



THERAPEUTIC EVALUATION OF *BĀDRANJBOYA* (*Melissa officinalis*) IN *FASĀDE TASHAHHUM FID DAM* (*Dyslipidaemia*) IN COMPARISON TO ATORVASTATIN

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Review Paper

Received: 02.08.2023

Revised: 20.08.2023

Accepted: 10.09.2023

ABSTRACT

Background and objectives: In the present era, Dyslipidaemia is one of the most common risk factor of cardiovascular diseases. This vulnerable disease is essentially an abnormal concentration of lipids or lipoproteins in blood. It leads to atherosclerosis, which is responsible for cardiovascular, cerebrovascular and peripheral vascular diseases. Nowadays, the treatment of Dyslipidaemia is lipid lowering agents with life style intervention, while lipid lowering agents are producing various side effects. Unani system of medicine (USM) provides comparatively safe drugs and needs to be validated on scientific parameters.

Study design: To evaluate the “Therapeutic evaluation of *Bādranjboya* (*Melissa officinalis*) in *Fasāde Tashahhum Fid Dam* (*Dyslipidaemia*) in Comparison to Atorvastatin” two drugs were selected, one was *Bādranjboya* (*Melissa officinalis*) which was taken as test drug and another was Atorvastatin which was taken as control drug.

Methods: The clinical trial study was conducted as an open labelled, randomized, comparative, pre and post analysis aimed to evaluate the efficacy of *Bādranjboya* in Dyslipidaemia. The scientifically chosen sample size was 40 which was divided in two groups; 20 patients were randomly allocated to test group and control group each. In test group, 25 g dried leaves of *Bādranjboya* was given in the form of *Joshanda* (decoction) empty stomach in the morning once a day orally and the control group received one tablet Atorvastatin 10 mg twice a day orally for 45 days. Treatment protocol was followed for every 15 days in both groups; subjective and objective parameters were recorded in each follow up i.e., 0, 15th, 30th and 45th day.

Results: The overall effect of the *Bādranjboya* was found quite encouraging in the treatment of Dyslipidaemia. Drastic improvement in subjective parameters like palpitation, breathlessness and joints pain was seen in patients placed in both test and control group with p value (<0.001*) is evident from statistical analysis, however, some parameters like cholesterol, triglyceride, HDL and LDL with p value >0.05 did not show significant improvement in either groups.

Conclusion: This study reveals that both the drugs are equally effective. But *Bādranjboya* did not show any toxicity and adverse effect on patients in test group.

No. of Pages: 11

References: 30

Keywords: Dyslipidaemia; *Melissa officinalis*; *Bādranj.boya*; *Quwate Tabaiya*; *obesity*.

INTRODUCTION

Dyslipidaemia is a metabolic disorder of lipid and lipoproteins, as well as increased concentration of

total cholesterol, triglycerides, LDL cholesterol and decreased concentration of HDL cholesterol.¹ Disturbance in normal levels of lipids in the human

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body causes dyspnoea, polydipsia, giddiness, tiredness and unconsciousness.¹⁰⁴ In other words, metabolic diseases are one of the major challenges of the twenty-first century and they are closely tied to the changes in human lifestyle. The prognosis for metabolic disorders is multi-organ system failure and damage to vital organs. They are considered as slowly progressing and silent killers. The Dyslipidaemia is not only a single morbid condition but also make a derangement at the vascular changes and visceral level including derangement in carbohydrate, protein, fat even of minerals and water metabolism. Dyslipidaemia is considered as an iceberg of many metabolic disorders including metabolic syndrome, as a result, Non-alcoholic Fatty liver disease (NAFLD), diabetes mellitus, hypertension and CAD may emerge as a co-morbid factor.^{3,4} Prevalence of Dyslipidaemia varies according to the age, sex, race, geographical conditions and association with other diseases. People with age group between 30 to 40 years tends to have a significant prevalence, but after the age of 60, it increases markedly. Male are more prone to Dyslipidaemia than female; rural population has less prevalence than urban in India. The prevalence with other disease association is high i.e. *Siman Mufrit* (obesity), *Ziabetus* (diabetes), *Amraz-e-kulliya* (renal disease) and *Amraz-e-Kabid* (liver disease) etc.^{20, 21, 22, 23}

