

Clinical Study on Dosha-Based Combinations in Essential Hypertension

Research Article

Jithesh Madhavan^{1*}, Gowrisankar P², Jayadevan C V³, Asha Karunakaran K⁴, Aswathy S⁵, Murali K⁶

Professor and Head, Kayachikitsa & PG Department Of Manasroga, V.P.S.V Ayurveda College Kottakkal, India.
 Professor and Head, Kayachikitsa, Vaidyarathnam Ayurveda College Ollur, Kerala, India.
 Principal, V.P.S.V Ayurveda College Kottakkal, India.

4. Professor, Department of Kayachikitsa, Government Ayurveda College, Tripunittura, India.
 5. Associate Professor, Department of Kayachikitsa, Government Ayurveda College, Thiruvanantapuram, India.
 6. Former Professor and Head, Department of Kayachikitsa, Government Ayurveda College, Tripunittura, India.

Abstract

Hypertension (HT) is one of the most vital modifiable risk factors for coronary heart disease, stroke, congestive heart failure, chronic kidney disease, and peripheral vascular disease. Data from HT trials indicate that most subjects need combination therapy to achieve sufficient BP control and in only 50% of trials, this goal was achieved. Addressing the contributory factors is the need of the hour rather than controlling blood pressure (BP) level only. Here the Ayurvedic drugs are having a definite scope in the management. HT may be considered as *tridoshaja vyadhi* with *Vatha* dominance with affection of the *rasa* and *raktha dhatus*. Ayurgenomics is having a crucial role in explaining how drugs can be used more effectively by targeting them on individuals of particular *Prakriti*. The unique method of administering the drug based on the *prakriti* and *dosha* in any clinical condition so as to enhance the effect is termed personalized medicine and based on the judgment that the *doshahara* drugs when added to *vyadhihara* drug enhances its efficacy potential. *Sarpagandha* was added with *brihat panchamoola, trina panchamoola* and *triphala* in *Vatha*, *Pitta and Kapha prakrithi*, satisfying the diagnostic criteria were administered with the drug, 6 gm twice daily after food, as per the *dosha* status for 45 days with BP assessments on 0th day, 15th, 30th, 45th and 60th day. Repeated Measures ANOVA was done for analysis. Result: The mean score reduced throughout the assessments and was significant at 0.01% level indicating the influence on *prakriti* in the outcome.

Key Words: Essential Hypertension, Sarpagandha, Ayurgenomics, Personalised medicine, Dosha based combinations, Prakriti.

Introduction

Ayurveda, the science for preserving life is not indicated for the management of disease conditions, but aimed at benefits such as health, happiness and harmony to the human kind. Hypertension (HT) or elevated blood pressure (BP) is a serious medical condition that significantly increases the risks of heart, brain, kidney and other diseases (1). An estimated 1.13 billion people worldwide have HT, among which the 2/3rd living in low and middle-income countries (2). Fewer than 1 in 5 people with identified HT have their BP under control. One of the global targets for noncommunicable diseases is to reduce the prevalence of HT by 25% between 2010 and 2025. HT is

Jithesh M

Professor and Head, Kayachikitsa & PG Department of Manasroga, V.P.S.V Ayurveda College Kottakkal, Kerala. India. Email Id: <u>drjitheshm@gmail.com</u> straightforwardly responsible for 57% of stroke deaths and 24% of coronary heart disease (CHD) deaths in India (3).

Essential HT is currently understood as a multifactorial disease arising from the collective action of several genetic, environmental and behavioral factors and the exact management not only includes controlling the BP, but also addressing the multifactors. (4) In the study, the already proven drug for HT, *sarpagandha* was combined with *dosha* specific combinations and tried in the three groups categorized on the basis of *dosha/ prakriti* in HT. This is based on the judgment that the *doshahara* drugs when added to *sarpagandha*, the *vyadhihara* drug enhance its potential in the action on the particular disease. The selected drugs are based on the assessment of *prakriti* or *dosha* of the included subjects.

