Efficacy of Unani Polyherbal Formulation (*Sharbat-e-Unnab)* In Grade I Primary Hypertension-An Open Labeled Randomized Standard Controlled Study

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ABSTRACT

Background and objectives:

Noncommunicable diseases in general and Cardiovascular diseases in particular are the major cause of mortality and morbidity worldwide. Hypertension is leading risk factor of all metabolic disease with a global prevalence of 1.39 billion. There are certain effective drugs available for hypertension in both conventional and traditional medicine. There is always a need of exploring better treatment for subjective and objective parameters related to hypertension. Present study was designed to determine the efficacy of *Sharbat-e-Unnab* in primary hypertension as antihypertensive drug in comparison with standard drug (Atenol 25 mg) on scientific parameters.

Methods: This study was design as randomised open labelled clinical trial with standard control, conducted up on forty cases for six weeks. Study outcome in both groups were assessed with objective and subjective parameters.

Result: The result of intervention was analyzed using paired & un-paired‘t’test and Chi-Square/Fisher Exact Test) test. Objective parameters (*viz.* reduction in Blood both systolic & diastolic pressure) analysis in both groups, exhibit statistically highly significant (p value <0.001**) without any difference in intergroup analysis. While subjective parameter (*viz.* Headache, Dizziness, Fatigue, Palpitation) analysis for test versus control groups reveals that test group is more significant than control group.

Conclusion& interpretation:

The study reveals that test drug is effective in reducing both subjective and objective parameters (B.P) without any adverse effect. Thus, it can be concluded that test drug is found equally effective with respect to control drug in the management of HTN.

Key words: Primary Hypertension; Essential HTN; *Sharbat-e-Unnab*; *Zaghtuddam Dam Qawi; Imtila.*

INTRODUCTION

Globally cardiovascular disease accounts for approximately 17 million deaths a year that is nearly one third of the total deaths worldwide. Of these, complications of hypertension account for 9.4 million deaths every year. Hypertension is responsible for at least 45% of deaths due to cardiac diseases and 51% of deaths due to stroke.[1]

Prevalence of hypertension in India is 25- 30% in urban area where as 10-20% in rural.[5] Raised blood pressure is a major cardiovascular risk factor. If left uncontrolled, hypertension causes stroke, myocardial infarction, cardiac failure, dementia, renal failure and blindness, causing human suffering and imposing severe financial and service burdens on health systems.[2] Prevention of hypertension, and control of blood pressure in patients with hypertension, is necessary for the reduction of cardiovascular morbidity and mortality.[3]

Unani Medicine is one of the oldest traditional medicines established by Hippocrates on the humoral doctrine, practiced largely in Indian subcontinent. Considering multi-factorial causation of hypertension and morbid to fatal consequences; it is needed to explore the hidden potential of Unani Medicines for prevention and treatment of hypertension in a holistic manner, which may prove more effective and safer. Hypertension is a term which does not exist as such in classical literature of Unani Medicine but most of the clinical features representing hypertension have been mentioned as a manifestation of a condition of plethora described as "*Imtela Bihasab Al Aw'eyyah*".[4,5,6] This condition may be defined as repletion or fullness of vessels with increased abnormal volume of sanguine humour (*Khilt Dam*). Unani treatment of this imtila consists of use of certain regimes as well as use of Moadillat Dam that are the drugs used for decreasing "*Imtela*". [4,5,6,7] Sharbat Unnab is one of such medicine described in classical unani texts.[7] The use of Moadillat dam is justifiable and mandates to be tested as such to assess the efficacy of employable treatment in primary hypertension.

METHODOLOGY

The present study was carried out at the Department of Moalajat, National Institute of Unani Medicine Bangalore. After soughting ethical clearance from Institutional Ethical Committee (IEC Reference No: NIUM/IEC/2015-16/003/Moal/03). Subjects were selected from OPD of NIUM on the basis of following inclusion and exclusion criteria and after getting written informed consent, patients were randomly allocated into test and control groups and all necessary investigations were done accordingly. This study stretched from April 2016 to February 2017.

Criteria for selection of Cases

Inclusion criteria:

- Known case of Primary hypertension with or without medication
- Patients with H/O hypertension (stage-1 hypertension, ranging between systolic pressure 140 mm Hg to 159 mm Hg and / or diastolic pressure 90 mm Hg to 99 mmHg) as per reference card from (JNC-7)
- Age between 35 to 50 years
- Both Gender (Male and Female)

Exclusion Criteria:

- Patients below 35 and above 50 years of age
- Pregnancy and Lactation
- Secondary Hypertension
- Diabetes Mellitus
- Other systemic and metabolic disorders
- History of Myocardial Infarction and Ischemic Heart Disease
- Bronchial Asthma and COPD

Investigations:

Following investigations were carried out with the aim to exclude the patients with pathological conditions mentioned under exclusion criteria and to assess the safety of the test drug. CBC; LFT (AST, ALT); KFT (Blood Urea, Serum Creatinine); RBS; Lipid Profile (TG, TGL, HDL, and LDL) and ECG.

SAMPLE SIZE OF ESTIMATION

Formula of calculating sample size is.[8,9]

$$n = [(Z_{\alpha/2} + Z_{\beta})^2 \times \{2(\sigma)^2\}] / (\mu 1 - \mu 2)^2$$

Where

n = sample size required,

μ1 = mean systolic BPin physical exercise group (132.3), [187]

μ2 = assumed mean systolic BP(126.1),

μ1-μ2 = clinically significant difference (6.2),

σ = standard deviation = 10.3

$Z_{\alpha/2}$: This depends on level of significance, for 5% this is 1.96

Z_{β}: This depends on power, for 80% this is 0.84

Based on the above formula, the sample size required group is calculated for single group was 43.Hence total sample size required is been set to 40 and it had been equally divided in two groups viz. test and control groups.

Procedure of Study

The study was designed as An open label randomized standard controlled study. Randomly allocated to test and control groups using computer generated tables with each group comprises of 20 patients. Test group was given *Sharbat e Unnab*- (A unani polyherbal medicine which is prepared by pharmacy of NIUM on standard procedures)[7] in the dose of 25 ml twice a day after meals for 6 weeks while control group was treated with Tab. Atenolol 25mg once (morning) a day orally after meals for same period.

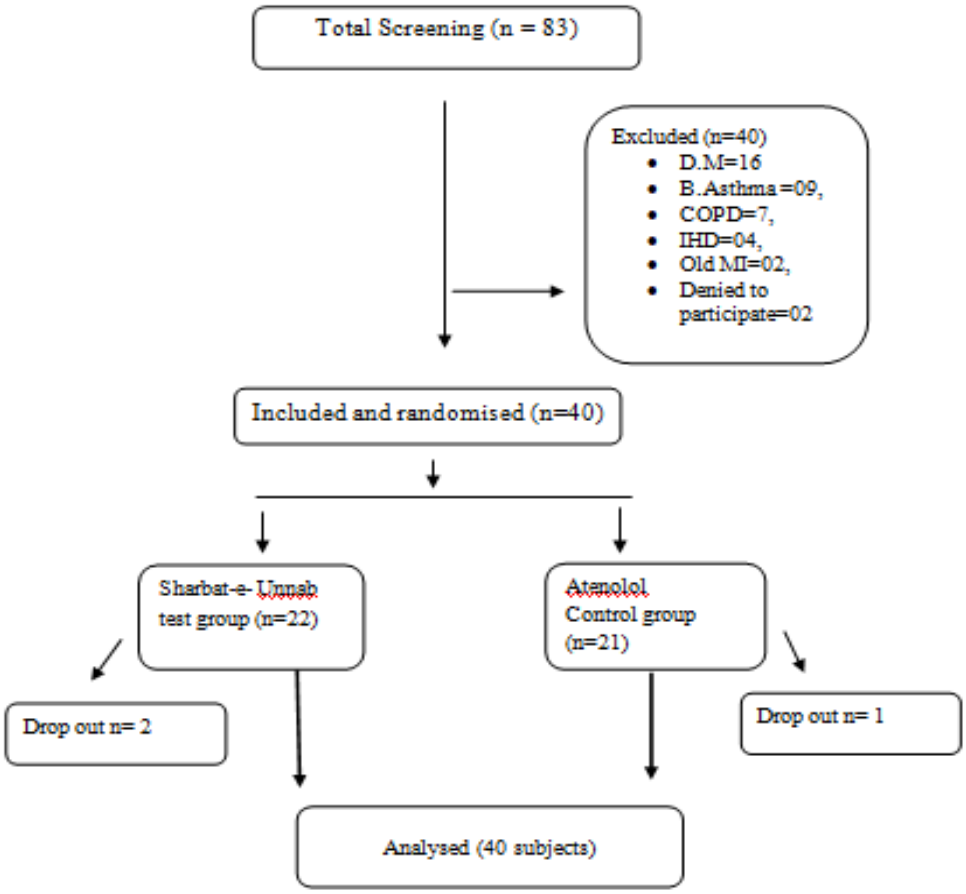

Figure 1

Test Drug

Sharbat-e-Unnab (Banuskha Hakeem Alvi-Khan) [7]

Composition of test Drug:

