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Research Article

A CLINICAL STUDY TO EVALUATE THE EFFICACY AND SAFETY OF *TUKHM-I KAHU* IN THE MANAGEMENT OF *ZAGHT AL-DAM QAWĪLĀZIMĪ* (ESSENTIAL HYPERTENSION)

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ABSTRACT

Aim of this study is to assess the efficacy of *Tukhm-ikahu* in *Zaght al-Dam Qawī Lāzimī* (Essential Hypertension) in comparison to Amlodipine (5 mg) tablet. Randomized, standard controlled clinical study was carried out. Patients of high blood pressure (n = 60) with age 35 to 55 years, with Stage-I Hypertension according to JNC 7 (Systolic BP 140-159 and Diastolic BP 90-99 mmHg) were randomized into study; *tukhm-ikahu* and control; amlodipine (5 mg) groups by block randomization method. Patients with SBP ≥ 160 mmHg and DBP ≥ 100 mmHg, Secondary Hypertension, Pregnant and Lactating women, Obese subjects – BMI > 30, Drug Addicts and Alcoholics were excluded from the study. Study group patients were given 5 gm of powder of *tukhm-ikahu* twice daily and those of control group Amlodipine 5 mg once daily. Duration of treatment was 6 weeks. Significant difference between *Tukhm-ikahu* and amlodipine was observed regarding improvement in headache (86.7% vs. 60%), P- value 0.039, vertigo (93.3% vs. 66.7%), P- value 0.021 and sleeplessness (96.67% vs. 73.3%), P- value 0.010. No significant difference was observed between the two regarding reduction in systolic and diastolic pressure at end point of study (P- value 0.675 and 0.552 respectively). No significant difference between the two was recorded regarding palpitation, laziness, anxiety, breathlessness, pulse rate, respiratory rate and temperature; P-value 0.080, 0.299, 0.748, 0.960, 0.858, 0.858 and 0.233 respectively. *Tukhm-ikahu* possesses efficiency and potency towards treating the high blood pressure and managing the symptoms linked with it.

Keywords: *Tukhm-ikahu*; Essential hypertension; Amlodipine; *Unani medicine*.

INTRODUCTION

Hypertension (*Zaghṭ al-Dam Qawī)* has emerged as the much commoner health trouble in developed as well as developing countries. About 7.5 million deaths have been estimated to be caused by hypertension according to WHO and 12.8% of all the deaths worldwide. This accounts for 57 million disabilities - adjusted life years.[1]

A number of surveys in last two decades have revealed the prevalence of hypertension in urban areas as 6.1% to 36.35% in men and 2%-39.4% in women, and in rural areas as 3%-36% in men and 5.8%-37.2% in women.[2] The prevalence of hypertension increases with age starting from around 15% -20% in early age to 75% -80% in individuals above 70 years of age.[3]

According to the WHO's World Health Report.[5] Hypertension is the foremost cause of death for ischemic heart diseases and cerebro-vascular stroke worldwide. In classical Unani literature, hypertension per se is not mentioned, but the symptoms simulating the clinical features of essential hypertension are described under the term *Imtilā'. Imtilā' baḥasb al-Aw'iya* (repletion in regard to vessels) is an increase in blood volume leading to increased vascular pressure. Unani physicians have described the symptoms of *Imtilā'* as heaviness of head and visual disturbances and complications as rupture of blood vessels in the form of epistaxis, haemoptysis and haemorrhage.[4-6]

MATERIAL AND METHODS

After getting approval from institutional ethics committee (Ethical Clearance Number is 38-18/ 2015-16/CRIUM/Hyd/IEC/01/M), a randomized, open label, standard controlled clinical study was conducted at our institution for a period of one and half year from December 2017. 60 patients of either sex between the age group 35 to 55 years with the complaint of increased blood pressure, headache, vertigo, palpitation, laziness, anxiety and insomnia were included in the study. Patients having SBP ≥ 160 mmHg and DBP ≥100 mmHg, Secondary Hypertension, pregnant and lactating women and/or having severe systemic illness, BMI > 30, Drug Addicts, Alcoholics, Patients not willing to give consent and Patients not willing to come for follow-up were excluded from the study.

A written informed consent was taken from the patients prior to enrollment into study. Patients were familiarized with the use of herbo-medicinal drug; *Tukhm-I kahu* and amlodipine (5 mg) and related adverse effects and outcomes. The patients were randomized into Group -A (study group; 30 in number) and Group-B (controlled group; 30 in number) using computer generated random table. Data were collected based on clinical interview, clinical observations and laboratory investigations.