Hypertension – Ayurvedic Understanding

A number of physiological mechanisms are involved in the maintenance of normal BP and their derangement plays a part in the development of essential HT. It is high time to propose with the possible

^{*} Corresponding Author:



Jithesh M et.al., Clinical Study on Dosha-Based Combinations in Essential Hypertension

medicines that control BP but also prevents complications as well as risks with the *Ayurvedic* understanding. HT is the result of *Rakta dushti* with *tridosha* involvement in which *Vata* and *Pitta* doshas are prominent.(5) The factors which influences HT include *Vyana Vatha, Sadhaka Pitta, Avalambaka Kapha, Rasa* as well as *Rakta dhatus*.

The decrease in the caliber of *Dhamanis* resulting from any cause including *Kapha vridhi* or *medovridhi* may also cause increased peripheral resistance. *Sadhaka Pitta* situated in *hridaya* is responsible for *budhi* (cognition), *utsaha* (alertness), *bhaya* (fear), *harsha* (pleasure) etc. and makes manas get rid of the raja and tama and helps optimum cardiac functions, the alteration may lead to deranged BP (6).

Hridaya is the *sthana* of *manas* and *atichinta* leads to *rasavaha srotodushti* (7). This points to the direct relationship of *manas* and its functional alterations contributory to the conditions such as HT. Stable condition of *manas* plays an important role in the regulation of BP and psychological factors are having a core role in the manifestation of HT. Alteration of the functioning of *manas* may also add to *dushti* of *ojus* which leads to variation including that of BP. Symptoms of *Oja kshaya* described in *Ayurvedic* parlance including *shrama* (lassitude), *moha* (disorientation), *murcha* (syncope) etc. are also observed in high BP. (8)

Avurveda gives more emphasis to the prevention and promotion of the health. The appropriate management includes not only reducing the BP but also modifying the risk factors so as to prevent the possible complications. Avoiding etiological factors of any disease is considered as the first line of management by Susrutha.(9) While treating this condition prasara tridosha and Rasa, Rakta and Meda avastha of dushti should be taken in to consideration and along with lifestyle modifications, appropriate Vata anulomana, Tridoshahara and Rasa, Rakta Prasadakara, Medohara chikitsa may be definitely adopted (10). For effective management of HT, lifestyle modifications should be given more emphasis and if necessary appropriate drug therapy should also be administered on a conditional basis.

Sodhana chikitsa is also helpful in HT in moderate to severe cases. Virechana have been observed useful peculiarly snigdha virechana which is capable of bringing Vathanulomya and also sudhi to Pitta and Kapha doshas (11). Also the sodhana helps to attain the clarity of the mind which helps in relieving the contributory psychological factors if any leading to the condition.

Aims and objectives

1. To explore *dosha*-based combinations for the management of essential hypertension (EHTN).

2. To postulate the possible *doshic* mechanism leading to EHTN.

Methodology

The project was entitled as "Clinical study on *dosha*-based combinations in essential hypertension", which was a multicentre trial in the selected Ayurveda colleges from Kerala to study the effect of *dosha* based drugs when added to the drug in routine use for HT, *Sarpagandha*. The drug was administered after the assessment of *prakriti* with a validated questionnaire for *prakriti* analysis. The *vyadhi vipareetha* drug, *sarpagandha* was added to *dosha* relieving combinations in the present study to assess its effect.

Diagnostic criteria

- A systolic BP reading of 140 mm Hg. or more
- A diastolic BP reading of 90 mm. Hg. or more
- At least two abnormal BP readings on different occasions over two week period or more (one week interval is adequate if the first reading higher than 180 systolic or 110 diastolic)

Laboratory Investigations

- Urine for albumin, RBC, Cast, sugar
- Blood Urea, Serum Creatinine, ESR, Hb, lipid profile
- FBS, PPBS
- ECG
- X-ray Chest
- · Serum potassium

Inclusion criteria

- Participants of EHTN with informed consent.
- Age group 30-60 years irrespective of gender, caste, religion etc.