S. NO	Unani Name	Scientific Name	Quantity
1	Unnab	*Zizyphus vulgaris*	60 Pc.
2	Gul-e-Banafsha	*Viola odarata*	18 gm
3	Gul-e-Neelofar	*Nymphea nucifera*	18 gm
4	Gul-e-Gauzaban	*Borago officinalis*	18 gm
5	Gul-e-Surkh	*Rosa damascena*	18 gm
6	Arqu-e-Gulab	*Rosa damascena*	2.88 L
7	Arqu-e-Baid-e-Mushk	*Salix caprea*	2.88 L
8	Turanjbeen	*Alhagi pseudalhagi*	480 gm
9	Sheer-e-Khisht	*Fraxinus ornus*	480 gm
10	Qand safed	*Saccharum officinarum*	480 gm

Dietry Adviced and life style:

Patients of both groups were subjected to following life style modification recommendations according JNC-7.[10]

- Weight reduction - Maintain normal body weight (body mass index 18.5–24.9 kg/m2).
- DASH eating plan -Adopt a diet rich in fruits, vegetables, and lowfat dairy products with reduced content of saturated and total fat.
- Dietary sodium reduction - Reduce dietary sodium intake to <100 mmol per day (2.4 g sodium or 6 g sodium chloride)
- Aerobic physical activity - Regular aerobic physical activity (e.g., brisk walking) at least 30 minutes per day, most days of the week.
- Moderation of alcohol consumption- Men: limit to <2 drinks per day. Women and lighter weight persons: limit to <1 drink per day.
- Cessation of smoking

Assessment and Follow up during trial:

Duration of study was six weeks with follow up made at interval of 7 days At every visit blood pressure was recorded through mercury sphygmomanometer as per JNC-VII criteria as an objective parameter whereas subjective parameters i.e. (Headache, Dizziness, Palpitation, Fatigue, Epistaxis, Loss of libido) were observed in each follow up. Patients were kept under strict observation and advised to come every week in OPD for the assessment of disease till the completion of study.

Results

After completion of study data generated was assessed using appropriate Statistical software namely SPSS 18.0, and R environment ver.3.2.2[8,9,11,12] For this trial, descriptive and inferential statistical analysis has been carried out and Significance level is set at 5%. Student t-test (two tailed, independent) has been used to Inter group analysis on metric parameters. Leven1s test for homogeneity of variance has been performed to assess the homogeneity of variance. Student t-test (two tailed, dependent) has been used to find the significance on continuous scale within each group. Chi-square and Fisher Exact test has been used to find the significance

of study parameters on categorical scale between two groups and Fisher exact test is used since cell samples are very small. After analysis it was evident that there was significant reduction ($p<0.001$) in objective parameters of Systolic & Diastolic blood pressure (Table 1 &2) for both control and test group, and no group is found to be better than other ($p > 0.005$) after inter group analysis (Table 1 &2).

After analysis it was evident that both groups were beneficial in improving subjective parameters of Headache, Dizziness, Fatigue, Palpitation, ($p<0.001$) but during inter group analysis it was revealed that results in control group are highly significant than that of test group($p<0.001$) however there is not any improvement observed in subject tive parameter of Epistaxis, Loss of Libido (Table 3). Hematological (Hb%,TLC,DLC,ESR), Bio-Chemistry (RBS, Blood-Urea, S-Creatinine), and Urine Analysis. Parameters were found within the normal range, and all safety parameters were found statistically insignificant.

SBP (mm Hg)	**Group A**	**Group B**	**Total**	**P value**
Results				
• Baseline	147.40±5.95	149.50±6.15	148.45±6.07	0.279
• 1wk	141.40±7.29	137.40±8.78	139.40±8.22	0.125
• 2wk	136.90±9.28	133.40±6.96	135.15±8.29	0.185
• 3wk	139.80±9.62	134.10±7.96	136.95±9.18	0.048*
• 4wk	135.10±9.55	131.50±8.68	133.30±9.19	0.220
• 5wk	136.50±9.60	131.50±8.58	134.00±9.34	0.091+
• 6wk	133.70±9.95	128.40±7.96	131.05±9.29	0.071+
Difference from baseline				
• 1wk	6.000	12.100	9.050	-
• 2wk	10.500	16.100	13.300	-
• 3wk	7.600	15.400	11.500	-
• 4wk	12.300	18.000	15.150	-
• 5wk	10.900	18.000	14.450	-

• 6wk	13.700	21.100	17.400	-
P value from Baseline				
• 1wk	<0.001**	<0.001**	<0.001**	-
• 2wk	<0.001**	<0.001**	<0.001**	-
• 3wk	<0.001**	<0.001**	<0.001**	-
• 4wk	<0.001**	<0.001**	<0.001**	-
• 5wk	<0.001**	<0.001**	<0.001**	-
• 6wk	<0.001**	<0.001**	<0.001**	-

Table 1: Objective parameter.Comparison of SBP (mm Hg) in two groups of patients studied in study time points