Group-A patients were treated with *Tukhm-I kahu* and Group-B with amlodipine (5 mg). All the patients underwent laboratory investigations like CBC, LFT, KFT, Serum electrolytes, lipid profile, ECG and urine routine and microscopic in an attempt to

exclude secondary hypertension.

The crude drugs required for the preparation of *sufuf* of *Tukhm-I kahu* was purchased from local crude drug market of Hyderabad city, and was identified and authenticated as *Lactuca sativa* Linn. by Survey of medicinal plant unit (SMPU), CRIUM, Hyderabad. Voucher specimen number SMPU/CRI-Hyd 13551. (Figure 1)

Sufuf of *Tukhm-I kahu* was prepared in CRIUM pharmacy. The seeds of *kahu* were cleaned by removing unnecessary particles mixed with them and then placed in sun light for at least one day. After it has been ensured that the seeds were dry enough to be powdered, they were made powdered by the machine. The *sufuf* (powder) of *tukhm-ikahu* was packed in pouches and given to patients to consume it as 5 gm orally two times a day with water. Amlodipine (5 mg) was purchased as trade name Amlodipine 5 mg from pharmacy store of Hyderabad city. One tablet of 5 mg was given to patient to consume it orally once a day with sips of water. No concomitant therapy/treatment to either test group patients or control group patients was allowed during the course of study.

Duration of treatment was 42 days and patients were instructed to visit hospital every week. At every visit, the patients were asked about the progression or regression in their symptoms and subjected to thorough clinical examination to assess clinical findings.

Measurement of blood pressure

Auscultator method of BP measurement was used. Persons were allowed to be seated quietly for at least 15-30 minutes in a chair, with feet on the floor, and arm supported at heart level. Caffeine, smoking and exercise are to be avoided for at least 30 minutes prior to measurement. An appropriately sized cuff (cuff bladder encircling at least 80% of the arm) was used to ensure accuracy. At least two measurements were made, and the average was recorded. SBP is the point at which the first of two or more Korotkoff sounds is heard (onset of phase 1), and the disappearance of Korotkoff sound (onset of phase 5) is used to define DBP. The pre-treatment and post-treatment values of different parameters, after 8 weeks of the treatment, were statistically analyzed to assess the efficacy of the treatment.

The arbitrary scale for all the symptoms like headache, palpitation, vertigo, laziness, anxiety, breathlessness and insomnia was used as for feasibility of assessment and regression of symptom (Table 1).

Table 1: Arbitrary scale of various parameters

Arbitrary scale of various parameters	
Headache	
1-3	Mild Headache
4-6	Moderate Headache
7-9	Severe Headache
Vertigo	
1-3	Mild Headache
4-6	Moderate Headache
7-9	Severe Headache
Palpitation	
1-3	Mild Headache
4-6	Moderate Headache
7-9	Severe Headache
Laziness	
1-3	Mild Headache
4-6	Moderate Headache
7-9	Severe Headache
Anxiety	
1-3	Mild Headache
4-6	Moderate Headache
7-9	Severe Headache
Breathlessness	
1-3	Mild Headache
4-6	Moderate Headache
7-9	Severe Headache
Insomnia	
1-3	Mild Headache
4-6	Moderate Headache
7-9	Severe Headache

Statistical analysis

Descriptive and inferential statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5 % level of significance. The following assumptions on data were made,

Assumptions

1. Dependent variables should be normally distributed
2. Samples drawn from the population should be random, and Cases of the samples should be independent.[7-10]

Student-t test (two tailed, independent) has been used to find the significance of study parameters on continuous scale between two groups (Inter group analysis) on metric parameters. Leven`s test for homogeneity of variance has been performed to assess the homogeneity of variance. Mann Whitney U test (two tailed, independent) has been used to find the significance of study parameters on continuous scale but non-parametric between two groups (Inter group analysis) on metric parameters. Chi-square/ Fisher Exact test has been used to find the significance of study parameters on categorical scale between two or more groups,

Non-parametric setting for Qualitative data analysis. Fisher exact test used when cell samples are very small.

Significant figures

Suggestive significance (P value: $0.05 < P < 0.10$)

Moderately significant (P value: $0.01 < P \leq 0.05$)

Strongly significant (P value: $P \leq 0.01$)

RESULTS

In this study, majority of the patients belonged to 40-50 years of age, female predominance, *Damvi Mizaj* followed by *Balghami*, suffered from elevated blood pressure (not more than 160 systolic and 100 diastolic) for 1 month to 3 years.