Exclusion criteria

Hypertension associated with:-

- Stage 3 hypertension
- Renal diseases
- Endocrinal disorders
- Related genetic abnormalities
- Pregnancy and lactation
- Collagen vascular diseases
- Patients already on hypotensive drugs or medications for cardiac disorders.
- Any condition that the investigator finds to jeopardize the study.

Withdrawal criteria

- Those with no hypotensive response within three weeks.(No reduction of 10mm. and 6mm in SBP and DBP respectively)
- Those wish to withdraw from the study
- Any other adverse effects during the study period

Duration of treatment and assessment

60 days, Assessment done on every fifteenth day with one follow-up



Form of medicine and intake

The medicines were prepared from Oushadi Pharmaceutical Corporation; Thrissur under expert supervision with duly identified drugs with the same batch number and was distributed to each centre of study.

Diet & Exercise

As per approved guidelines of DASH (Dietary Approach to Stop Hypertension) (12)

Study period

Two years

Study setting

Multicentre study involving Department of *Kayachikitsa* of the Ayurveda Colleges - Kottakkal, Thiruvananthapuram, Tripunithura and Ollur.

Intervention

- *Vathika Sarpagandha* 1 gm and *Brihat panchamula churna –* 5 gm
- *Pittaja Sarpagandha* 1 gm and *Trina panchamula churna* 5 gm
- *Kaphaja Sarpagandha* 1 gm and *Triphala churna –* 5 gm
- Dosage twice daily 1 hour before food with warm water as anupana

The medicines were prepared from Oushadi Pharmaceutical Corporation Thrissur under expert supervision with duly identified drugs with the same batch number and was delivered to each centre of study.

Study design

Single group – Pretest – Post test Design

Sample size

150 (36 each in two centers and 39 each in other two centers) with equal distribution in each *dosha/ prakriti* type

It was a single blind Clinical trial. *Prakriti* was assessed with TNMC *prakriti* questionnaire. The BP was assessed with the same type of Diamond Non mercuric type Sphygmomanometer purchased for the project. The duration of the study was 60 days. BP assessment was done on 0th, 15th 30th, 45th and 60th days. The mean of the three assessments were taken as the actual value.

Ethical clearance was obtained from the respective Institutional Ethical Committees of all the study centers prior to inclusion.

Statistical Analysis

For continuous variables, the summary statistics included mean, minimum, maximum and standard deviation. The discrete variables were summarized through frequency distribution. The measurements under *Vatha*, *Pitha*, *Kapha* for Systolic and Diastolic BP by locations were subjected to Repeated Measures ANOVA. Decision tree and cluster analysis was also done (13).

Observations regarding the disease

The distribution of the symptoms in relation with HT was analyzed among the three groups. Disturbed sleep was more prominent among the Vatha group, headache, dizziness was seen more in the Pitta group and palpitation, fatigue, chest pain in the Kapha group while emotional disturbances were distributed almost equally among the groups. One fifth of the female subjects were having the history of HT during pregnancy. Among the psychological factors, the Vatha group was having more stress, Pitta group was having fear and irritability and the Kapha group was having grief and also fear among them. 75% of all the subjects were non vegetarians with more frequency among the Vatha group between them. They were using katu, amla and lavana rasa in excess in their diet. Lack of exercise or insufficient exercise was observed in 2/3 rd of the subjects. Sleep was disturbed in several subjects, more in the Vatha group. 1/4th of the subjects were having the habit of frequent alcohol intake.

