined as a plasma (or serum) urate concentration > 6.8mg/dl. Hyperuricemia can result from increased production or decreased excretion of uric acid or from the combination of the two processes. The risk of developing gouty arthritis or urolithiasis increases with higher urate levels and escalates in proportion to the degree of elevation. Hyperuricemia is present in 2 to 13.2% of ambulatory adults and is even more frequent in hospitalized individuals (Harrisons: Principles of Internal Medicine, 18th edition). Although hyperuricemia is a sine qua non for the development of gout, it is not the sole determinant. More than 10% of the population of the western hemisphere has hyperuricemia, but gout develops in less than 0.5% of the population (Robbins and Cotran, 7th edition). Hyperuricemia can be classified as primary or secondary depending on whether the cause is innate or is the result of an acquired disorder. However, it is more useful to classify hyperuricemia in relation to the underlying pathophysiology, i.e. whether it results from increased production, decreased excretion or a combination of the two. Hyperuricemia does not necessarily represent a disease, nor is it a specific indication for therapy. The decision to treat depends on the cause and the potential consequences of the hyperuricemia in each individual (Harrisons: Principles of Internal Medicine, 18th edition). The most recognized complication of hyperuricemia is gouty arthritis. In the general population, the prevalence of hyperuricemia ranges between 2.0 and 13.2%, and the prevalence of gout is in between 1.3 and 3.7%. The higher the serum urate level, the more likely an individual is to develop gout. In one study, the incidence of gout was 4.9% for individuals with serum urate concentrations > 9.0 mg/dl compared with 0.5% for those with values between 7.0 and 8.9 mg/dl. The complications of gout correlate with both the duration and severity of hyperuricemia. Hypruricemia also causes several renal problems: (1) Nephrolithiasis; (2) Urate nephropathy, a rare cause of renal insufficiency attributed to monosodium urate crystal deposition in the renal interstitium, and (3) Uric acid nephropathy, a reversible cause of acute

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renal failure resulting from deposition of large amount of uric acid crystals in the renal collecting ducts, pelvis and ureters (ibid). Various allopathic medicines are used for the management of hyperuricemia/gout. Colchicine, Allopurinol, Probenecid, etc. are most commonly used drugs but have many serious adverse effects, e.g., overdose of colchicine produces kidney damage, CNS depression, and intestinal bleeding and death is due to muscular paralysis and respiratory failure. Chronic therapy with colchicine is not recommended because it causes aplastic anaemia, agranulocytosis, myopathy and loss alopecia. If hyperuricemia is increasing persistently it will develop into gout. In Ayurvedic texts, gout can be correlated with *Vatarakta* and to cure the *Vatarakta* various line of treatment has been given in *Charaka Samhita.* So, *Bodhi Vriksha Kashaya Paan* (Agnivesha *et al*., 2009) was taken for the management of hyperuricemia.

MATERIALS AND METHODS

Bodhi Vriksha Kashaya has been selected for the treatment of *Vatarakta* which is a classical reference mentioned in the *Carak Samhita Vatashonitacikitsaadhyaya*.

BODHI VRIKSHA (Dravyaguna-Vijanana, 2006):
Properties and its details

Botanical name- *Ficus religiosa*

Family- Moraceae

Synonyms- *Bodhidru, Pippala, Calapatra, Gajasana.*

Classical Categorization

Carak: *Mutrasangrahaniya, Kashaya skandha*
Susruta: *Nyagrodhadigana*

Parts used: Bark, leaf, fruit, leaf bud.

Major Chemical Constituents: Bark-β-sitosterol-D-glucoside, Vit.K, n-octacosanol, Methyloleanolate, Lanosterol, Stigmasterol, lupeon-3-one.

Properties:

Rasa- *Kashaya, Madhura*
Guna- *Guru, Ruksha*
Virya- *Sita*
Vipaka- *Katu.*
Karma: *Kapha-pittahara, Varnya, Vrishya, Vranasodhana* and *Ropana.*
***Matra* (Dose)**

***Kwath* (Decoction) –** 50 to 100 ml.

KASHAYA PREPERATION (Shailaja Srivastava *et al.*, 1999): Standard procedure of kwath preparation has been followed i.e. 10 gms crude powder (*Yavakuta*) of *Bodhi Vriksha* root bark were taken and mixed in 160 ml of water. This mixture was boiled until it remains 40 ml.

Aims and objectives

The aim and objective of the study is

1. To evaluate the efficacy of *Bodhi Vriksha Kashaya* in the management of Hyperuricemia.
2. Compare the efficacy of *Bodhi Vriksha Kashaya* with standard drug.

Patients were selected on the basis of the presence of classical symptoms of Hyperuricemia/*Vatarakta* from the O.P.D. / I.P.D. department of *Panchakarma,* Rishikul Campus, Haridwar. Patients were randomly categorized in 2 equal groups irrespective of their gender, age, income status etc. Some routine haematological examinations had been carried out in order to select the patients and to rule out any other pathology and to exclude the organic disorders. Special research proforma had been prepared and after detail history taking and examinations, selected 30 patients were randomly categorized in two groups on the basis of inclusion and exclusion criteria.

Criteria for selection of patients

(A) INCLUSION CRITERIA

1. Serum Uric Acid more than 6.8mg/dl
2. Patient age between 20-60 years
3. Patients fit for *Bodhi Vriksha Kashaya Paan.*

(B) EXCLUSION CRITERIA

1. Age < 20 years or > 60 years
2. Secondary hyperuricemia due to leukaemias, lymphomonas, polycythemia.
3. Patient with uncontrolled diabetes or serum glucose level >125mg/dl (fasting) and >180mg/dl (post prandial)
4. Tophaeceous gouty arthritis.
5. Patient with renal impairment.

LABORATORY INVESTIGATIONS

Investigations were carried out before, in between and after completion of therapy.

1. S. Uric Acid
2. Hb%
3. T.L.C
4. D.L.C
5. E.S.R
6. B.Sugar – Fasting and Post Prandial
7. B. Urea
8. S. Creatinine

WITHDRAWAL CRITERIA

Personal Matters

1. Inter-current Illness
2. Aggravation of symptoms
3. He / She develops any serious adverse effect (necessitating hospitalization)

Randomization & Blindin

Patients were randomized in a 1:1 ratio. This is an open study. The study protocol was reviewed and approved by an

Institutional Review Board at the institution level. From patients, written informed consent was taken before entering into study. The importance of them for adherence to the treatment, *Pathya-Apathya* associated with the disease, schedule for follow up, dates for visits to hospital was issued.

INTERVENTIONS

- Drug : *Bodhi Vriksha Kashaya*
- Dose : 40 ml
- Time of administration : Twice in a day (morning and evening empty stomach)
- Duration of therapy : 60 days
- Patients were guided regarding *Pathya/Apathya* regimen

Methodology of administration of standard drug

Allopurinol was administered in group B in the dose 100 - 200 mg twice a day for 60 days after breakfast/meal.

FOLLOW UP- After the completion of the therapy, patient was advised to visit O.P.D. at interval of 15 days for one month.

CRITERIA FOR EXAMINATION AND ASSESSMENT - Parameters were employed for assessment of the impact of the treatment produced in respective groups. Objective parameter of uric acid for Hyperuricemia and some special subjective parameters of *Vatarakta* were looked into for assessment.

A. Objective parameter: Serum Uric Acid
B. Subjective Parameters: Following subjective parameters of *Vatarakta* were taken for the assessment-

1. *Kandu* (Itching)
2. *Daha* (Burning sensation)
3. *Ruja* (Pain)
4. *Toda* (Pricking sensation)
5. *Sandhi Sotha* (Swelling of the joints)
6. *Stabdhta* (Stiffness)
7. *Sparshasahishnuta* (Tenderness)
8. *Twakvaivarnya* (Discoloration of skin)
9. *Raga* (Redness of the joints)

Observations

- Total 30 patients were registered. Out of which 90% patients had completed the treatment and 10% patients discontinued the treatment.
- Maximum No. of patients were females i.e. 56.67% and 43.33% of patients were males.
- Maximum No. of patients were urban i.e. 86.67% and 13.33% of patients were rural.
- Out of 30 patients 50% patients were belonging to middle class, 23.33% patients were belonging to lower middle class, 10% patients were from upper middle class where as 16.67% patients were very poor. None of the patients were registered from rich class.
- Maximum No. of patients were of Pittaja-Kaphaja Prakriti i.e. 40%, 36.67% of patients were Vata-Pitta and minimum were Vata-Kaphaja 23.33%.
- Majority i.e. 50% patients were having *Krura Koshta*, while 20% patients were having *Madhyam Koshta* and 30% were having *Mridu Koshta*.

RESULTS

Statistical analysis

The information gathered on the basis of above observations was subjected to statistical analysis using Graph Pad Instat. Software Version 3.10. As the criteria selected for analysis were non-parametric hence 'Paired "t" test' was applied for statistical improvement analysis in the clinical features of Hyperuricemia/Vatarakta in single group and 'unpaired "t" Test' for statistical status of inter group differences of clinical features. The results were interpreted.

The obtained results were interpreted as:

No improvement: $P > 0.05$
Improvement: $P < 0.05$
Significant: $P < 0.01$
Highly significant: $P < 0.001$

Relief in *Kandu*, *Daha*, *Ruja*, *Toda*, *Sandhi Sotha* and *Stabdhta* were 87.5 %, 70 %, 83.333 %, 84.615 %, 81.818 % and 85.714 % respectively. All these results were statistically extremely significant ($P < 0.001$). Relief in *Sparshasahishnuta* was 62.5 % which was statistically very significant ($p < 0.01$). Relief in *Raga* was 57.143 % which was statistically significant ($p < 0.02$). Relief in *Twakvaivarnya* was 50 % which was statistically insignificant.

Relief in *Kandu, Daha, Ruja, Sandhi Sotha* and *Stabdhta* were 77.778 %, 80 %, 87.5 %, 63.636% and 84.615 % respectively. All these results were statistically were extremely significant ($p < 0.001$). Relief in *Toda* was 87.5 % which was statistically very significant ($p < 0.01$). Relief in *Sparshasahishnuta*, *Twakvaivarnya* and *Raga* were 75 %, 66.667 % and 60 %. All these results were statistically insignificant ($p < 0.10$ or $p > 0.10$).

The improvement in Uric Acid percentage was more in group A than group B. There was statistically insignificant difference between both the treatments ($p<0.05$).

1. *Kandu:* - The improvement in *Kandu* grading was more in group A than group B but there was statistically insignificant difference between both groups of the treatments ($p<0.05$).
2. *Daha:* - The improvement in *Daha* grading was more in group B than group A but difference was statistically insignificant ($p<0.05$).
3. *Ruja*: - Improvement in both groups A and B were almost similar. Statistically, the difference was insignificant ($p<0.05$).
4. *Toda:* - Improvement in both groups A and B for the grading *Toda* was almost similar. Statistically, the difference was insignificant ($p<0.05$).
5. *Sandhi Sotha:* - Although relief in group A was more than group B, statistically the difference was not significant ($p>0.05$).

Table 1. Effect on Uric Acid in Group A

Objective Parametre	Mean Score		$\bar{X}$	%	SD	SE	T	P
	BT	AT						
Uric Acid (n=14)	7.6371	6.1093	1.5279	20.006	0.9037	0.2415	6.3259	<0.001

Relief in uric acid were 20.006 %. This result was statistically extremely significant (P < 0.001).

Table 2. Effect on chief complaints in Group A

Chief Complaints	Mean Score		$\bar{X}$	%	SD	SE	T	P
	BT	AT						
KANDU (n=6)	1.3333	0.1667	1.1667	87.5	0.4082	0.1667	7	<0.001
DAHA (n =6)	1.6667	0.5	1.1667	70	0.4082	0.1667	7	<0.001
RUJA (n=14)	2.1429	0.3571	1.7857	83.333	0.4258	0.1138	15.691	<0.001
TODA (n=11)	1.1818	0.1818	1	84.615	0.4472	0.1348	7.4162	<0.001
SANDHI SOTHA (n=8)	1.375	0.25	1.125	81.818	0.3536	0.125	9	<0.001
STABDHATA (n=13)	1.6154	0.2308	1.3846	85.714	0.5064	0.1404	9.859	<0.001
SPARSHASAHISHNUTA (n= 6)	1.3333	0.5	0.8333	62.5	0.4082	0.1667	5	<0.01
TWAKVAIVARNYA (n=3)	1.3333	0.6667	0.6667	50	0.5774	0.3333	2	> 0.10
RAGA (n=5)	1.4	0.6	0.8	57.143	0.4472	0.2	4	<0.02

Table 3. Effect on Uric Acid in Group B

Objective Parametre	Mean Score		$\bar{X}$	%	SD	SE	T	P
	BT	AT						
Uric Acid (n=13)	8.0085	6.5015	1.5069	18.817	0.8527	0.2365	6.3718	<0.001

Relief in uric acid were 18.817 %. This result was statistically extremely significant (P < 0.001).

Table 4. Effect on chief complaints in Group B

Chief Complaints	Mean Score		$\bar{X}$	%	SD	SE	T	P
	BT	AT						
KANDU (n=9)	1	0.2222	0.7778	77.778	0.441	0.147	5.2915	<0.001
DAHA (n =7)	1.4286	0.2857	1.1429	80	0.378	0.1429	8	<0.001
RUJA (n=13)	1.8462	0.6154	1.6154	87.5	0.9608	0.2665	6.0622	<0.001
TODA (n=7)	1.1429	0.1429	1	87.5	0.5774	0.2182	4.5826	<0.01
SANDHI SOTHA (n=8)	1.375	0.5	0.875	63.636	0.3536	0.125	7	<0.001
STABDHATA (n=12)	1.0833	0.1667	0.9167	84.615	0.2887	0.0833	11	<0.001
SPARSHASAHISHNUTA (n= 4)	1	0.25	0.75	75	0.5	0.25	3	>0.10
TWAKVAIVARNYA (n=3)	1	0.3333	0.6667	66.667	0.5774	0.3333	2	< 0.10
RAGA (n=4)	1.25	0.5	0.75	60	0.5	0.25	3	>0.10

Table 5. Comparison of intervention effect on objective parameter (Group A vs Group B)

Objective Parameter	Mean±SD		% RELIEF		Df =N1 + N2- 2	Unpaired t test	p value	Signifi-cance
	Gr. A	Gr. B	Gr. A	Gr. B				
Uric Acid	1.5279±0.9037	1.5069±0.8527	20.006	18.817	25	0.06199	0.9511	>0.05

Table 6. Comparative Effect of Invtervention on subjective parameters (Group A vs Group B)

Chief complaints	Mean±SD		% RELIEF		Df =N1 + N2- 2	Unpaired t test	p value	Signifi-cance
	Gr. A	Gr. B	Gr. A	Gr. B				
KANDU	1.1667±0.4082	0.7778±0.441	87.5	77.778	13	1.721	0.1089	>0.05
DAHA	1.1667±0.4082	1.1429±0.378	70	80	11	0.1091	0.9151	>0.05
RUJA	1.7857±0.4258	1.6154±0.9608	83.333	87.5	25	0.6032	0.5518	>0.05
TODA	1±0.4472	1±0.5774	84.615	87.5	16	0.0	>0.9999	>0.05
SANDHI SOTHA	1.125±0.3536	0.875±0.3536	81.818	63.636	14	1.414	0.1792	>0.05
STABDHATA	1.3846±0.5064	0.9167±0.2827	85.714	84.615	13	2.805	0.0101	>0.05
SPARSHASAHISHNUTA	0.8333±0.4082	0.75±0.5	62.5	75	8	0.2901	0.7791	>0.05
TWAKVAIVARNYA	0.6667±0.5774	0.6667±0.5774	50	66.667	4	0.0	>0.9999	>0.05
RAGA	0.8±0.4472	0.75±0.5	57.143	60	7	0.1584	0.8786	>0.05

Table 7. Comparison of overall relief in chief complaint after follow up (percentage)

Follow up study

Relief	GROUP A				GROUP B			
	AT		After 1 month		AT		After 1 month	
	No.	%	No.	%	No.	%	No.	%
Moderately Improved (41% to 70%)	12	85.71	12	85.71	9	69.23	6	46.15
Mildly Improved (16% to 40%)	2	14.28	2	14.28	4	30.76	7	53.85

6. *Stabdhta*: - On comparison of both groups A and B the improvement was almost similar. Therefore statistically insignificant difference was found ($p<0.05$).
7. *Sparshasahishnuta*: - The improvement in *Sparshasahishnuta* in group B is more than group A. The difference insignificant ($p>0.05$).
8. *Twakvaivarnya:* - The improvement in group B were more than group A but statistically the difference was insignificant ($p<0.05$).
9. *Raga:* - The improvement in group B were slightly more than group A but statistically the difference was insignificant ($p<0.05$).

In Group A there was no change in the result after completion of the treatment and after follow up of one month. In Group B, there was decrease in number of patients in moderately improved i.e. from 9 to 6, while increase in number of patients in mildly improved criteria i.e. from 4 to 7. In Group B, moderately improved patient decreases from 69.23% to 46.15% while mildly improved patient's increases 30.76% to 53.85%. Table shows Group B patients having relapse of symptoms after follow up study. In both the groups A and B no patient got complete remission and markedly improved result. The number of patient was shown result as unchanged and got worsened was none.