There was statistically significant difference between Test (*Tukhm-iKahu*) and Control (Amlodipine) groups in relieving headache at the end of treatment (86.7% vs. 60%), P-value 0.039. Highly significant difference between Test and Control groups in reducing the symptom of vertigo at the end of treatment (93.3% vs. 66.7%); P- value 0.021 was observed. Statistically highly significant difference between Test and Control groups in reducing the symptom of sleeplessness at the end of treatment (96.67% vs. 73.3%), P- value 0.010 (Highly significant) was noted.

In test group, the mean systolic pressure (Mean ± SD) before treatment was 148.53 ± 1.17, which reduced to 124.53 ± 0.86 after treatment (P-value < 0.00001, Highly Significant). In control group, the mean systolic pressure (Mean ± SD) before treatment was 144.73 ± 0.82, which reduced to 125.20 ± 1.32 after treatment (P-value < 0.00001 highly significant). There is no statistically significant difference between study and control groups regarding improvement in systolic pressure at end point of study (60% vs. 53.3%), P- value 0.675 (which is > 0.05). In test group, the mean diastolic pressure (Mean ± SD) before treatment was 95.47 ± 0.82, which reduced to 80.90 ± 0.41 after treatment (P-value < 0.00001, strongly significant). In control group, the mean diastolic pressure (Mean ± SD) before treatment was 95.53 ± 1.00, which reduced to 81.47 ± 0.85 after treatment (P-value < 0.00001 strongly significant). There is no statistically significant difference between study and control groups regarding improvement in diastolic pressure at end point of study (96.67% vs. 73.3%), P- value 0.552 (which is > 0.05).

There was no statistically significant difference between test and control groups regarding effect on palpitation, laziness, anxiety, breathlessness, pulse rate, respiratory rate and temperature (P-value 0.080, 0.299, 0.748, 0.960, 0.858, 0.858 and 0.233 respectively).

There was no statistically significant difference between test and control groups in relation to all parameters of *Nabz*, i.e. *Miqdar-al-inbisat* (a) and (b), *Kayfiyat-al-kara', zamana-i-harkat, qiwam-i-ala, khala-o-imtila, malmas, nizam-o-adam nizam* and *wazan* (P-value 0.240, 1.000, 0.606, 1.000, 0.789, 0.267, 0.492, 1.000 and 1.000 respectively).

Comparison of various important parameters before and after treatment in study and control group has been illustrated in Table 2.

Reduction in the systolic and diastolic blood pressure as well as the symptoms related to hypertension by administration of *Tukhm-iKahu* is attributed to its important properties that have been proved beneficial and effective against hypertension, like *Mudirr-I Bawl*,[11-13] *Musakkin*,[14,15] *Munawwim*,[16] *Daaf'-iḥiddatṣafrā' waJosheKhoon*,[13-16] *Muqawī Qalb, Mufarrah Qalb*,[13,17] and Angiotensin converting enzyme inhibitor like property as evidenced by a clinical study carried out in Persia to find out the antihypertensive property of *Tukhm-iKahu* based on *in vitro* bio assay for ACE inhibition. The result suggested that *Tukhm-iKahu* exhibited the activity of inhibition of angiotensin converting enzyme.[18,19]

Table 2: Comparison of various parameters in two groups of patients studied

Parameters	Case			Control		
	BT	AT	P- Value	BT	AT	P- Value
SBP	148.53 ± 1.17	124.53 ± 0.86	< 0.00001	144.73 ± 0.82	125.20 ± 1.32	= 0.00001
DBP	95.47 ± 0.82	80.90 ± 0.41	< 0.00001	95.53 ± 1.00	81.47 ± 0.85	<0.00001
Headache	4.23 ± 0.65	0.13 ± 0.06	< 0.00001	4.40 ± 0.57	0.70 ± 0.20	< 0.00001
Vertigo	2.97 ± 0.53	0.07 ± 0.05	< 0.00001	3.00 ± 0.56	0.57 ± 0.16	= 0.00005
Palpitation	3.43 ± 0.59	0.07 ± 0.05	< 0.00001	2.90 ± 0.53	0.37 ± 0.12	< 0.00001
Laziness	3.67 ± 0.50	0.13 ± 0.08	< 0.00001	3.07 ± 0.52	0.53 ± 0.21	= 0.00004
Anxiety	4.33 ± 0.51	0.27 ± 0.13	< 0.0001	3.63 ± 0.43	0.43 ± 0.18	< 0.00001
Breathlessness	2.57 ± 0.53	0.20 ± 0.11	= 0.00005	1.40 ± 0.39	0.13 ± 0.06	= 0.00152
Sleeplessness	3.57 ± 0.47	0.03 ± 0.03	< 0.00001	2.03 ± 0.43	0.73 ± 0.25	= 0.0036

SBP: Systolic blood pressure, **DBP**: Diastolic blood pressure, **BT**: Before treatment, **AT**: After treatment

DISCUSSION

In a Meta-Analysis of 94 Randomized Placebo-Controlled Trials With 24 000 Participants conducted by Law *et al*., it was found that only 1 in 30 treated persons benefited by having headache prevented.