Table -1, Descriptive Statistics of Vatha, Pitta and
Kapha groups

		Sys	stolic	Diastolic			
Location	Statistic	Mean	Std. Deviation	Mean	Std. Deviation		
Kottakal	Time1	153.2231	15.69661	95.5231	5.81752		
	Time 2	145.7154	9.15977	89.8231	6.23914		
	Time 3	138.4462	10.69857	82.7508	8.75053		
	Time 4	135.6177	10.00108	80.2792	9.88300		
	Time 5	131.6231	11.55611	79.3915	9.28961		
	Time1	148.8663	4.16805	85.0413	2.17698		
	Time 2	142.2875	5.00558	83.2038	1.82704		
Ollur	Time 3	138.2913	7.29949	83.5369	3.27671		
	Time 4	135.1250	7.58837	82.2850	1.67428		
	Time 5	133.1206	7.57028	82.0763	1.85203		
	Time1	147.8000	7.23564	98.3083	5.30702		
	Time 2	139.0775	10.02586	81.7492	4.47366		
Tripunithura	Time 3	138.4075	10.01799	77.9250	6.07620		
1	Time 4	134.6250	5.24094	79.4667	6.29276		
	Time 5	132.4583	6.63961	78.8000	4.74131		
Thiruvanatha	Time1	144.7667	7.65190	82.5000	2.11058		
	Time 2	144.4167	9.15014	82.4417	2.13519		
	Time 3	141.8250	9.32681	81.3833	1.56137		
puram	Time 4	137.3167	10.97475	81.1417	2.07910		
	Time 5	136.0500	11.35994	81.2417	1.63899		

Time 1: 0th Day, Time2: 15th Day, Time 3: 30th Day, Time 4: 45th Day, Time 5: 60th Day

The average age in *Vatha* group was 48.14 with a minimum of 29 years and maximum of 70 years, while *Pitta* group had an average of 49 with age ranging from 27 to 76. In *Kapha* group, the average age was 48.7 ranging from 19 to 70 years. The mean weight was 64.7 in *Vatha* group, 64.1 in *Pitta* group and 71.5 in *Kapha* group. *Kapha* group had the highest BMI among the three groups (27.37) while *Pitta* group had 24.42 and *Vatha* group have 24.31 as the mean BMI.

Jithesh M et.al., Clinical Study on Dosha-Based Combinations in Essential Hypertension

The mean systolic BP on inclusion was 149.5 in the *Vatha* group, 148.45 in the *Pitta* group and 148.76 in the *Kapha* group. The mean Diastolic BP on inclusion was 89.3 in the *Vatha* group, 90.76 in the *Pitta* group and 89.1 in the *Kapha* group. The mean systolic BP on the last assessment was 136 in the *Vatha* group, 135 in the *Pitta* group and 133 in the *Kapha* group. The mean Diastolic BP on the last assessment was 82 in the *Vatha* group, 82 in the *Pitta* group and 80.5 in the *Kapha* group.

Observations regarding alteration in BP Vatha group

Table 2: Effect of the intervention in Vatha group

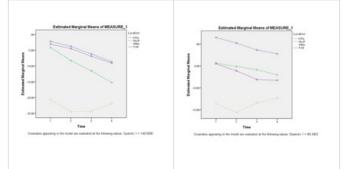
	Change in Systolic Pressure			Change in Diastolic Pressure			
With-in Subjects	df	F	P Value	df	F	P Value	
Time	2.5	5.028	0.005	2.3	0.165	0.872	
Time * Pressure1	2.5	5.885	0.002	2.3	0.297	0.771	
Time * Location	7.5	1.703	0.110	6.8	2.158	0.460	
		Betwo	een Sub	jects			
Intercept	1	5.071	0.029	1	63.373	<0.00 1	
Pressure1	1	8.326	0.006	1	78.235	<0.00 1	
Location	3	18.257	< 0.001	3	35.676	<0.00 1	

In the *Vatha* group, mean systolic BP reduced from 149.5 to 136.25 in the last assessment. The diastolic BP reduced from 100.6 to 96.7 in the final assessment.

Table 3 - Changes in BP in Vatha group - Friedman's Test

	Mean Rank	Chi- Square	Df	P Value	
Pressure at Time Point 0	3.81				
Pressure at Time Point 1	3.18				
Pressure at Time Point 2	3.03	68.427	4	< 0.001	
Pressure at Time Point 3	2.59				
Pressure at Time Point 4	2.39				

Graph 1 - Distribution of Systolic Pressure and diastolic pressure through out the centres



There was statistically significant change in the group at 0.1% level

Pitta group

Table 4: Effect of the intervention in Pitta group

	8							
	Change in Systolic Pressure			Change in Diastolic Pressure				
With-in Subjects	df	F	P Value	df	F	P Value		
Time	3	4.021	0.009	2.2	1.022	0.369		
Time * Pressure1	3	4.707	0.004	2.2	1.043	0.361		
Time * Location	9	1.144	0.336	6.6	1.631	0.138		
		Betwe	een Subj	ects				
Intercept	1	4.391	0.041	1	17.394	<0.00 1		
Pressure1	1	7.347	0.009	1	22.377	<0.00 1		
Location	3	5.824	0.002	3	3.268	0.29		

In the *Pitta* group, the mean systolic BP reduced from 148.46 to 135.11 while the last assessment. The diastolic BP reduced from 90.76 to 82.12 during the last assessment.

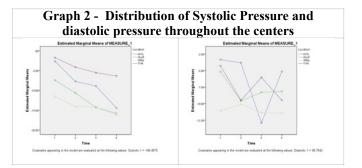


Table 5 - Changes in BP in Pitta group - Friedman's Test

		9 · · F		
	Mean Rank	Chi- Square	Df	P Value
Pressure at Time point 0	3.88			
Pressure at Time Point	3.15			
Pressure at Time Point 2	3.02	70.021	4	< 0.001
Pressure at Time Point 3	2.56			
Pressure at Time Point 4	2.38	_		

There was significant change in the BP level in the group at 0.1% level.

Kapha group Table 6: Effect of the intervention in *Kapha* group

	Change in Systolic Pressure			Change in Diastolic Pressure				
With-in Subjects	df	F	P Value	df	F	P Value		
Time	2.1	5.872	0.004	2.3	0.227	0.826		
Time * Pressure1	2.1	7.828	0.001	2.3	0.530	0.964		
Time * Location	6.2	0.994	0.660	6.8	4.952	< 0.001		
	Between Subjects							
Intercept	1	31.606	< 0.001	1	130.877	< 0.001		
Pressure1	1	39.960	< 0.001	1	158.219	< 0.001		
Location	3	1.211	0.316	3	1.645	0.191		

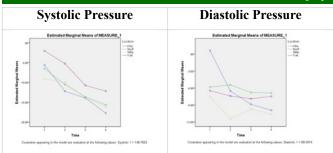


Table 7 - Changes in BP in Kapha group -Friedman's Test

		~ •		
	Mean Rank	Chi- Square	Df	P Value
Pressure at Time point 0	4.08			
Pressure at Time Point1	3.37			
Pressure at Time Point 2	2.85	96.914	4	< 0.001
Pressure at Time Point 3	2.52			
Pressure at Time Point 4	2.19			

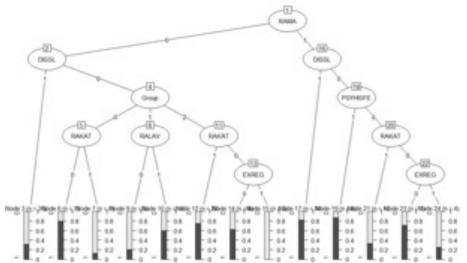
In the *Kapha* group the mean systolic BP reduced from 148.77 to 133.27 during the last assessment. The diastolic BP reduced from 90.05 to 80.49 during the last assessment. The changes were statistically significant at 0.1% level.

Decision Tree analysis

The same trend of systolic and diastolic pressure reducing from time point 1 to 4 can be seen across *prakriti* groups. The same trend of decrease in the values of BP was observed in the three groups of the study.

Discussion

HT is to be considered as *tridoshaja vyadhi* with *Vatha* dominance with affection of mainly, the *rasa* and *raktha dhatus*. Thus the causative factors leads to alteration in function of the three *doshas* and *rasa rakta dhatu dushti* leading to the manifestation. Sudden or severe HT produces symptoms such as headache, giddiness, palpitations, excessive sweating, fatigue, exertional dyspnoea and insomnia as per the involvement of *doshas* based on the etiological factors and the *prakriti* of the subject(14) *Vatha* dominant manifestation were presenting with head ache, giddiness, tremor, sleep disturbances etc. *Pitta* dominant with excess sweating, blackouts, palpitation etc. and *Kaphaja* with lassitude, heaviness of body, lack of energy etc. among the affected (15).



The group or *prakriti* has a decisive influence at level 3 on the outcome of the study. Disturbed sleep has an influence at level 2 and *amla rasa* have influence at level 1 in the study.

If disturbed sleep is present in a *Vatha* group subject, there is 30% chance of not responding to the treatment. If a *Vatha prakriti* subject is using *amla rasa* and has sleep disturbances, there is less chance to respond with the intervention. In a *Pitta prakriti* subject using *lavana rasa*, there is 60% chance of no changes in BP after the intervention. Excess use of *Katu rasa* in *Kapha prakriti* is also lessening the response. If a *Kapha prakriti* subject is having no exercise regime, there is 60% chance of getting no response.

If a *Vatha prakriti* subject is having excess *amla rasa* use and also having fear, there is 80% chance of not getting the response of the treatment. If a *Vatha*

subject is using excess *katu rasa* also, the chances of getting changes in BP will become less. If a *Vatha* subject is using *amla rasa* and is also lacking exercise, the chance of reducing BP will come down by almost 70%.

Cluster analysis

Hierarchical clustering was carried out using Jaccard similarity index as distance measure, all the variables being in dichotomous state. Proximity values were obtained between all the variables. The identified clusters indicate their significance in contributing to the condition of HT. The gender and the *rasas – katu, amla and lavana* are similar in contributing to the condition. Similar is the case of sleep and its duration. In the same way the psychological history and the duration of non veg intake belongs to a cluster. Similar is the case of

Jithesh M et.al., Clinical Study on Dosha-Based Combinations in Essential Hypertension

irritability and grief in contributing to the illness. In the same manner the food habit, duration of hotel food intake, nature of the sleep and sleep duration behaves in the same manner as contributory. The leisure type and time of leisure also belongs to the same cluster. The range of Jaccard index is from 0 to 1, with 1 indicating perfect similarity (16).

Outcome of BP

The diastolic and systolic were used to group the patient's outcome into Normal or High pressure and Friedman's test was done for analysis.

The mean score reduction was observed and it was significant as well in the *Vatha* group, indicating the effect of the therapy in the group. In the *Pitta* group also, the mean score reduced throughout and was also statistically significant as well. In the *Kapha* group, there was significant reduction in mean scores after the intervention. This indicates to the fact that, in all the groups, the intervention was effective as well as statistically significant in managing HT.

Mode of action of the drug

The effect of the therapy was analyzed in the *Vatha, Pitta and Kapha* groups separately for systolic pressure as well as diastolic pressure. It was not able to compare between the groups as the intervention was dissimilar in the groups. The mean score reduction was observed throughout and it was statistically significant as well in the *Kapha, Pitta* as well as *Vatha* groups, indicating the effect of the therapy in the group in managing HT.

Prakriti assignment involves phenotyping of an individual based on several characteristics including body frame, food and bowel habits, disease resistance, memory retention, metabolism, etc. (17) being the foundation of personalized medicine, by which the combination in the study was selected. Such combinations are designed for attaining the purpose of vyadhiharatwa as well as doshaharatva contributing to absolute recovery from any clinical condition. Prakriti phenotyping can function as a potential stratifier of the gut microbiome in a published study and may provide evidence for the conceptual framework of personalized medicine in Ayurvedic system of medicine. This may also bring light to the importance of koshta and agni in the medicine selection in such conditions including HT. (18)

Sarpagandha is described in the Samhitas as Kapha Vatha Shamana, Nidra Karaka, and Uccharaktachapahara; thus, it alleviates the Vata, Pitta, and Kapha and act as Mastiska Shamaka, Hridaya avasaadaka and Nidrajanaka. Sarpagandha has an action on the sareerika as well as manasika contributory aspects of HT. (19).

Mode of action of Brihat Pancamula is based on their rasa pancaka. Drugs of Brihat Pancamula are ushna in virya and laghu, ruksha in guna. Due to kashaya, tikta rasa Brihat Pancamula is Kapha samaka and due to ushna in virya it is Vata samaka and agni deepaka and can be used in diseases such as Svasa, kasa and Shotha (20). The drugs in *Trina panchamula* generally have the properties of *madhura*, *kashaya rasa*, *snigdha laghu guna*, *madhura vipaka*, *sheeta virya* and *tridoshahara* property. These drugs acts as *Jeevaniya*, *Rasayana*, *Mutrala*, *Agnidipana*, *Ruchivardhaka* and *Rakta Shodhaka* and useful in *Prameha*, *Daha*, *Jvara*, *Trishna*, *Arshas*, *Hridroga*, *Vatarakta* etc (21)

Triphala promotes proper digestion and absorption of food, reduces serum cholesterol levels, improve circulation, relax bile ducts, prevent immunosenescence, maintain homeostasis of the endocrine system, and increase production of red blood cells and hemoglobin. The major constituents of the formula are the tannins, gallic acid, ellagic acid, and chebulinic acid, which are potent antioxidants that may account, at least in part, for the observed immunomodulatory activity of the formula (22).

These well studied drugs along with *sarpagandha* may be enhancing the action of the same in the HT and also alleviating the *dosha* related symptoms associated with respective *dosha/ prakriti* features, which is being explained as the reason behind the observed effect.

Conclusion

The selected intervention was effective, statistically significant as well as safe in reducing the systolic and diastolic BP of the Vatha, Pitta and Kapha group of subjects, in the study conducted in the four Ayurveda Colleges across the state. The current study is an initial step towards assessing the effect of prakriti based combinations of sarpagandha in EHT. Ayurveda not only offers personalized treatment but personalized nutrition and personalized lifestyle by way of both drug and non drug modalities suited to an individual's prakriti for ultimate efficacy.(23) Further studies are to be planned in this area for generalization of the observations with appropriate proven control drugs. Use of techniques such as dietary alterations, psychological support and adoption of healthy life style when supplemented with the drugs will be quite effective in the management of such conditions. (24). This seems to be an area with scope of further research by which the principles of Ayurveda will be popularized for the help of the diseased.

Conflicts of interest: Nil

Acknowledgement: The project was sanctioned and funded by Kerala University of Health sciences, Thrissur, Kerala. The authors acknowledge the heartily support by the KUHS Vice chancellor and the whole team of SFRA till the completion of the project.

References

- 1. Oparil S, Acelajado MC, Bakris GL, Berlowitz DR, Cífková R, Dominiczak AF, et al. Hypertension. Nat Rev Dis Primer. 2018 Mar 22; 4: 18014.
- 2. WHO | A global brief on hypertension [Internet]. [cited 2021 Jan 21]. Available from: https:// www.who.int/cardiovascular_diseases/publications/