DISCUSSION

SEX (Ioannou and Boyko, 2012) **-** Maximum patients were females (56.67 %). It is believed that premenopausal women's are less susceptible to Hyperuricemia because of the normal estrogens level in their body which helps in excretion of uric acid, but post menopausal women's are more prone to develop Hyperuricemia/Gout then men's because of low level of estrogens. Recent studies also have shown that women's in 70-80 age groups are 3 times more prone than males.

Habitat - Maximum number of patients was residents from the urban region 86.67 % where as only 13.33% of patients were residents from rural area. The possible reason may be faulty dietary habits of the patients.

Socio-Economic status (Desideri et al., 2015; Meneses-Leon et al., 2014) - Incidence of socio-economic status reveals that maximum (50 %) belonged to middle class followed by 23.33 % were belonging to the lower middle class. This may be due to lack of awareness about the disease and also due to stressful life. To overcome the stress drinks alcohol and consumes other beverages. Alcohol is also responsible for the Hyperuricemia.

Sharirika prakriti **-** Most of the patients i.e. 40 % patients had *Pitta-Kaphaja Prakriti*, while 36.67 % patients had *Vata-Pitta Prakriti.* As *Vatarakta* is *Vata* and *Pitta Doshaja Vyadhi*, incidence of occurrence of this disease in *Vata-Pitta* and *Pitta-Kapha Prakriti* were more. This data possibly reveals the predominant role of *Vata Dosha* in development of *Vatarakta* also *pitta* due to *Sahadharmita* to *Rakta* is responsible for vitiation of *Rakta* and causing the disease. *Prakriti* always supports vitiation of same *Dosha* very easily.

Kostha **-** In the case of categorization of *Koshtha, Krura Koshtha* people were more (50 %). This may be due to aggravated *Vata* and *Krura Koshtha* is more prone to constipation which is also one of the causes of Hyperuricemia as excretion of the uric acid through gut is hampered.

RESULTS

Both the interventions are found to be significantly effective in reducing Serum Uric Acid on objective parameter. *Bodhi Vriksha Kashaya* was found to be quite significant in providing percentage relief in symptoms. *Bodhi Vriksha* has *Kashaya (pungent)* and *Madhura Rasa (sweet taste), Virya Sita* and *Vipaka Katu*. It act as *Raktashodhaka (purification of blood)* and pacify the *Rakta Dosha*. It acts on very first level at *Dosha-Dusya Sammurcchana (first step of pathogenesis)* by decreasing vitiated *Vata* and *Rakta. Madhura, Kashaya Rasa* has *Pitta Shamaka* and *Sita Virya* of *Bodhi Vriksha* is *also Pitta Shamaka. Madhura Rasa* also has *Vata* and *Pitta Shamaka* properties. *Rakta* and *Pitta* has similar properties (*Tulya Guna).* So, *Rakta* were pacified by the similar way. Hyperuricemia is a disorder of Purine metabolism and hence it can be considered as a disorder of *Agni Dushti*. *Katu Vipaka* of *Bodhi Vriksha* was helpful in correction of Agni. This may be the possible explanation of mode of action of *Bodhi Vriksha Kashaya*. *Bodhi Vriksha Kashaya* was given empty stomach for better absorption of the drug. In this study *Kwath* (Decoction) were prepared for the *Paan*. During the process of

Kwath preparation *Samsakaranuwartana (alteration of properties)* were happened and this may be the *Prabhava* of the drug which was useful in the treatment of Hyperuricemia.

The standard drug (Allopurinol) was found to be quite effective in providing immediate relief from the symptoms. But during the follow up after one month, there is reduction in percentage relief and relapse of symptoms occurs with the standard drug while treatment with Ayurvedic palliative medicine more sustained relief was found.

Conclusion

Bodhi Vriksha Kashaya was proved to be promising treatment of Hyperuricemia as that of the standard drug. After one month of treatment more sustained response was observed in patients treated with *Bodhi Vriksha Kashaya.* Repeated application of these treatment procedures may be conducted to evaluate further study. This study should be conducted on large sample and longer duration for better and more accurate results. In this way new Ayurvedic palliative drugs may be arise as a new ray of hope in management of Hyperuricemia safely.

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