In Unani literature there is a indication of *tukhm-ikahu* in headache[69] and Our study shows the outstanding results of *tukhm-i-kahu* in preventing headache in 86.7% (26 out of 30) patients at the end point of the study, P < 0.00001, which is much better as compared to the finding postulated by Law *et. al*.[20]

In a long-term double-blind comparison of doxazosin and atenolol in patients with mild to moderate essential hypertension conducted by M.H. Frick *et. al*. it was concluded that palpitation was one amongst other side effects caused by doxazosin.[21]

The data is supported by Unani literature which suggests the *tukhm-ikahu* as useful drug in palpitation.[13]

Our study supports the benefit of *tukhm-i-kahu* in controlling the condition like palpitation, 93.3% patients (28 out of 30) got relieved, P-value < 0.00001 rather giving rise to the side effect like palpitation.

No further comparable data of laziness, anxiety, breathlessness, sleeplessness, *miqdar-al-inbisat, kayfiyat-e-kara', zamana-i-harkat, qiwam-i-ala, khala-o-imtila, malmas, nizam-o-adam nizam, wazan,* pulsus planus, temperature, respiratory rate and pulse rate was found to correlate our findings.

In an open label clinical study conducted by Sane R *et. al*. it was found that mean SBP was significantly lesser at the endpoint of study (141.86 ± 12.54 mm Hg) as compared to the mean SBP recorded on day 1 (155.48 ± 19.37 mm Hg).[22]

In a clinical study Verma RS *et. al*.; where the Unani coded drug UNIM-902 was given to assess the efficacy of the same in hypertensive patients, it was found that UNIM-902 significantly reduced systolic blood pressure from 150.48 mm of Hg ± 2.44 to 130.48 mm of Hg ± 13.29.[23]

Our study shows much potent results in favor of *tukhm-i-kahu* in reducing systolic blood pressure up to 124.53 ± 0.86 mmHg at the endpoint of study as compared to the findings given by Sane R *et.al*; where systolic pressure reduced to upto141.86 ± 12.54 mm Hg and Verma RS *et.al*; where systolic pressure reduced upto130.48 ± 13.29 mmHg.

In an open label clinical study conducted by Sane R *et. al*; it was found that the mean DBP at the endpoint of study (89.66 ± 6.8 mm Hg) was lesser than that on day 1 (90.34 ± 7.44mm Hg).[22]

In a clinical study Verma RS *et. al*; where the Unani coded drug UNIM-902 was given to assess the efficacy of the same in hypertensive patients, it was found that UNIM-902 significantly reduced diastolic blood pressure from 90.00 ± 1.35 mmHg to 77.14 ± 1.17 mmHg.[23]

Our study shows much potent results in favor of *tukhm-i-kahu* in reducing diastolic blood pressure up to 80.90 ± 0.41 mmHg at the endpoint of study as compared to the findings given by Sane R *et. al*. Where diastolic pressure reduced to up to 89.66 ± 6.8 mm Hg and analogous to the result given by Verma RS *et. al*; where diastolic pressure reduced up to 77.14 ± 1.17 mmHg.

CONCLUSION

With the significant positive results, it can be inferred that *Tukhm-iKahu* is more effective and potent Unani drug working against *Zaghṭ-al Dam Qawī Lāzimī* (Essential Hypertension), showing better results in increased systolic and diastolic blood pressure as well as the symptoms related to increased blood pressure. Moreover, *Tukhm-iKahu* was found safe, as no adverse effects were observed and the safety parameters, i.e., Haemogram, LFTs and KFTs remained within normal limits during the study. This experience in the study suggests that *Tukhm-iKahu* is the safe, potent and effective Unani antihypertensive drug. *Tukhm-iKahu* was also effective in improving quality of life in hypertensive patients. It can be used as a monotherapy or as an adjuvant with the other antihypertensive drug (in stage 2 and resistant hypertension). However, long-term study with larger sample size is required, for further assessing the anti-hypertensive activity of the test drug (*Tukhm-iKahu*).

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