WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 9, Issue 12, 1236-1243. Research Article ISSN 2277– 7105

EVALUATION OF AYURVEDIC FORMULATION- NIA/DG/2015/01 IN THE SUSTAINABLE MANAGEMENT OF NEWLY DIAGNOSED STAGE -1 ESSENTIAL HYPERTENSION

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Article Received on
20 August 2020,

Revised on 10 Sept. 2020,
Accepted on 30 Sept. 2020

DOI: 10.20959/wjpr202012-18772

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ABSTRACT

Hypertension is a widely prevalent disease affecting a significant population globally. Hypertension is a major risk factor for the development of cardiovascular disease, cerebrovascular disease causing high rate of mortality and morbidity and renal diseases etc. One in three adults worldwide has high blood pressure. Therefore hypertension is a global health challenge and a lot of effort is devoted to keep the population normotensive. Against the backdrop drug of these facts, the holistic formulation containing *arjuna*, *ashwagandha*, *jatamansi*, *shankhpushpi*, *punarnava* was formulated and named NIA/DG/2015/01(trial drug). A single center, randomized, double-blind, clinical trial (90 days total duration) has been conducted in order to evaluate the action of trial drug–GV (GhanVati) in group A, trial drug – ME (standard extract) in group B of hypertension. The trial drug showed highly significant reduction in Blood pressure in both the groups.

KEYWORDS: *Arjuna*, *ashwagandha*, *jatamansi*, *shankhpushpi*, *punarnava*, hypertension.

INTRODUCTION

Hypertension, also known as high or raised blood pressure, is a condition in which the blood vessels have persistently raised pressure, includes both hypertension (defined as 140/90 mm of Hg or above) and "high normal" (between 130/85 mm of Hg and 140/90 mm of Hg).[1] It is classified as either *primary* (essential) or secondary. About 90 to 95% of cases are termed

primary HTN, which refers to high BP for which no medical cause can be found.[2] The remaining 5 to 10% of cases, called *secondary* HTN, are caused by other conditions that affect the kidneys, arteries, heart, or endocrine system.[3]

The prevalence of hypertension in the urban Indian population was estimated to be 40.8% (95%CI: 40.5%-41.0%) and that of hypertension in the rural population was 17.9% (95%CI: 17.5%-18.3%).[4] Globally, the overall prevalence of hypertension or raised blood pressure in adults aged 25 and above was around 40% in 2008.[5] Worldwide, hypertension is estimated to cause 7.5 million deaths, about 12.8% of the total deaths. Hypertension accounts for 57 million disability adjusted life years (DALYS) or 3.7% of total DALYS. The World Health Organization (WHO) has estimated that globally about 62% of cerebrovascular diseases and 49% of ischemic heart diseases are attributable to suboptimal blood pressure (systolic > 115 mmHg), with little variation by sex.[6]

There are different opinions regarding Ayurvedic nomenclature of this clinical condition such as *vyanabala, raktagatavata, siragatavata, avritvata, Dhamani prapurnata, Vaishamya avrut vata, Raktavata, Vyanabala vaisamya etc. Acharya Charaka* has advised to treat such a disease without nomenclature by judging the involvement of *dosha dushya* only.[7] Essential hypertension has been screened as *Vata pitta pradhana raktaprdoshaja vikara.*

Antihypertensive drugs in modern medicine are not effective owing to dependence, side effects and cost effectiveness. *Ayurvedic* medicines do play role in management of hypertension but practically as an adjuvant therapy because of the serious emergency consequences of uncontrolled hypertension. Though practically adopted, there is very little scientific and systemic data available for the role and efficacy of *Ayurvedic* medicines as an adjuvant therapy in hypertension. Against the backdrop drug of these facts, the holistic formulation containing *Arjuna, Ashwagandha, Jatamansi, Shankhpushpi, Punarnava* was formulated and named NIA/DG/2015/01.

Need of study

Two studies have been conducted for trial drug NIA/DG/2015. One was pre-clinical for assessing the toxic effect and to know the anti-hypertensive effect in rat model. No toxic effect and significant anti-hypertensive effect was found in albino rats. Another study was clinical for evaluation of anti- hypertensive effect in human and was found significant result

when used @ 1 g BD for 30 days (published data of MD Thesis of Dr Dipti – Kayachikitsa Dept, NIA year 2017).

In previous study, the effect was observed within 7-10 days from start of drug administration. But, the effect was not sustained after the withdrawal of the drug. Considering the multifactorial and metabolic etio-pathology of hypertension, it is hypothesized that drug intervention for a longer period might be able to produce sustenance in anti-hypertensive activity. Therefore, the present study is planned to be undertaken by drug administration for 3 month and follow up for 1 month in human subjects of newly diagnosed stage-1 essential hypertension.

OBJECTIVE

To assess role of NIA/DG/2015/01 formulation in Newly Diagnosed (1-3mnth) Stage-1 Essential Hypertension.

MATERIAL AND METHODS

Study design

single center, randomized, double blind, interventional type clinical trial.