Siman Mufrit is another well-known disease since Greco Arab period and was first described by *Buqrat* (Hippocrates), later on other Unani physicians like *Jalinoos*,⁵ *Ibn Sn*,⁶ *Zakariya Razi*,⁷ *Rabban Tabri*⁸ etc, mentioned *Siman Mufrit* in their treatises. They defined etiological factors, symptoms, signs and complications of *Siman Mufrit* expansively. *Ibn Sn* especially pointed out that obese people are more prone to develop cardiac and cerebral complications like stroke, syncope, coma, palpitation, breathlessness, concealed haemorrhage and sudden death.^{6,9} As per the Unani philosophy, *Siman Mufrit* develops due to increased *Rutūbat* (moisture/wetness) and *Burdāt* (coldness) leading to imbalance of humours in the body and increases tendency of accumulation of *Akhlt-i-Fasida* (morbid humours) particularly *Mdda-i-Balghamiyya* (morbid phlegm). It is an established fact that hyperlipidaemia is associated with *Siman Mufrit* and atherosclerosis.⁶ Currently, available anti-hyperlipidaemic drugs or lipid lowering agents like statins (Atorvastatin, simvastatin, pravastatin and lovastatin etc.) are modestly effective in some subjects but administration of these pharmacological agents

produces several life-threatening adverse effects or side effects along with antilipidaemic activity.^{15,16} The side effects include hepatotoxicity, myopathy, renal dysfunction, dyspepsia, bloating, constipation, flushing, pruritus of the face and upper trunk, skin rashes, acanthosis nigricans, urticaria, hair loss, myalgias, fatigue, headache, impotence and anaemia. Consequently, there is a pressing need for novel therapeutic agents for better management to prevent these adverse effect of conventional therapy. As a result, there is a growing need to develop effective, safe and well-tolerated drugs to reduce atherosclerotic complications in Dyslipidaemia.¹⁷ In USM, there is concept of *Qwwat-i-Ṭabī'iyya* (Natural faculty), which serves the functions of nutrition, growth and reproduction in the body, and expel out *Fuzlat* (waste products) from the body. Liver is the chief organ of *Qwwat-i-Ṭabī'iyya*. *Qwwat-i-Ghidh'iyya* (Nutritive faculty) is one of the types of *Qwwat-i-Ṭabī'iyya* which is responsible for ingestion, digestion, absorption, transformation and assimilation of *Ghidh'* (food) and excretion of waste products. *Qawwat-i-Ghidh'iyya* is served by four kinds of sub-ordinative faculties. *Hadm Kabidī* (hepatic digestion/Chyle formation) is one of the parts of *Qawwat Hadm* (faculty of digestion) i.e. type of subordinative faculty of *Qwwat Ghazia*. *Hadm Kabidī* is aimed at benefitting the liver cells themselves as well as the entire body.¹⁸

Dyslipidaemia, as such has not been described in Unani literature but it may be interpreted with the abnormalities of entire mechanism of *Hadm Kabidī*. There are three conditions which affects *Hadm Kabidī* namely (1) *Burdāt Jigar* (excessive coldness in liver), it causes hindrance in digestion of *Ghidh'*(food), which reaches liver from intestine (2) obstruction by viscous matter or any inflammation which causes partial digestion of nutrients (3) the poor nutrition resulting from alteration in *Kammiyat* and *Kaifiyat* (quantity or quality) of food.¹⁹ Despite remarkable advancement in Dyslipidaemia therapy, it continues to raise significant economic and personal burden to patient. In USM, Unani physicians have recommended a number of single and compound drugs, which are *Har* (hot) in *Mizaj* (temperament) to modulate liver functions and also scientifically reported to have lipid lowering effects, such as *Badranjboya* (*Melissa officinalis*), *Guggul* (*Commiphora mukul*), and *Lehsun* (*Allium sativum*) and *Piyaz* (*Allium cepa*),²⁴ *Haldi* (*Crucuma longa*), *Lilly* of the Kashmir (*Convallaria majalis*) *Filfil siyah* (*Piper nigrum*), etc.²⁵ These are being used in the management of *Amr Sawdwiyya* (melancholic diseases) and *Amr Balghamiyya*

(phlegmatic diseases) since antiquity. Since, it is widely accepted by Unani scholars that *Ghayr* [ab] *Burūdat* (aberrant coldness) and *Yub* [sat] *Mizaj* (aberrant dry temperament) are responsible for the development of *Dyslipidaemia*, *Amr* [Sawd] *wiyya* and *Balghamiyya*. Therefore, if any drug which possess *Munzij* (concoctive) and *Mushil* (purgative) properties of *Balgham* (phlegm) and *Sawd* (black bile), eventually reduces the *Salabat* (hardness) of specific organ, particularly of *Sharaeen* (arteries) The same hypothesis may be applied in case of *Tasaddud Shah* [mī] *Kilsī* (atherosclerosis) in *Dyslipidaemia*. Some studies carried out in recent past also demonstrated very promising result and explored the potentiality of Unani drugs to be used as effective hypolipidaemic agent. Researchers have shown interest to investigate drugs that can prove better than currently available conventional drugs.^{6,26,14,27} The USM offers tripartite approach of treatment i.e. '*Ilaj bi'l Ghidha*' (dietotherapy), '*Ilaj bi'l Tadbir* (regimenal therapy) and '*Ilaj bi'l Dawa*' (Pharmacotherapy),²⁸ which are the mainstay of treatment of hyperlipidaemia. Fundamentally, dietotherapy is very important. This purpose can be achieved by the use of *Qalilul Taghaziya Kasirul Kammiyat* (low calorie) diet, *Riyazat-i-Kasira* (exercise), *Hammam*²⁹ and *Tareeq* (sweating) in order to burn extra calories deposited in the body and to eliminate *Mawad-i-Fasida* (morbid matter) and correction of *Sue Mizaj Barid* (aberrant temperament). Furthermore, Unani physicians recommended *Ilaj bid Dawa* for this purpose. Therefore, the drugs possessing action like *Munzij*, *Mushil*, *Mufatteh* (deobstruent), *Jaali* (detergent) and *Muhallil* (resolving) properties may be beneficial for the treatment of *Dyslipidaemia*. As per Unani philosophy, *Salabat-i-Nabz* (hardness of pulse) develops due to production of temperament of aberrant nature particularly due to *Ghalbae Balgham wa Sawd*.²⁶

As a matter of fact, any drug which can ameliorate the derangement of temperament and helps to evacuate *Fasid Maddae Balghamiyya wa Sawdāwiyya* will definitely be effective in the management of *Dyslipidaemia*.

Although, above mentioned drug is being used by Unani physicians, from time immemorial. But the efficacy of these drugs have not been scientifically evaluated so far. Therefore, an open labelled, randomized, comparative, pre and post analysis study was done to evaluate the efficacy of *Bādranjboya* in the management of *Dyslipidaemia* on scientific

parameters.

The present clinical study was conducted at Regional Research Institute of Unani Medicine, Srinagar, Jammu and Kashmir, India. Before commencing study, the protocol was put forth for ethical consideration. After obtaining the clearance from Institutional Ethical Committee (IEC), the study was conducted on 40 diagnosed patients of *Dyslipidaemia*.

The patients were randomly allocated in two groups, i.e test group (group A) and standard control group (group B) comprising 20 patients in each group. Group A was given test drug while group B was treated with standard control drug for the period of 45 days. All the patients were kept under observation and advice strict dietary control and moderate exercise. For the assessment of efficacy of test drug, joint pain, palpitation, breathlessness, xanthelesma, were used as a subjective parameters and serum cholesterol, serum triglyceride, LDL, HDL were used as an objective parameter. The clinical improvement was recorded fortnightly on the Case Report Form (CRF) especially designed for the study.

Apart from efficacy parameters that are related for assessment of improvement in *Dyslipidaemia* such as haemogram, ESR, blood sugar fasting and PP, LFT, KFT, urine, TSH and USG examination and ECG were also carried out in all patients in order to determine toxic effects of the test formulation. The overall effect of the *Bādranjboya* was found quite encouraging in the treatment of *Dyslipidaemia*. Significant improvement in subjective parameters like palpitation, breathlessness and joints pain was seen in patients placed in both test and control group with p value is (<0.001*) is evident from statistical analysis, however, some parameters like; cholesterol, triglyceride, HDL and LDL with p value is (>0.05) did not show significant improvement in either groups. Interestingly, it is observed that in test group, safety parameters remained under normal range after the administration of *Bādranjboya* which rules out any possible side effects or toxicity of the drug. The compliance to the treatment was found good. These results conclude that the test drug is quite safe in the treatment of *Dyslipidaemia*.

MATERIAL AND METHODS

Trial design

The present clinical study has been conducted with the intention to evaluate the *Dyslipidaemia* effect and safety profile of *Bādranjboya* and atorvastatin, whose efficacy and safety was evaluated through an open

labelled, randomized, comparative, pre and post analysis trial on 40 patients at the Department of Moalajat in Regional Research Institute of Unani Medicine (RRIUM), University of Kashmir, Srinagar, Jammu and Kashmir, India. Both the test and control groups underwent therapy for 45 days. The study was registered with Clinical Trial Registry-India (CTRI) (vide Registration No. REF/2020/07/035404 dated 25.07.2020). The study was conducted according to the protocol approved by the Institutional Ethical Committee (IEC) (Ref. No. RRIUM/KU/2018-19/Tech/IEC dated 29.03.2019). Apart from clinical

examination with detailed history of the disease and necessary haematological, biochemical investigations, clinical symptoms, history and investigations were recorded on the prescribed CRF designed for the study with specific inclusion criterion. After the ethical clearance, clinical study was started by enrolling eligible patients into test and control groups by randomisation with the help of computer generated method from the OPD of Regional Research Institute of Unani Medicine (RRIUM) Hospital. This study was stretched between September 2019 to December 2020. A detailed study

INCLUSION CRITERIA	EXCLUSION CRITERIA
<ul style="list-style-type: none"> • Diagnosed patients of Dyslipidaemia. • Patients irrespective of gender • Total Cholesterol \geq 240mg /dl • Triglycerides < 499 mg / dl (High) • LDL 160-189 mg / dl • HDL < 40 mg / dl in men and <50 in woman • Age group between 20-50 years of age • Patients able to participate in the study who follow the protocol • Known cases of DM type -II with Dyslipidaemia • Fasting blood sugar (FBS) \geq 126 mg/dl - < 150mg/dl • Post Prandial blood sugar (PPBS) \geq 140 mg/dl - < 250mg/dl³ • Normotensives (< 130 – 80 mm of Hg) • Patients who follow the protocol 	<ul style="list-style-type: none"> • Known cases of Dyslipidaemia, with disease history of > 3 years • Total Cholesterol \leq 240 mg / dl • Triglycerides > 499 mg / dl (High) • LDL > 189 mg / dl • HDL > 70 mg / dl • Known cases of Type 2 Diabetes Mellitus. • Known cases of hypertension, diabetes mellitus type I, hypothyroidism • Patients on corticosteroids, and contraceptives. • History of cardiovascular, renal, liver diseases, AIDS and T.B. • History of alcoholism • Pregnant and lactating mothers • Age < 20 and > 50 years of age

Procedure

Case detection and subject selection

Patients diagnosed with Dyslipidaemia, irrespective of gender having total cholesterol \geq 240mg /dl, triglycerides < 499 mg / dl (High), LDL 160-189 mg / dl, HDL < 40 mg / dl in men and <50 in woman were selected for the study. Patients with 20-50 years of age group and non-pregnant (in case of females), were screened for the study. Selection of the patients was done on the basis of 3 subjective parameters, i.e. palpitation, breathlessness, joint pain and two objective parameters i.e. ECG and Blood investigations. During selection procedure complete history (Present, past, family, personal and socio-economic history) was taken. General physical and systemic examinations was also done. For socioeconomic strata, Kuppuswami socioeconomic

scale (2007) was used. It has been attached with the Case Report Form in annexure. Vitals were checked and recorded in the medical case files. The laboratory data was collected from the hospital and patient case files. The inclusion and exclusion screening criteria used for this study are in table.1. Patients fulfilling all the criteria were made aware of the study and informed consent was taken from those who were willing to participate. Patients enrolled in the study were given the informed sheet containing details regarding the nature of the study, the drug to be used, method of treatment etc. They were given enough time to go through the contents of informed consent sheet. They were given the opportunity to ask any question, and if they agreed to participate in the study, were asked to sign the informed consent form. Subsequently, the patients were randomized into the test and control groups.

Randomization

In accordance with the scientifically established sample size of 40 patients, 20 patients from each of the two groups were randomly assigned to the test group and the control group using computer generated data. On an empty stomach, the test group was given 25 g of dried Bādranjboya leaves in the form of a decoction, once daily, while the control group was given one tablet of atorvastatin 10 mg twice daily orally for 45 days.

Investigation

Various parameters like lipid profile, total cholesterol, triglycerides, low density lipoprotein (LDL) and high density lipoprotein (HDL) were determined. Above mentioned investigations were done in each and every patient before starting the trial and as well as after completing the trial. To exclude the patients other than Dyslipidaemia due to some pathological condition, investigations like Haemogram (Hb %, TLC, DLC), ESR, blood sugar fasting, blood sugar post prandial, liver function test (SGOT, SGPT), serum bilirubin, alkaline phosphatase, KFT (blood urea, serum creatinine), urine routine and microscopic, ECG, TSH and USG were done to rule out alcoholic fatty liver, cirrhosis of liver and renal calculi. All these biochemical parameters were measured according to routinely employed procedures in pathological laboratories.

Treatment and drug administration

Criteria for selection of drugs

Single drug Bādranjboya (*Melissa officinalis*) was selected for the present study due to its pharmacological properties like *Mufarre Qalb* (exhilarant), *Muqawwi Qalb* (cardiotonic), *Mufatti* (deobstruent), *Muqawwi-i-Dimāgh* (brain tonic) and *Muqawwi-i-Mi'da* (stomachic) properties.

Dosage and mode of administration of test drug

The *Joshānda* (decoction) of the leaves of test drug Bādranjboya was given to the test group patients. Drug was provided by the Unani pharmacy of Regional Research Institute of Unani Medicine (RRIUM) Srinagar. Before dispensing, the test drug was properly identified from Botany Department RRIUM, Srinagar, to determine its originality. The patient was given 25 g of dried leaves in zip packed polythene bags and was guided to soak it in 200 ml of water throughout night and boil in the morning till the water remained half of its quantity and this decoction was then advised to be taken in an empty stomach orally for the period of 45 days with a follow up for every 15 day.

Administration of control drug

The control drug atorvastatin 10 mg (prepared by certified company LUPIN LTD Bhasmey Block, Duga ilaka, East Sikkim – 737132, INDIA given dose was) was advised to take one tablet once a day, after meal for the period of 45 days. Apart from the above-mentioned treatment, no other intervention was provided to the patients.

Follow up monitoring and investigations

Duration of 45 days study, was divided into 4 visits of follow up including baseline. i.e. 0, 15th, 30th and 45th days. At every visit, patients were enquired about the progression or regression in their symptoms and were subjected to examination for the assessment of clinical findings.

Safety assessment

The safety of the treatment was assessed at every visit of follow up by clinical evaluations, vitals (pulse, BP, temperature) and biochemical assessment like Hb%, TLC, DLC, ESR, FBS and PPBS, KFT, LFT, TSH, urine (R/M), ECG and alkaline phosphatase.

Criteria for safety evaluation:

Any adverse event or reaction appearing during the study either in test or control group was recorded.

Data collection

Collection of data was made through clinical history, physical examination and laboratory investigations which were recorded in the CRF. Data was collected at Regional Research Institute of Unani Medicine (RRIUM), University of Kashmir, Srinagar, Jammu and Kashmir, India. A proforma was made to collect the data. Data was cross-checked to ensure error proofing.

Assessment of efficacy

The assessment of efficacy in the test and control groups was based on subjective and objective parameters. Subjective parameters include palpitation, breathlessness and joint pain. Objective parameters are serum cholesterol, triglycerides, HDL and LDL cholesterol. The subjective parameters were assessed at every visit, while objective parameters before and after the completion of trial. A Visual Analogue scale was adopted for the assessment of joint pain in both test and control group. However, for palpitation and breathlessness parameters, we adopted arbitrarily scale given below.

Arbitrarily scale

For palpitation and breathlessness are enlisted in

Table 2: Arbitrarily scale for palpitation and breathlessness, scores and its interpretation.

Palpitation and breathlessness	Scores	Interpretation
Normal	0	no symptom
Mild	1+	mild symptoms but not enough need of remedial therapy to continue daily activities
Moderate	2+	moderate symptoms which interfere in daily activities and require medical attention
Severe	3+	severe symptoms which don't allow to carryout daily activities in spite of taking drug

For the assessment of pain, we used VAS index (10 points Likert's Scale).

Withdrawal criteria

Patients who failed to follow the protocol, any adverse drug reaction and poor compliance to the treatment.

Statistical analysis

For statistical analysis, recorded data was compiled and entered in a spread sheet and then exported to data editor of SPSS version 20.0 and Graph pad prism software. The continuous variables were expressed as mean \pm standard deviation and categorical variables were expressed in terms of frequency and percentage. Student's independent t- test was employed for inter-group analysis of data and for intra-group analysis paired t- test was applied. Chi-square test was employed for comparison of categorical variables. A p-value of less than 0.05 was considered statistically significant.

RESULTS

All baseline characteristics are summarized in 01. Most of the parameters are within the acceptable range. Likewise, the blood biochemical parameters and serum levels of creatinine reflecting normalcy of kidney functioning and those of alanine transaminase (ALT/SGPT) and aspartate aminotransferase (AST/SGOT), bilirubin (suggestive of normal liver function) of the test group before and after treatment. These values were found to be within their respective normal ranges. Comparison between the baseline hematological parameters, liver-kidney function tests and their corresponding values showed no significant change, suggesting that there was no undesirable effect due to the treatment in both control and test group. From these observations, it is deducible that the administered treatment did not exert any observable adverse side effects. This also depicts that there is an insignificant difference before and after the treatment within the test group and control group with respect to safety parameters.

Table 3: Comparison of Objective parameters before and after the treatment with in Test group.

Objective parameters		Mean	N	Std. Deviation	P value
Sr. Chol (mg/dl)	BT	174.9500	20	48.63016	0.650
	AT	182.3000	20	55.33829	
Sr. TGL (mg/dl)	BT	261.0750	20	198.38891	0.378
	AT	223.9100	20	81.75849	
Sr. HDL (mg/dl)	BT	71.3050	20	89.13655	0.331
	AT	51.5200	20	7.99701	
Sr. LDL (mg/dl)	BT	144.7400	20	29.39453	0.391
	AT	137.5050	20	34.74641	

Table 4: Shows that there is an insignificant difference before and after the treatment with respect to Objective parameters with in the Test group since p value <0.001.

Objective parameters		Mean	N	Std. Deviation	P value
Sr. Chol (mg/dl)	BT	179.5000	20	38.78755	0.162
	AT	162.5500	20	52.70022	
Sr. TGL (mg/dl)	BT	256.7700	20	116.41720	0.090
	AT	214.9650	20	87.60699	
Sr. HDL (mg/dl)	BT	53.6450	20	10.08472	0.695
	AT	52.6250	20	10.17566	
Sr. LDL (mg/dl)	BT	142.6350	20	29.08594	0.002
	AT	106.9200	20	37.76355	

Table 5: Shows descriptive statistics of Objective parameters for Test and Control group at base line and last follow up. We observe that both the treatments are almost equally effective because there is no significant difference between the two groups as p value is >0.05.

Objective parameters	Group	N	Mean	Std. Deviation	P value
Sr.Chol BT	Test Group	20	174.95	48.63	0.745
	Control Group	20	179.50	38.79	
Sr.Chol AT	Test Group	20	182.30	55.34	0.255
	Control Group	20	162.55	52.70	
Sr. T.G BT	Test Group	20	261.08	198.39	0.934
	Control Group	20	256.77	116.42	
Sr. TG.AT	Test Group	20	223.91	81.76	0.74
	Control Group	20	214.97	87.61	
Sr. HDL BT	Test Group	20	51.11	9.31	0.413
	Control Group	20	53.65	10.08	
Sr. HDL AT	Test Group	20	51.52	8.00	0.705
	Control Group	20	52.63	10.18	
Sr. LDL BT	Test Group	20	144.74	29.39	0.821
	Control Group	20	142.64	29.09	
Sr. LDL AT	Test Group	20	137.51	34.75	0.011
	Control Group	20	106.92	37.76	
	Control Group	20	106.92	37.76	

DISCUSSION

The present study entitled as “Therapeutic evaluation of *Bādranjboya (Melissa officinalis)* in *Fasāde Tashahhum Fid Dam* (Dyslipidaemia) in Comparison to Atorvastatin” has been carried out at the Department of *Moalajat* in Regional Research Institute

of Unani Medicine, (RRIUM) University of Kashmir, Srinagar.

Before starting study, the protocol was submitted for ethical clearance. Accordingly, Institutional Ethical Committee had approved the protocol. Subjects were

selected from OPD of RRIUM Hospital, after clinical examination with detail history of the disease and necessary haematological, biochemical investigations, Clinical symptoms, history and investigations were recorded on the prescribed Case Record Form (CRF) designed for the study with specific inclusion criterion. The clinical study was started by enrolling eligible patients in test and control groups by randomisation with the help of computer generated method.

The clinical study was conducted to evaluate the efficacy of *Bādranjboya* (*Melissa officinalis*) in Dyslipidaemia. This was an open labelled, randomized, Comparative, pre and post clinical study, with 40 patients (20 in test group and 20 in control group) belonging to 20-50 years of age, irrespective of gender. out of 47 patients 40 completed, 45 days protocol, 7 patients (3 in test and 4 in control) were dropped out. The test group was treated with *Joshandae* (Decoction) *Bādranjboya* (25 gm of dried leaves) empty stomach in the morning once a day orally, whereas control group was managed, with one tablet of Atorvastatin 10 mg once a day orally for 45 days. Subjective parameter (joint pain) were assessed based on Visual Analogue Scale (VAS) on every 15th day of follow up and Objective parameters were carried out before and after treatment in each group. This study stretched from July 2019 to December 2020.

Palpitation and breathlessness was assessed on the severity of disease and extent of involvement were assessed by using (Arbitrarily Scale) graded as severe, moderate, mild and absent/normal and was coded as 3+, 2+, 1+ and 0 respectively.

Present result on palpitation and breathlessness reveals that the both the treatments are almost equally effective because there is no significant difference between the two groups as p value is >0.05 at 45th day on all subjective parameters.

In control group there is a significant difference before and after the treatment with respect to subjective parameters within the control group since p value is <0.001 at 45th day with respect to control day 0, and also significant difference (p value <0.001) at 45th day with respect to control day 15.

In test group there is a significant difference before and after the treatment with respect to subjective parameters within the test group since (p value

<0.001) at 45th day with respect to test day 0, and also significant difference (p value <0.001) at 45th day with respect to test day 15.

Objective parameters were as follows:

Serum Cholesterol was assessed before and after treatment in both test and control group. The Mean \pm SD score of test group was (174.95 \pm 48.63) on base line and (182.30 \pm 55.34) on 45th day. In control group Mean \pm SD score was (179.50 \pm 38.79) on baseline and (162.55 \pm 52.70) on 45th day respectively (Table No. 11). We analysed intra group data comparison by Paired-t test for inter group comparison we applied student independent t-test. We observed that Serum Cholesterol level in both the groups at base line and found that they were comparable with a p-value of 0.745. However, we also observed that there was an insignificant difference between the two groups with respect to the effect on Cholesterol levels after the treatment as the p-value was >0.05 .

Serum Triglyceride was assessed before and after treatment in both test and control group. The Mean \pm SD score of test group was (261.08 \pm 198.39) on base line and (223.91 \pm 81.76) on 45th day. In control group Mean \pm SD score was (256.77 \pm 116.42) on baseline and (214.97 \pm 87.61) on 45th day respectively (Table No. 11). We analysed intra group data comparison by Paired-t test for inter group comparison we applied student independent t-test. We observed that Serum Triglyceride level in both the groups at base line and found that they were comparable with a p-value of 0.934. However, we also observed that there was an insignificant difference between the two groups with respect to the effect on Triglyceride levels after the treatment as the p-value was >0.05 .

HDL cholesterol was assessed before and after treatment in both test and control group. The Mean \pm SD score of test group was (51.11 \pm 9.31) on base line and (51.52 \pm 8.00) on 45th day. In control group Mean \pm SD score was (53.65 \pm 10.08) on baseline and (52.63 \pm 10.18) on 45th day respectively (Table No. 11). We analysed intra group data comparison by Paired-t test for inter group comparison we applied student independent t-test. We observed that HDL. Cholesterol level in both the groups at base line and found that they were comparable with a p-value of 0.413. However, we also observed that there was an insignificant difference between the two groups with respect to the effect on HDL. cholesterol levels after the treatment as the p-value was >0.05 .

