Indian Journal of Traditional Knowledge
Vol. 13 (2), April 2014, pp. 313-318

Assessment of efficacy of *Sankhahuli* (*Convolvulus pluricaulis* Chois.) and *gokhru* (*Tribulus terrestris* L.) in the management of hypertension

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Received 21.02.13, revised 19.08.13

Although, the allopathic drugs are very useful to control hypertension and prevent cardiovascular morbidity and mortality; the adverse metabolic effects of antihypertensive drugs have raised questions that challenge the traditional approaches for the management of hypertension. This was the main aim behind this study that prompted us to look for a safe and effective antihypertensive drug. Randomized, active control, single blind trial was carried out on 40 subjects. Experimental group was subjected to dried aqueous extract of *Sankhahuli* (*Convolvulus prostratus* Forssk syn. *C. microphyllus* Sieb. ex Spreng.*; C. pluricaulis* Chois.) and *Gokhru* (*Tribulus terrestris* L.). Control group was subjected to Benzthiazide and Triamterene. Blood pressure levels were measured by using sphygmomanometer at 0, 14th and 28th day. For safety evaluation liver function test, kidney function test, Serum electrolyte and ECG (Electrocardiogram) were obtained before and after treatment. After 28th day of therapy a significant difference ($P < 0.0001$) was noticed in both experimental and control group. The results in this preliminary study suggested that the drugs are effective and safe. However, the power of this study was limited because of low number of patients to draw a valid conclusion. Further studies are warranted with large number of patients before this drug could be recommended for therapy.

Keywords: Hypertension, Temperament, Essential hypertension, *Sankhahuli*, *Gokhru*

IPC Int. Cl.[8]: A61K 36/00, A01D 20/00

The incidence of hypertension is increasing very rapidly. It is considered to be a major health problem throughout the globe. This is due to high prevalence and its association with increased risk of cardiovascular complications.

As estimated in the Framingham Heart Study, the residual lifetime risk of incidence of hypertension was 90% for both 55 and 65 yrs old subjects and lifetime probability of receiving antihypertensive was 60%[1]. It is also emerging as a major health problem in India; the prevalence of hypertension in recent studies was almost similar to USA[1,2] About > 90 % of cases of hypertension are idiopathic in nature and are labeled as essential or primary hypertension, whereas, remaining have a definitive cause of the disease and are called as secondary hypertension cases[3-9] However, ancient Unani scholars did not describe the term hypertension, mentioned the treatment of manifestation of hypertension in their books.

Most of Unani scholars were familiar to manifestation of hypertension, as they described the most of symptoms such as headache, vertigo, epistaxis, due to *imtela* (excessive intravascular blood). Some of them described vascular pressure caused by increased blood volume and decrease in lumen of blood vessels.

Basheezak[10] is described by Al-Razi. It is more closely related to hypertension in comparison to *imtela*. The manifestations of *basheezak* as described by him are as follows:

1 Production of tension in blood vessels
2 Redness of eyes

He also described management of *basheezak* as:

1 Sleep decreases symptoms
2 *Fasad* (Venesection)
3 Use of *Mushillat-e- Safra* (Purgatives of yellow bile)

The drug *Sankhahuli* (*Convolvulus prostratus* Forssk syn. *C. microphyllus* Sieb. ex Spreng.*; C. pluricaulis* Chois.) is prostrate, sub-erect, spreading, hairy, perennial herb, with a woody root stock, found throughout India. The plant is used as memory enhancer, to reduce mental tension, as a psycho-stimulant and tranquillizer and in diabetes. Decoction

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of the plant is used as aphrodisiac. The leaves are beneficial in haemoptysis, urinary diseases, calculi, fever, cough, dyspnoea and anorexia. The leaves are one of the major constitutents of herbal formulation '*shankhpushpi*', used as antiepileptic. The drug has been used in Unani system of medicine since centuries in various heart diseases[11,12]. Besides hypertension and palpitation, this drug is also used as brain tonic, and tranquilizer[11,13]. It contains alkaloids convolvine, convolamine, phyllabine, convolidine, confoline, convoline, subhirsine, convosine, and convolvidine along with scopoline, flavons coumarin, beta-sitosterol, fatty acid, wax and hydrocarbons[14,15]. It has been established that convolvine blocks the M-receptors of the heart and intestine, but raises the sensitivity of the M-receptors of the salivary gland and of the CNS[16]. Mishara *et al.* concluded that it showed maximum hypotensive activity during spring season[17].

Tribulus terrestris L. is a variable, prostrate annual, up to 90 cm in length, commonly found thought out India, up to an altitude of *c*. 5,400 m. Roots slender, cylindrical, somewhat fibrous, 10-15 cm long, light brown and faintly aromatic; leaves paripinnate: leaflets 5-8 pairs, subequal, oblong to linear-oblong; flowers leaf-opposed, solitary, pale-yellow to yellow; fruits globose, consisting of 5-12 woody cocci, each with 2 pairs of hard, sharp, divaricate spines, one pair longer than the other; seeds several in each coccus with transvers partitions between them.

The drug *Gokhru* (*Tribulus terrestris* L.) has also been used in classical literature of Unani medicine as diuretic[18-20] for hypertension, palpitation and other cardiovascular diseases[11]. It has been shown to have a high angiotensin converting enzyme inhibition suggesting the possible mechanism of action of controlling hypertension[21]. These herbs have been used for controlling symptoms of hypertension for centuries. Thus it seems worthwhile to investigate into their possible properties of lowering elevated blood pressure.

Material and methods

This was a randomized, single blind, active controlled clinical study, approved by the institutional ethical committee of Jamia Hamdard, New Delhi. Newly diagnosed patients of grade I essential hypertension (as classified in JNC VII report)[22,23], have no treatment for it were enrolled in the out patients department (OPD) of Majeedia hospital. Patient of either sex between 18 - 70 yrs of age and who voluntarily consented were included in the study. The patients with secondary hypertension, diabetes mellitus, hypothyroidism, taking oral contraceptive pills, having CVS and CNS complications, liver and kidney insufficiency, pregnant women and lactating mothers, and terminally ill patients (Tuberculosis, Hepatitis-B and C, HIV and Carcinomas) were excluded from the study. Blood pressure was measured by using standardized techniques[23]. The BP was the average of two seated measurements of right arm. After obtaining the informed consent, patients were randomized by using simple randomization (tossing a coin) into two groups, i.e., experimental (A) and control (B). Each of them was given patient ID number. The experimental group was subjected to dry aqueous extracts of *Gokhru* (*Tribulus terrestris* L.) and *Sankhahuli* (*Convolvulus pluricaulis* Chois.) in capsule form, orally. Both herbs (in crude form) were procured from the market and authenticated by Taxonomist (Dr Javed Ahmad; DB/FOS/JH/I/2005/01), Jamia Hamdard, New Delhi. Extraction, drying of extract and filling of capsules were done at trial center. Dried and powdered aqueous extract of 7 gm of *Gokhru*[20] (that was equivalent to 500 mg) was filled in gelatin capsules of 500 mg capacity. Likewise dried and powdered aqueous extract of 3 gm of *Sankhahuli*[24] (that was equivalent to 375 mg) was filled in 500 mg capacity gelatin capsules. The patients of experimental group was advised to be taken one capsule of *Gokhru* once a day (in the morning) orally and one capsule of *Sankhahuli* twice daily (in the morning and evening) orally. The capsules were dispensed from outpatient department in small poly packs that could be snapped airtight. The combination of 25 mg benzthiazide and 50 mg triamterene (filled in capsules having similar characteristics as the experimental drugs) was given to the control group in the morning. The duration of protocol therapy was 28 days. Systolic and diastolic blood pressures were the primary outcome parameters. There were no secondary outcome parameters for this study. The study outcome was assessed after 14 and 28 days of protocol therapy and the results were analyzed by using Wilcoxon Macthed Pair Signed Rank Test (for same group) and Mann Whitney Test (between different groups). Results are presented as the mean value ± SEM. Values of $p < 0.05$ were considered significant. The *Mizaj* (temperament) was assessed at first visit only to evaluate the prevalence of hypertension among four types of personalities (Sanguine, Phlegmatic, Bilious and Melancholic) described in classical literature. To

assess the *Mizaj* (temperament of patients) a questionnaire based on classical Unani literature was developed (**Table 1**). The maximum number of right ticks given by a patient to the questions in a particular column was used as indicative of temperament for that individual.

Results

Out of total number of patients enrolled 31 in experimental and 20 in control group) 40 patients (25 in experimental and 15 in control group) completed the study, 7 patients (4 in experimental and 3 in control group) did not come for proper follow up and 4 patients (2 in experimental group and 2 in control group) were dropped out from the study due to development of angina and were advised proper treatment. **Table 2** represents the baseline characteristics of the participants. Out of total number of patients (40) who completed the study *Safravi* temperament was attributed most frequently (16 patients, 11 in experimental and 05 in control group) followed by *Damvi* temperament (12 patients, 08 in experimental and 04 in control) (**Table 2**).