Study population

The study was explained clearly to the subjects and their signed, written informed consent was taken before starting the trial. A total of 60 subjects completed the trial out of 63 subjects registered for the trial. Subjects were randomly assigned in two groups 30 in each group. Trial was conducted after approval of IEC of National Institute of Ayurveda with approval no. (No.IEC/ACA/2017/12 dated 26/04/2017). The trial was also registered in CTRI with registration no. CTRI/2018/10/016005.

Trial drug

Sr. No.	Ingredient	Part used	Quantity
1	*Convolvulus pleuricaulis* Chois	Whole plant	1 part
2	*Nordostachys jatamansi* DC	Rhizome	1 part
3	*Terminalia arjuna* Roxb.	Bark	1 part
4	*Withania somnifera* Linn.	Root	1 part
5	*Boerhaavia diffusa* Linn.	Root	1 part

The above ingredients will be pulverized and mixed in equal proportions which will be then subjected to extraction methods- 1) Traditional extraction method (Ghan vati method) 2) Modern extraction method.

Extraction of the ingredients will be obtained in aqueous medium. The obtained extract will be filtered and dried suitably**.** The extracts will be filled into 500mg capsules. The capsules containing Ghan Vati will be named as NIA/DG/2015/01 – GV and the capsules containing the standard extract will be named as NIA/DG/2015/01 – ME.

Dose, duration, and administration

The trial drug was given as capsules of 500 mg, twice daily, before food, with normal water, for 90 days.

Grouping, Randomization & Blinding

After the screening through complete examination and investigation, selected patients will be enrolled for the trial. The enrolled patients will be divided randomly into two groups; one group (Group – A) will receive Ghan Vati Capsules and other group (Group – B) will receive Extract Capsules.

Blinding will be done by a person who is not related to study team. Fictitious names will be assigned by him/her and all the records will be stored in his/her safe custody. After completion of the trial, de-blinding will be done by the same person.

Inclusion criteria

1. Patients belonging to either sex between the age group 18 to 60 yrs.
2. Patients who newly diagnosed as E.H.T (within 1-3 month duration) will be selected.
3. Mild to moderate grade patients of hypertension as per 7^{th} JNC & WHO criteria will be include.
4. Isolated grade-1 Systolic or Diastolic hypertension.

Exclusion criteria

1) Secondary hypertension.
2) Renal diseases, Diabetic Mellitus.
3) Pregnancy induced hypertension.
4) Drugs like Oral Contraceptive Pills, steroids.
5) Ventricular hypertrophy, co-arctation of aorta.

6) Portal hypertension.
7) Renal artery stenosis induced hypertension.

Criteria for Assessment

a. Subjective parameters

Sign and symptom Rating Scale

b. Objective parameters

1) Assessment of change in Blood Pressure in supine position.
2) Complete Blood Picture
3) Renal Function Test (Blood urea, Serum Creatinine) and
4) Lipid profile (Total lipids, Serum Triglyceride, Serum Cholesterol)

Statistical method

The values of the above parameters were recorded before and after the treatment for both the groups and were analyzed by using the Student's paired 't' test.

Assessment of Clinical Result

Duration of clinical trial will be of 4 month. (3month intervention and 1 month follow up)
All patients were followed up 15th and 30th day after withdrawal the drug.

OBSERVATION AND RESULT

The effect of therapy was assessed on each sign and symptom of the disease. These sign and symptoms had scored before and after treatment and assessed statistically to see the significance. The effect of therapy in all the groups in each sign and symptom is followings

Intra Group comparison

Table no. 4.29: Showing Effect of therapy in subjective parameters.

Variable	Group	Mean		Mean Diff.	% Relief	SD±	SE±	P	Significance
		BT	AT						
Shirshool	A	0.97	0.57	0.43	44.83	0.5040	0.0920	<0.0001	HS
	B	1.47	0.60	0.83	56.82	0.6989	0.1276	<0.0001	HS
Bhrama	A	0.53	0.27	0.27	50.00	0.6397	0.1168	<0.05	S
	B	1.03	0.63	0.43	41.94	0.6261	0.1143	<0.0001	HS
Klama	A	0.63	0.30	0.33	52.63	0.4795	0.0875	<0.0001	HS
	B	0.77	0.30	0.47	60.87	0.6814	0.1244	<0.0001	HS
Hritspandana	A	0.57	0.37	0.20	35.29	0.5509	0.1006	>0.05	NS
	B	0.47	0.23	0.23	50.00	0.4302	0.0785	<0.0001	HS
Anidra	A	0.50	0.27	0.27	53.33	0.4498	0.0821	<0.0001	HS

	B	0.33	0.17	0.17	50.00	0.3790	0.0692	<0.05	S
Krodha	A	0.40	0.20	0.20	50.00	0.4068	0.0743	>0.05	NS
	B	0.50	0.23	0.27	53.33	0.5208	0.0951	<0.0001	HS

Table no. 2: Showing effect of therapy on objectives parameter (Paired 't' Test).

Variable	Group	Mean		Mean Diff.	% Relief	SD±	SE±	T	P	S
		BT	AT							
Hb% (gm%)	A	12.75	13.00	-0.25	-1.93	0.3980	0.0727	3.394	<0.05	S
	B	12.85	12.91	-0.06	-0.44	0.3380	0.0617	0.9182	<0.05	NS
TLC	A	7761.67	7732.67	29.00	0.37	331.28	60.483	0.4795	<0.05	NS
	B	7803.3	7893.33	-90.00	-1.15	290.48	53.034	1.697	<0.05	NS

Variable	Gr	Mean		Mean Diff.	% Relief	SD±	SE±	T	P	S
		BT	AT							
Sr Urea	A	30.73	29.40	1.50	4.88	1.978	0.361	4.325	<0.0001	S
	B	32.63	30.37	2.27	6.95	3.205	0.585	3.874	<0.0001	HS
Sr.Ceat.	A	0.93	0.83	0.21	23.02	0.163	0.030	4.014	<0.0001	HS
	B	0.75	0.61	0.14	18.75	0.175	0.032	4.372	<0.0001	HS

Variable	Gr	Mean		Mean Diff.	% Relief	SD±	SE±	T	P	S
		BT	AT							
Sr.Chol.	A	209.72	205.16	4.557	2.35	5.365	0.9795	4.652	<0.0001	HS
	B	210.59	203.71	7.11	3.38	8.507	1.553	4.345	<0.0001	HS
Sr.Tri.	A	174.09	170.33	3.763	9.08	4.710	0.8599	4.377	<0.0001	HS
	B	174.30	157.17	17.13	9.83	5.991	1.094	15.665	<0.0001	HS

Table No. 3 Showing effect of Therapy on Systolic and Diastolic Blood Pressure (Objectives parameter): (Paired't' Test).

Variable	Group	Mean		Mean Diff.	% Relief	SD±	SE±	T	P	S
		BT	AT							
Systolic BP	A	141.00	126.67	14.33	10.17	7.6759	1.4014	10.228	<0.0001	HS
	B	142.70	125.67	17.03	11.94	6.8907	1.2581	13.539	<0.0001	HS
Diastolic BP	A	95.83	89.50	6.33	6.61	6.4237	1.1728	5.400	<0.0001	HS
	B	97.33	89.00	8.33	8.56	4.0115	0.7324	11.378	<0.0001	HS

DISCUSSION

These five drugs had been selected for the present study due to their established role in management of hypertension (Pratibha et al; Dipti et al), broad spectrum action at different levels of etiologies and different mechanisms, wide therapeutic window and easy availability.

Regarding subjective parameters , In Group A, patients treated with *Ghan vati* of Trial drug formulation, showed statistically highly significant results (p value <0.0001) regarding subjective parameter–*Shirashool, Klama* whereas *Bhrama, Anidra* showed significant result and *Hridspanadana, Krodha* showed non significant results. While In Group B, patients

treated with aqueous extract of Trial drug TF-2 showed highly significant results regarding subjective parameters – *Shirshool*, Klama, *Hritspandan*, *Bhrama* and Krodha whereas in case of *Anidra* showed non significant result.

Regarding objective prameters In Group A, Hb% showed significant results (p value <0.05) whereas in Blood Urea, Sr. Creatinine, Sr. Cholesterol, Sr. triglyceride showed highly significant results (p value<0.0001) and non significant (p value>0.05) result in TLC. In Group B Blood urea, Sr. Cholesterol, Sr. Creatinine, Sr. Triglyceride showed highly significant (P value <0.0001) whereas in Hb and TLC showed non-significant (P value >0.05) result. Blood pressure is the most important objective parameter regarding the clinical trial of Hypertension in which both groups gave highly significant result.

The patients were followed up after withdrawing the trial drugs for 1 month with measurement of BP on 15^{th} and 30^{th} day from the date of drug withdrawal.

In Group A- 15 patients (50%) remained normotensive after the withdrawal of the intervention where as in 15 patients (50%) rise on blood pressure was observed. In Group B- 20 patients (66.7%) remained normotensive after the withdrawal of the intervention where as in 10 patients (33.3%) rise on blood pressure was observed.

Though beyond the scope of the work, the follow up is still continuing. The normotensive patients are still normotensive till the last follow up. The longest follow up is 3 months from the withdrawal of the drug. The willing patients in whom BP was raised upto 140/90 mm of hg again were given the medicine again and became normotensive within one week of re-administration of the drug.

Each of these herbs has been reported to be safe by toxicity study. Acute oral toxicity of above mention drug formulation had been carried out in rats1. It had shown no toxic effect both in animals and humans.

CONCLUSION

The trial drug showed highly significant reduction in Blood pressure in both the groups when given at a dose of 2 capsules (1 gm) twice a day after meal for 90 days. Since both Ghanavati and Modern Extract showed similar results, it can be concluded that drug A (Ghanvati) can be used for the patients of EHT to offer an cost effective drug in comparison to Modern extract. The study showed that 58.3% patients sustained the effect of becoming normotensive

up to 30 days after withdrawal of drug whereas rise in BP was observed in rest 41.67% patients. Thus the study suggests that the medication can be attempted to be withdrawn after 3 months of treatment but with close monitoring and follow up. The trial drug was well tolerated by all the patients and no toxic or unwanted effects were observed in any patient.

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