global_brief_hypertension/en/ dated 04-10-2020 time 13:04 IST

- 3. Gupta R. Trends in hypertension epidemiology in India. J Hum Hypertens. 2014 Feb; 18(2):73–8.
- Kannel WB. Hypertension: reflections on risks and prognostication. Med Clin North Am. 2009 May; 93(3): 541–58
- Dipti Kalangutkar et.al. Essential Hypertension An Ayurvedic View, International Journal of Science and Healthcare Research 168 Vol.4; Issue: 2; April-June 2019: 33-36 pp
- 6. Astanga Hrdayam of vagbhata, Edited by Bramhanand Tripathi, Chaukhamba Sanskrit Pratishthan Delhi, Reprint-2009, 173pp
- Caraka Samhita, Agnivesha with Ayurveda Dipika Samskrit commentary Edited by Laxmidhar Dwivedi, B. K. Dwivedi, P.K. Goswami, Part-1, Choukhamba Krishnadas Academy, Varanasi Print-2014, 829 pp.
- Caraka Samhita, Agnivesha with Ayurved Dipika Samskrit commentary Edited by Laxmidhar Dwivedi, B. K. Dwivedi, P.K. Goswami, Part-1, Choukhamba Krishnadas Academy, Varanasi Print-2014, 832 pp
- 9. Susruta, Nibandhasangraha commentary by Dalhana, edited by Vaidya Jadavaji Trikamaji Acharya, 7th edition, Chaukhamba publications, 2002, .64pp
- 10. Agnivesha, Charaka Samhita. Dipika commentary of Chakrapanidatta, edited by Vaidya Jadavaji Trikamaji Acharya, 5th edition, Varanasi Chaukhamba publications 2001,144pp
- 11. Astanga Hrdayam of Vagbhata, Edited by Bramhanand Tripathi, Chaukhamba Sanskrit Pratishthan Delhi, Reprint-2009, 58pp
- 12. Juraschek SP, Miller ER, Chang AR, Anderson CAM, Hall JE, Appel LJ. Effects of Sodium Reduction on Energy, Metabolism, Weight, Thirst, and Urine Volume: Results From the DASH (Dietary Approaches to Stop Hypertension)-Sodium Trial. Hypertension. 2020 Mar; 75(3):723-729.
- 13. Kamatani N. Using statistics to make personalized medicine a reality. 2007;2. '*FRONTLINES*', *Riken Research*. 2007;2 pp

- 14. Katz JN, Gore JM, Amin A, Anderson FA, Dasta JF, Ferguson JJ, *et al.* Practice patterns, outcomes, and end-organ dysfunction for patients with acute severe hypertension: the Studying the Treatment of Acute Hypertension (STAT) registry, Am Heart J, 158 (4) (2009), 599-606 pp
- Gadre RK, editor. Pune, India: Aryabhushan Mudranalaya; 1963. Ashtanga Hridaya of Vagbhata; Chaukhamba Sanskrit Pratishthan Delhi, Reprint-2009, 223 pp
- 16. Tan PN, Steinbach M, Kumar V (2005). Introduction to Data Mining. Pearson Publishers, 2019, 25-28 pp
- 17. Dey S, P. Pahwa, Prakriti and its associations with metabolism, chronic diseases, and genotypes: possibilities of new born screening and a lifetime of personalized prevention, J Ayurveda Integr Med, 5 (2014), 15-24pp
- Wallace RK. The Microbiome in Health and Disease from the Perspective of Modern Medicine and Ayurveda. *Medicina*. 2020; 56(9):462 pp
- 19. Kaptchuk TJ, Eisenberg DM, The persuasive appeal of alternative medicine, Ann Intern Med 1998;129: 1061-5 pp.
- 20. Bhavna Gupta, Anil Kumar Singh, Insightful Exploration of Brihat Panchamula from Brahatrayi and Nighantu, Mukt Shabd Journal, 9/VII (2020), 86-90pp
- Nagarajnaik Chavhan, Shashirekha H.K, Bargale Sushant Sukumar, S.N.Belavadi, Tejashwini Hiremath. Comprehensive Documentation and Critics on Trinapanchamula. Ayushdhara, 2019;6(6): 2458-2463pp
- 22. Baliga MS, Meera S, Mathai B, Rai MP, Pawar V, Palatty PL. Scientific validation of the ethnomedicinal properties of the Ayurvedic drug Triphala: a review. *Chin J Integr Med*. 2012;18(12):946-954pp
- 23. Ozdemir V, Shear NH, Kalow W. What will be the role of pharmacogenetics in evaluation of drug safety and minimizing adverse effects? Drug Saf 2001; 24:75-85 pp.
- 24. Yarnell E, Abascal K. Treating hypertension botanically. *Altern Complement Ther.* 2001;7(5):284–290 pp.