Effect on systolic blood pressure

For systolic blood pressure experimental drug showed extremely significant ($P < 0.0001$) results. Before starting the treatment, 100% patients in both groups (experimental & control) had systolic hypertension. The mean bold pressure of experimental group was 150.7 mm of Hg and mean blood pressure of control group was 152.7 mm of Hg. After the 14 days of treatment out of total (40) patients, 29 (72.5 %) patients (17 from the experimental, respectively 12 from the control group) became normotensive (≤ 139 mmHg) while in the other (27.5 %) blood pressure level decreased significantly. The mean blood pressure decreased to 130.4 mm of Hg in experimental and 130.6 mm of Hg in control group. After completion of study out of total (40) patients, 38 (95 %) patients (24 from the experimental, respectively 14 form the control group) became normotensive while the other (5 %) failed to do so. The mean blood pressure further decreased to 125.4 mm of Hg in experimental and 124.0 mm of Hg in control group. After completion of study the relative decrease of mean blood pressure was 16.8% in the experimental; respectively 18.8% in the control group **(Table 3)**. The mean systolic blood pressure decreased more after 28 days than 14 days.

Effect on diastolic blood pressure

For diastolic blood pressure experimental drug showed extremely significant ($P < 0.0001$) results. Before starting the treatment, 100% patients in both

Table 2—Basic characteristics of participants

Characteristics	Experimental group	Control group
Age in year (Mean± SEM)	44.5±1.4	48.0±1.2
Sex		
Male	14	06
Female	11	09
BMI (Mean± SEM) kg/m^2	24.5±0.5	24.1±0.3
Significant past history (+ve)	09	07
Significant family history (+ve)	10	05
Temperament		
Damvi	8	04
Balghami	5	04
Safravi	11	05
Asudavi	01	02

Table 1—Assessment of temperament of patients

Parameters	Sanguine	Phlegmatic	Bilious	Melancholic
Complexion	Rudy (Radish)	Chalky (Whitish)	Pale (Yellow)	Purple (Blackish)
Built	Muscular & Broad	Fatty & Broad	Muscular & Thin	Skeletal
Touch	Hot & Soft	Cold & Soft	Hot & Dry	Cold & Dry
Hair	Black lustrous thick rapid growth	Black thin slow growth	Brown thin rapid growth	Brown thin slow growth
Movement	Active	Dull	Hyperactive	Less active
Diet	Cold & Dry	Hot & Dry	Cold & Moist	Hot & Moist
Weather	Spring	Summer	Winter	Autumn
Sleep	Normal (6-8) hrs	Excess	Inadequate	Insomnia
Pulse	Normal (70-79)	Slow (60-69)	Rapid (≥80)	Slow (60-69)
Emotions	Normal	Calm & Quiet	Angry	Nervous

Maximum number of right ticks given by the patient in a particular column is indicative of temperament of that patient.

groups (experimental & control) had diastolic hypertension. The mean blood pressure was 95.8 mm of Hg in experimental and 94.5 mm of Hg in control group. After 14 days of treatment 22 (55 %) patients (12 in the experimental, respectively 10 in the control group) became normotensive (≤ 89 mmHg) while in the other (45 %) blood pressure level decreased significantly. The mean blood pressure decreased to 84.6 mm of Hg in experimental and 84.0 mm of Hg in control group. After completion of study, 26 (65 %) patients (14 in the experimental, respectively 12 in the control group) became normotensive while the other (35 %) failed to do so. The mean blood pressure further decreased to 83.2 mm of Hg in experimental and 81.7 mm of Hg in control group. After completion of study the relative decrease of mean blood pressure was 13.6% in the experimental; respectively 13.2 % in the control group **(Table 4)**. The mean diastolic blood pressure decreased more after 28 days than 14 days.

Effect on safety parameters

The experimental as well as control drugs found to be very safe for this duration of treatment, however, control drugs showed significant effects on some parameters. Laboratory finding is presented in **Table 5**. Both drugs (experimental and control) showed none significant (P > 0.05) change in liver function tests (Serum Bilirubin, Serum Aspartate, Alanine Aminotransferase and Serum Alkaline Phosphatase). On kidney function tests (Serum Creatinin and Blood Urea) experimental drugs showed none significant (P > 0.05) changes but control drugs showed mixed results there was a

Table 3—Effect on systolic blood pressure in both groups

	Control group			Experimental group		
F/U Visits	0 Day	14ht Day	28th Day	0 day	14th Day	28th Day
Mean±SEM	152.7 ± 1.6	130.6 ± 2.7***	124.0 ±2.9***	150.7 ±1.3	130.4 ±2.3***	125.4 ±1.4***
% of Change		14.9	18.8		13.5	16.8

†P>.05(NS) *P<0.05(S) **P<0.01(MS) ***P<0.001(ES) (Wilcoxon Matched Pair Signed Rank Test)
P (E/C) at 14th day & at 28th day was > 0.05 (NS) (Mann-Whitney Test)