DBP (mm Hg)	**Group A**	**Group B**	**Total**	**P value**
Results				
• Baseline	96.10±2.38	96.20±2.14	96.15±2.24	0.890
• 1wk	93.00±3.46	89.30±4.78	91.15±4.53	0.008**
• 2wk	90.30±5.00	85.00±5.17	87.65±5.69	0.002**
• 3wk	89.40±5.39	83.80±5.15	86.60±5.93	0.002**
• 4wk	86.00±5.43	84.50±5.31	85.25±5.35	0.382
• 5wk	87.20±5.44	83.80±6.86	85.50±6.35	0.091+
• 6wk	85.60±5.30	82.00±5.19	83.80±5.49	0.036*
Difference from baseline				
• 1wk	3.100	6.900	5.000	-
• 2wk	5.800	11.200	8.500	-
• 3wk	6.700	12.400	9.550	-
• 4wk	10.100	11.700	10.900	-
• 5wk	8.900	12.400	10.650	-

• 6wk	10.500	14.200	12.350	-
P value from Baseline				
• 1wk	<0.001**	<0.001**	<0.001**	-
• 2wk	<0.001**	<0.001**	<0.001**	-
• 3wk	<0.001**	<0.001**	<0.001**	-
• 4wk	<0.001**	<0.001**	<0.001**	-
• 5wk	<0.001**	<0.001**	<0.001**	-
• 6wk	<0.001**	<0.001**	<0.001**	-

Table 2: Objective parameter.Comparison of DBP (mm Hg) in two groups of patients studied in study time points

	Before	**After**	**Total**	**P value**
Group A (n=20)				
Headache	16(80%)	6(30%)	-50.0%	0.013*
Dizziness	7(35%)	2(10%)	-25.0%	0.044*
Fatigue	13(65%)	3(15%)	-50.0%	0.001**
Palpitation	7(35%)	3(15%)	-20.0%	0.044*
Epistaxis	0(0%)	0(0%)	0.0%	-
Loss of Libido	2(10%)	2(10%)	0.0%	-
Group B (n=20)				
Headache	13(65%)	8(40%)	-25.0%	0.138
Dizziness	7(35%)	4(20%)	-15.0%	0.183
Fatigue	10(50%)	7(35%)	-15.0%	0.235
Palpitation	10(50%)	6(30%)	-20.0%	0.159
Epistaxis	1(5%)	1(5%)	0.0%	-
Loss of Libido	1(5%)	1(5%)	0.0%	-

Table 3: subjective parameter, distribution in two groups of patients studied (before /after assessment)

Discussion & Conclusion

Test drug reduced SBP and DBP due to *Moadil Dam, Mudirre Baul, Mufattite Sudad, Musakkin, Mufarreh wa Muqavvi Qalb* activity [13] which may be understood as diuretic, cardio protective and hypnotic activity. *Siddiqi HS et al* reported that the *Viola odorata* contains alkaloids, saponins, tannins, phenolics, coumarins and flavonoids responsible for antihypertensive activity due to its possible diuretic activity.[14] test drug ingredients (*Viola odorata, Rosa damascena*) possess analgesic, anti-inflammatory, sedative, antioxidant, and diuretic activities along with other beneficial effects such as antihypertensive, antipyretic, diaphoretic which is affirmed by finding of Feyzabadi (2014)[15] and Hajhashemi V et al (2010).[16] *Rosa damascene* and *Borago officinalis* also exhibit antioxidant, cardio protective activity due to presence of flavonoids, coumarins, sterols and tannins which possess vasodilator effect and claimed by Nayabi N et al (2017) and Gilani AH (2007).[17,18] All above said cumulative effects of test drug is found useful in reducing both SBP and DBP. The test drug is also found to be very effective in relieving subjective parameters of Dizziness, Fatigue, Palpitation these parameters are more attributed to unani medicinal concept of *Tadeel Dam, Tafreeh wa Taqwiyat e Qalb* and *Taskeen.*[4,5,6,7,13] Since *Sharbat Unnab* posses acitivities *Musakkin, Mufarreh-Wa-Muqavvi Qalb, Dafe Suda and Mudir* as described by Ibn Baitar[19], Ibn Hubal Baghdadi [20], Hakim Azam Khan [21], and Hakim Najmzmul Ghani[13] so it is believed to reduce stress, dizziness and work as antidepressants and anticonvulsants resulting in feeling of well being. [22,23] Moreover the test formulation ingredients exhibit antioxidant [24,25], immunomodulator[26] activity which prevents the formation of lactic acid thus reducing muscle fatigue.

The study found that the two drugs, control and the test were safe during the treatment period, concluded safe, effective, oriented and they may be used in the management of Hypertension. Test drug being found more effective in reducing subjective parameters may be used in patients of grade I primary hypertension for better patients care. However clinical trials based on large number sample size may be needed in future to explore further benefits of test drug.

Conflicts of Interest: None

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