Therapeutic efficacy and safety of Unani formulation in patients of Fasaad-e-tashahhum-e-dam (dyslipidemia): a randomized open standard controlled clinical study

Syed Sabahat*, Naquib Ul-Islam

ABSTRACT

Background: Hyperlipidemia which is interchangeably used with the term dyslipidemia essentially refers to the condition of abnormality of lipid levels measured in the blood typically due to the disorder of lipoprotein metabolism. The objective of this study was to determine the therapeutic effect and safety of newly formulated drug on patients with Fasaad-e-Tashahhum-e-Dam (dyslipidemia) and compare it with the effect of Unani formulation and rosavastatin.

Methods: The present study was open randomized controlled clinical study. The study subjects were divided in two groups, one group was given test drug (test group) and another group was given control drug (control group). All the patients who qualified the inclusion criteria were randomly placed in either test or control group.

Results: In the present study we observed that both the groups were comparable with respect to age, sex lifestyle, family history and mizaj. We found that both Unani formulated drug and standard drug rosavastatin significantly improves the lipid parameters after the treatment with a p value of (<0.001*).

Conclusions: We concluded that the overall effect of the proposed Unani formulated drug was found quite fascinating in the treatment of dyslipidemia. Apart from drug safety, visible improvements were evident in objective parameters like cholesterol, triglyceride and LDL, VLD. However, the present study did not revealed that Unani drug is superior to standard drug instead both the treatments are equally effective on the improvement of lipid profile parameters.

Keywords: Fasaad-e-tashahhum-e-dam, Lipid, Unani, Rosavastatin

INTRODUCTION

Hyperlipidemia which is interchangeably used with the term dyslipidemia essentially refers to the condition of abnormality of lipid levels measured in the blood typically due to the disorder of lipoprotein metabolism. Dyslipidemia which includes either overproduction or deficiency of lipoproteins or both manifests an elevation of serum total cholesterol or triglyceride or both, or low density lipoprotein (LDL) and decrease in high density lipoprotein (HDL) concentration. Evidently, health care providers face a great deal of challenge to deal with dyslipidemia and its associated comorbidities, since it plays a significant role in development of coronary artery disease (CAD) and immensely contributed to the annual death rates globally. There is a 4 fold prevalence of coronary heart disease in Asia as compared with general USA population. The unattended dyslipidemia vulnerably invites certain catastrophic consequences like atherosclerosis, stroke and ischemic heart disease (IHD). The cause responsible for such lipid disorder could be primary, and more commonly secondary to diabetes mellitus, nephrotic syndrome and hypothyroidism. It is important for a patient with dyslipidemia to have a full clinical assessment and thereby timely appropriate treatment so that the life-threatening consequences of disease may be controlled or halted optimally. Despite
remarkable advancement in dyslipidemia therapy, it continues to raise significant economic and personal burden as risk factor of cardiovascular disease. The management of dyslipidaemia is a two-way process; non-pharmacological and pharmacological. The non-pharmacological approach includes diet, food and additives and reduction of weight and exercises. The pharmacological approach consists of drug therapy to aim at maintaining lipids in recommended range. Currently available drug classes that affect lipoprotein metabolism are listed in Table 1.

**Table 1: Available drug classes that affects lipoproteins metabolism.**

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Daily close</th>
<th>Mechanisms</th>
<th>Lipid/lipoprotein in effects</th>
<th>Side effects</th>
<th>Contraindications</th>
</tr>
</thead>
<tbody>
<tr>
<td>HMGCoA Reductase inhibitors (statin)</td>
<td>Lovastatin (20-80 mg), pravastatin (20-40 mg)</td>
<td>Cholesterol synthesis, hepatic</td>
<td>LDL-C 18-55%, HDL-C 0%-15%</td>
<td>Myopathy, increased liver enzymes</td>
<td>Absolute: active or chronic liver disease relative</td>
</tr>
<tr>
<td>Bile acid sequestrant</td>
<td>Ezetimibe (10 mg)</td>
<td>Intestinal cholesterol absorption</td>
<td>LDL 17% HDL, TG-minimal change</td>
<td>Elavated tranaminases, angioedema, headache</td>
<td>Hypersensitivity</td>
</tr>
<tr>
<td>Nicotinic acid</td>
<td>Cholestyramine (4-32 g), cholesterol (5-40 g), colesvelem (3750-4375 mg)</td>
<td>Bile acid excretion and LDL receptors</td>
<td>LDC-C 15-30%, HDL-C n3-5%, TG no change or increase</td>
<td>Gastrointestinal distress, constipation, decreased absorption of other drugs</td>
<td>Absolute: dysbetalipoproteinemia TG&gt;400 mg/dl, relative TG&gt;200 mg/dl</td>
</tr>
<tr>
<td>Fibric acid</td>
<td>Gemfibrozi (600 mg BID), fenofibrate (200 mg), clofibrate (1000 mg bid)</td>
<td>VLDL hepatic synthesis</td>
<td>LDL-C 5-20% (may be increased in patients with high TG) HDL-C 10-20% TG 20-50%</td>
<td>Dyspepsia, gallstones, myopathy</td>
<td>Absolute severe renal disease, severe hepatic disease</td>
</tr>
</tbody>
</table>