Table 4—Effect on diastolic blood pressure in both groups

	Control group			Experimental group		
F/U Visits	0 Day	14ht Day	28th Day	0 day	14th Day	28th Day
Mean±SEM	94.5 ± 1.6	84.0*** ± 1.6	81.7** ± 1.6	95.8 ± 0.6	84.6*** ± 1.2	83.2*** ± 1.3
% of Change		11.7	13.2		11.1	13.6

†P>.05(NS) *P<0.05(S) **P<0.01(MS) ***P<0.001(ES) (Wilcoxon Matched Pair Signed Rank Test)
P (E/C) at 14th day & at 28th day was > 0.05 (NS) (Mann Whiteny Test)

Table 5—Effects on safety parameters in both groups

Parameters	Control group		Experimental group	
F/U Visits	0 Day	28th Day	0 day	28th Day
S. Bilirubin (mg/dl)	0.7± 0.1	0.8±0.1†	0.8±0.1	0.8±0.0†
AST (Units/Lt)	28.7±2.9	23.4±2.1†	33.9±3.8	29.7±2.6†
ALT (Units/Lt)	36.2±5.8	31.7±2.7†	34.5±3.1	33.6±2.9†
S. ALP (Units/Lt)	163.5±11.5	178.2±13.6†	163.7±11.4	176.6±21.1†
S. Createnin (mg/dl)	1.7±0.5	1.3±0.1*	1.2±0.0	1.2±0.1†
Blood Urea (mg/dl)	21.7±1.3	28.6±2.5*	29.7±1.9	25.5±1.5†
S. Potassium (meq/L)	4.2±0.1	4.4±0.2†	4.4±0.1	4.3±0.1†
S. Sodium (meq/L)	137.3±1.3	137.9±1.4†	138.6±1.0	138.1±1.0†
S. Chloride (meq/L)	103.6±0.9	104.3±1.2†	105.5±0.7	105.3±0.8†

†P>.05(NS) *P<0.05(S) (Wilcoxon Matched Pair Signed Rank Test)

significant ($P < 0.05$) decrease in serum creatinin level and significant ($P < 0.05$) increase in blood urea. Both drugs (experimental & control) showed none significant ($P > 0.05$) changes in serum electrolytes (Serum Potassium, Serum Sodium and Serum Chloride) and electrocardiogram.

Discussion

The present study was carried out to evaluate the hypotensive effect of Unani medicines (*Sankhahuli* and *Gokhru*). Participants of the study were adults of both sexes having grade I essential hypertension. There was a significant improvement in systolic as well as diastolic blood pressure after 14 and 28 days of treatment. Experimental ($P < .0001$) as well as control drugs ($P < .0001$) showed comparable effects on systolic blood pressure after 14 and 28 days of treatment. After 14 days of treatment control drugs ($P < .0001$) showed slightly batter effects than experimental drugs ($P < .001$) for diastolic blood pressure, however, results were equally comparable after 28 days of treatment. Due to some methodological shortcomings like very short length of therapy, outcome parameters (traditional blood pressure measurements: Only right arm and no 24 hrs ambulatory blood pressure monitoring) and unblinding of patients, these data suggest short period non-inferiority of the experimental Unani drug composition to the conventional combination of diuretics chosen in this trial. Safety of both drugs (experimental as well as control) was evaluated after 28 days of treatment. There was no statistically significant difference on safety parameters before and after treatment. No adverse effect was reported by participants of this study.

Traditional significance of study

Although the allopathic drugs are very useful to control hypertension and prevent cardiovascular morbidity as well as mortality, they have adverse metabolic effects on electrolyte, glucose/insulin, lipid and uric acid[25,26]. On the other hand experimental drugs, *Sankhahuli* and *Gokhru* neither showed adverse metabolic effects nor have reported toxicity in Unani classical literature. Upon the basis of results of this study and survey of Unani medical literature, it is supposed that experimental drugs may have significant role in controlling hypertension without having adverse metabolic effects. As observed in this study maximum patients (40%) were of *Safravi Mizaj* (temperament), this may be useful for physicians while treating patients and researchers for future studies.

Conclusion

Experimental drugs were found to be effective and safe on these limited numbers of patients for given time period. However, the sample size was not large; therefore the preliminary level of this study suggested that the drugs may be effective and safe in the management of essential hypertension. This data has limited importance for long term endpoints such as stroke, M I, etc. however, provides scope for future long term studies with improved outcome parameters and long term observations to evaluate the significant results for long term assessment of hypertension.

Acknowledgement

Authors are very thankful to Dean Faculty of Medicine, Jamia Hamdard, New Delhi for his valuable guidance and support during the study. We are also thankful to Jamia Hamdard (Hamdard University) to provide funds for the study.

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