LDL cholesterol was assessed before and after treatment in both test and control group. The Mean \pm SD score of test group was (144.74 \pm 29.39) on base line and (137.51 \pm 34.75) on 45th day. In control group Mean \pm SD score was (142.64 \pm 29.09) on baseline and (106.92 \pm 37.76) on 45th day respectively (Table No. 11). We analysed intra group data comparison by Paired-t test for inter group comparison we applied student independent t-test. We observed that LDL cholesterol level in both the groups at base line and found that they were comparable with a p-value of 0.821. However, we also observed that there was an insignificant difference between the two groups with respect to the effect on LDL cholesterol levels after the treatment as the p-value was >0.05 . We observed that both the treatments are almost equally effective because there is no significant difference between the two groups as p value is >0.05 at 45th day.

The exact mechanism of action of *Melissa officinalis* needs to be evaluated, however, the chemical constituents like flavonoids (luteolin, quercitrin, rhamnocitrin) monoterpene aldehyde, triterpenes (ursolic and oleanolic acids), polyphenolic compounds (rosmarinic acid, caffeic, and protocatechuic acid), monoterpenoid aldehydes, sesquiterpenes, tannins and monoterpene glycosides present in *Melissa officinalis* could possibly be correlated with the therapeutic effect as they play a key role in heart disease prevention by their antioxidant activity.^{164,165}

In this study *Bādranjboya* has effect on most of the parameters which is evident from statistical analysis, since the p-value is $<0.001^*$ for almost all the parameters including palpitation, breathlessness and joint pain, however, there was an insignificant difference before and after the treatment with respect to some parameters like Cholesterol, Triglyceride and HDL in both test and control group except for LDL showed some improvement in control group. In case of safety parameters, we observed they remained within normal range before and after the treatment which indicates that both the treatments are safe to patients. However, haemoglobin level among patients in test group improved which is evident from the statistical analysis as the p value is <0.001

CONCLUSION

The overall effect of the *Bādranjboya* was found quite encouraging in the treatment of Dyslipidaemia. Drastic improvement in subjective parameters like

palpitation, breathlessness and joints pain was seen in patients placed in both test and control group as the same is evident from statistical analysis, however, some parameters like; cholesterol, triglyceride, HDL and LDL did not show significant improvement in either groups. In conclusion, we observed that both the treatments are almost equally effective on parameters like palpitation, breathlessness, joint pain and equally not effective on cholesterol, triglyceride, HDL and LDL. However, for test group patients there was a significant improvement in haemoglobin level of patients since the p-value corresponding to haemoglobin level (before and after) is $<0.001^*$. Interestingly, we observed that in test group, safety parameters remained under normal range after the administration of *Bādranjboya* which rules out any possible side effects or toxicity of the drug. The compliance to the treatment was found good. These results conclude that the test drug is quite safe in the treatment of Dyslipidaemia. However, long term study on larger sample size is required for further exploration of the effects of *Bādranjboya*, and also to determine their mechanism of action with modified methodology.

Authors contribution

The corresponding author attest that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted. All data were generated in-house, and no paper mill was used. All authors agree to be accountable for all aspects of work ensuring integrity and accuracy.

Funding

This study in Regional Research Institute of Unani Medicine, Srinagar, Jammu and Kashmir, India, got funding from Central Council for Research in Unani Medicine, Ministry of AYUSH, Government of India. No other external funding organization was involved in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Ethical approval

This study was approved by the Institutional Ethical Committee (IEC) (Ref. No. RRIUM/KU/2018-19/Tech/IEC dated 29.03.2019) of Regional Research Institute of Unani Medicine, Srinagar, Jammu and Kashmir, India and registered with Clinical Trial Registry-India (CTRI) (CTRI No. Registration No. REF/2020/07/035404 dated 25.07.2020). Patient consent was acquired as per IEC and CTRI guidelines.

Consent to participate and publish

Written informed consent of the participants was obtained for participation in the study and publication of the data.

Declaration of Competing Interest

Authors declare no conflict of interests with regards to the submitted work.

Acknowledgments

We acknowledge the dedication and commitment of the staff, providers and personnel at RRIUM, Srinagar, Jammu and Kashmir. We are thankful to Assistant Director-Incharge (Dr Seema Akbar) for her relentless support. We express our gratitude to the patients who gave consents to participate in this study and diligently followed up, without them this research would not have been possible. We thank Central Council for Research in Unani Medicine, Ministry of AYUSH, Government of India, for their funding and support to accomplish this study.

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