Presently, the treatment of dyslipidemia is lipid lowering agents; these are statins (atorvastatin, simvastatin, pravastatin andLovastatin, etc), bile-acid sequestrants (cholestyramine and colestipol), resins, niacin, fibric acid analogs (fenofibrate, bezafibrate, and ciprofibrate) and ezetimibe. Administration of these pharmacological agents produces several adverse effects or side effects along with antilipidemic activity like hepatotoxicity, myopathy, renal dysfunction, dyspepsia, bloating, constipation, flushing, pruritus of the face and upper trunk, skin rashes, acanthuses nigricans, urticaria, hair loss, myalgias, fatigue, headache, impotence, and anaemia.8,10 Hence, there is pressing need for novel therapeutic agents for better management to prevent from adverse effect of conventional therapy. In conventional Unani system of medicine, there are large number of drugs; like Gugulipid (Camifora mukal), Alfalfa (Medicago sativa), Asian ginseng (Panax ginseng), and Fenugreek (Trigonella foenum graecum), Garlic (Allium sativum) and onions (Allium cepa), Turmeric (Curcuma longa), Lilly of the valley (Convallaria majalis), Black cumin (Nigella sativa), etc.

These drugs are Haar (hot) in mizaj (temperament) to modulate liver functions and also scientifically have been reported to have lipid lowering effects, like Gugulipid.
(Camifora mukul), Alfalfa (Medicago sativa), Asian ginseng (Panax ginseng), Garlic (Allium sativum) and onions (Allium cepa), Turmeric (Curcuma longa), Lilly of the valley (Convallaria majalis), Black cumin (Nigella sativa), etc.\textsuperscript{11}

**Aim and objectives**

The aim of the study was to determine to evaluate the therapeutic effect and safety of a newly formulated Unani drug in the patients with Fasaad-e-tashahhum-e-dam (dyslipidemia) and to compare it with the effect of rosavastatin by open randomized controlled clinical study.

**METHODS**

The Present study was conducted at postgraduate department of Moalijat, Regional Research Institute of Unani medicine (RRIUM), Srinagar, University of Kashmir from 2018-2019. A newly established Unani drug consists of several botanical ingredients- Zeera (Carum carvi), Tukhm Karafs (Apium graveolens Linn), Marzenjosh (Oliganum vulgare Linn), Boora surkh (Armenianbole), Tukhm Suddab (Rutagraweolanslinn) and Nankhaw (Trachyspe rumnunammi Linn). These ingredients were first dried at 40°C and then grounded to powder and thereafter were taken in different quantity, mixed together properly and then packed.

The active investigation product was supplied to the patients in the powder form on each visit in small disposable poly packs from the day one. The investigational products were stored in dry and cold place and the patients of test group were also instructed for the same, the daily dosage of 4.5 g was advised orally for two months. The standard drug rosavastatin in the form of tablet with daily dosage of 10mg orally was administered to control group for two months.

**Sample size calculation**

Using GPOWER software (version 3.0.10), it was estimated that the least number of patients required in each group with 80% power, 0.91 effect size and 5% significance level is 20. Since we had to include two groups in our study, therefore a total of 40 samples was included in our study.

**Statistical methods**

The recorded data will be compiled and entered in a spreadsheet (Microsoft excel) and then exported to data editor of SPSS version 20.0 (SPSS Inc., Chicago, Illinois, USA). Categorical variables will be summarized as frequencies and percentages and continuous variables will be expressed as mean±SD.

Unpaired t-test for difference between two independent groups will be applied to analyze the recorded data and paired t-test will be employed to analyze the difference within groups.

**Inclusion criteria**

Patients with following criteria’s were included (a) known case of dyslipidemia with disease history of <3 years with or without anti hyperlipidemia medication- total cholesterol ≥240 mg/dl, triglycerides <499 mg/dl (high), LDL ≥189 mg/dl, HDL ≥40 mg/dl in men and ≥50 in woman, VLDL <0.930-1.006 g/l, ratio LDL to HDL <6.3 in man and 5 in woman; (b) patients of both sex; (c) age between 20-50 years; and (d) patients who follow the protocol.

**Exclusion criteria**

Patients with following criteria’s were excluded- (a) known case of dyslipidemia with disease history of >3 years total cholesterol <240 mg/dl, triglycerides >499 mg/dl (high), LDL <189 mg/dl, HDL <40 mg/dl in men and <50 in woman, VLDL>0.930-1.006 g/l, ratio LDL to HDL >6.3 in man and >5 in woman; (b) known cases on use of corticosteroids and contraceptives; (c) history of cardiovascular, renal, liver disease, AIDS and TB; (d) history of alcoholism; (e) pregnant and lactating mothers; and (f) age <20 and >50 years of age.

To minimize the selection bias, participants fulfilling the inclusion criteria and willing to participate in the study were randomly divided into test and control group. Due to time constraint, lottery method was used for randomization. The study was carried out strictly according to guide lines of good clinical practices, embodying the principles mentioned in Declaration of Helsinki. Informed consent was obtained from all participants and approval from the Institutional Review Board was obtained.

![Figure 1: Displays graphical justification of sample size determination.](image)
RESULTS

The age distribution of patients of test group and control group is shown in Table 2. Mean age was 23.55±0.762 years, among test group and 23.6±1.110 years, among control group. Maximum numbers of patients were between the age group of 31-40 years in both test and control group.

Table 3 displays sex wise distribution of patients among test group and control group. The above table indicated that in test group 55% were male and 45% were female while in control group 65% were male and 35% were female.

Table 4 exhibits lifestyle distribution among test and control group. We observe that majority of patients accounting about (50%) was having sedentary lifestyle and (35%) participants were had hardworking lifestyle followed by (15%) who were very hard working in test group. In control group (60%) of patients were having sedentary lifestyle followed by (20%) in hard working and (20%) very hardworking.

Table 5 shows family history among test and control group. In test and control group, majority of participants had family history of hyperlipidaemia (60%) and (75%) respectively. Only (40%) and (15%) had no family history of hyperlipidaemia in test and control group respectively.

It is evident from above Table 6, that majority of patients i.e.; 40% patients among test group while in control group (50%) had balghami temperament. In the present study, 40 patients of hyperlipidaemia were registered and were randomly placed under test and control group. 20 patients were treated in test group with Unani formulation and 20 patients in control group were treated with rosavastatin. The effect of these treatment on the subjective and objective parameters are presented. In
21.59%, LDL was reduced by 18.02%, VLDL was reduced 33.75% which were all statistically significant at p<0.0001 whereas HDL was raised by 4.01%. The change that occurred with the treatment is not great enough to exclude the possibility that the difference is due to chance p=0.072. In Table 9, the comparison of test and control group with respect to cholesterol, triglyceride, HDL, LDL and VDL.

### DISCUSSION

In present study, we observed that the incidence of patients with dyslipidaemia were highest in the age group of 31-45 years constituting (52.5%) of total numbers of patients followed by (40%) patients in the age group of 46-50 years and (7.5%) were in the age group of 16-30 years. This is in concurrence with the increased incidence of dyslipidaemia in the middle age group. This data shows that more prevalence of dyslipidaemia found in age group of 31-45 years, second high incidence was found in age over 50 years. Our study is closely related with the study conducted by Sawami et al (2008) who reported that prevalence of dyslipidaemia is high in 31-40 years of age group.
Marked improvements were evident in objective parameters like cholesterol, triglyceride and LDL, VLD. Both test and control drugs have same effects on lipid profile parameters.

Statistically no side effect was observed in test group, compliance to the treatment was found good. These results conclude that the test drug is quite safe in the treatment of dyslipidaemia. Hence, we recommend practitioners to opt for proposed Unani formulated drug for optimal results.

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Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES