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A prospective open label randomized clinical study of *Safoof-e-Mohazzil* in the cases of primary hyperlipidemia (*Fart-e-Tadassum-Fid-Dam*)

Md Razi Ahmad[1*], Md Najibur Rahman[2], Jamal Akhtar[3], Akhtar Hussain Farooqui[4].

[1]Dept. of Moalijat, Salfia Unani Medical College & Hospital Laheriasarai Darbhanga, Bihar, INDIA.
[2]Dept. of Moalejat, Govt. Tibbi College & Hospital, Patna, Bihar, INDIA.
[3]Dept. of Moalejat, Z.V.M. Unani Medical College & Hospital, Pune, M.S., INDIA.
[4]Dept. of Moalejat, Z.V.M. Unani Medical College & Hospital, Pune, M.S., INDIA.

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ABSTRACT

Background: The concept of Hyperlipidaemia (Fart-e-Tadassum-Fid-Dam) is new and based on the biochemical changes in the blood i.e. distributed lipid metabolism and as a result, there is an increasing concentration of lipids in the blood. It was a prospective open-label randomized clinical study of Safoof-e-Mohazzil in the cases of primary hyperlipidemia (Fart-e-Tadassum-Fid-Dam).
Subjects and methods: All patients were randomly divided into two groups (test group and standard group). The patients of test groups were received Safoof-e-Mohazzil 05 gram OD in morning and the standard group were received Atorvastatin (Atorva) 10 mg OD (HS).
Results: All the baseline parameters were patients divided did not differ significantly between two intervention groups. After Intervention comparing to the test group v/s standard group, improvement of subjective parameters did not differ significantly. On objective parameters, improvement is very significant in both groups. All the biochemical parameters in each intervention groups P=0.001. On the comparison between test group v/s standard group by using unpaired "t" test.
Conclusion: This result suggesting the effect of test drug and the standard drug is not equally effective. Test drug is more effective than control drug for the increment on HDLc, lowering of BMI and WHR. The HDL Cholesterols considered as good Cholesterols and lowering of BMI and WHR so this is also the beneficial effect of the test drug.

*AUTHOR FOR CORRESPONDENCE
E-mail address: dr.razi.ahmed@gmail.com

INTRODUCTION

Hyperlipidemia (*Fart-e-Tadassum-Fid-Dam*) is a common metabolic disease seen in clinical practice. It is mentioned that increased lipid level is associated with the pathogenesis of atherosclerosis. (Lipid Research Clinics Programme, 1984) It can cause CHD, IHD, CVA, and PVD (Howard et al., 1999). The incidence of CHD in Indians reported to the two folds higher than other US populations with early age of onset due to genetic and environmental factors (Ashavaid et al., 2005). Additionally, steadily rising PVD is a major concern to health workers. Modified lifestyle and genetic susceptibility make the condition worse for Indians (Park's, 2002; Gan et al., 2006).

Theory of Hyperlipidaemia meets similarly on the basis of etiology, presentation, complications, pathophysiology and non-pharmacological management with Saman-e-mufrit (obesity), which is a highly predisposing factor of hyperlipidemia. The

Hippocrates (Jalinoos 1903), Rofas (Ibne-Rushd 1986), Galen (Jalinoos 1903), Razes (Zakaria Razi 1999) and Avicenna (Ibne Cena 1929) described the obesity (Saman-e-mufrit), which is due to the excess of the phlegm (Khilt-e-Balgham). They describe the causes of that obesity are hereditary (Kirmani Nafees bin Auz, 1935) lack of exercise (Riyazat) and luxurious life style (Iqsari Jamaluddin 1907), diet (Ghiza) (Antaki Dawood, 1930), the excess of alcohol, especially after the meal. Shareef, 1931) and Baroodat-e-Mizaj (Firozuddin, 1939). Saman-e-mufrit is a predisposing factor of paralysis, stroke, narrowing of blood vessels, hemorrhage and sudden death (Lopez, 1993; Abbott et al., 1988). "Galen" recommended the main stay of treatment is to be evacuation (Istefragh by laxative), increasing body heat (Harrarat) breath holding exercises and the moderate amount of alcohol(Jalinoos 1903), "Avicenna" emphasized on Istefrag, exercise and low calories diet in the management of obesity. (Ibne Cena 1929), "Razes" Grains and vegetables reduce the body weight (Zakaria Razi 1999).

This concept seems very true in the light of modern advances because many obese individuals with apparently normal glycemic control have a syndrome characterized by insulin resistance, leads to hyperinsulinemia, which stimulates sympathetic nervous system, resulting in retention of sodium and water, vaso-constrictions, and hyperlipidemia (Wilsons et al., 1998; Stamler, 1986; Thomas, 2006).

Primary hyperlipidaemia is caused by inherited single gene multiple genetic factors whereas Secondary hyperlipidaemia develops in response to some metabolic disturbances caused by Diabetes Mellitus, Hypothyroidism, Hepatic/ Renal parenchymal disorder, Use of drugs like contraceptive pills, corticosteroid and antipsychotics etc. (Parveen Kumar & Michael Clark 1998; Sainani, 2002; Davidson, 2002; Farnier and Picard, 2001).

Textbooks of the Unani system of medicine described many possible treatments of metabolic disorders like DM and obesity. But most of the drugs have not been subjected to scientific evaluation. Safoof-e-Mohazzil has been selected for management of primary hyperlipidemia on the basis of some preliminary animal and human trials (Khan, 1954; Jamaluddin A, 1954).

SUBJECTS AND METHODS

The study was approved by Institutional Ethical Committee (MMERC/EC/2009/5) and conducted during the session 2009-2012, and the study was designed as a standard-controlled open labeling trial in successive patients with primary hyperlipidemia diagnosed on presentation, history, examination, and investigations. Sixty patients were selected by random sampling, of age between 20-60 years who were belonging to inclusion criteria registered. All patients were randomly divided into two groups (test group and standard group). The patients of test groups were received Safoof-e-Mohazzil 05 gram OD in morning and the standard group were received Atorvastatin (Atorva) 10 mg OD (HS), respectively for 90 days. Follow-up planned 0 days, 45th-day middle and on the 90th day, at the end of the trial. A low-fat diet, moderate exercise, cutting down sweet, alcoholic beverages and cessation of smoking were advised. Subjective and objective parameters were recorded. Complication and side effects treated accordingly and data collected. An official approval of study proposal was taken by College and Hospital ethical committee; later on by MUHS, Nashik (M.S.) before starting the trial. The statistical analysis of data and Test of significant calculated by the help of computer software "GraphPad InStat using paired and unpaired "t" test].

RESULTS

The higher incidence of hyperlipidemia is found in the age group of 31-50 years. That is 86.7% in group "A" and 100% in group "B". The higher incidence of hyperlipidemia is found in the male that is 66.66% in group "A" and 50% in group "B". The higher incidence of hyperlipidemia is found in Muslims that is 66.66% in group "A" and 70% in group "B". The higher incidence of hyperlipidemia is found in lower middle and upper middle class that is 83.33% in group "A" and 93.33% in group "B" and less common in lower class that is 3.33% in group "A" and 6.66% in group "B". Hyperlipidaemia is more common in Non-vegetarian that is 80% each in both groups and less common in vegetarian that is 20% each in both groups. In our observation, there are 70.0% in group "A" and 80.0% in group "B" of mizaj-e-Balghami demonstrates that there is a higher incidence of hyperlipidemia in mizaj-e-Balghami persons. In our observation, there are 63.3% in each group person suffered to anxiety and depressive disorders that, there is a higher incidence of hyperlipidemia in those subjects. During the study, it is observed that 43.33% patients in each group have a habit of smoking, and 10.0%in group "A" and 20.0% in the group were alcoholic, also 16.7% in group "A" and 20.0% in group "B" were habits of tobacco use.

The present study demonstrates that patients with primary hyperlipidemia are more susceptible to hypertension. Most of the patients are either pre-

hypertensive (16.7% group "A" and 33.3% group "B"), or mild hypertensive (53.33% group "A" and 50.0% group "B"), and some patients also suffering from moderate (6.7% group "A" and 3.3% group "B"), severe (3.3% in group "A" only) or isolated hypertension (6.7% group "A" and 3.3% group "B"). Present study demonstrated the higher incidence of hyperlipidaemia in those patients who have the family history of hypertension (76.7% group "A" and 86.7% group "B"), DM (33.3% group "A" and 53.3% group "B") and Obesity (73.3% group "A" and 76.7% group "B").

Subjective parameters

After Intervention, most of the subjective parameters like chest pain, palpitation, exertional dyspnoea, and joint pain improved significantly in both interventional groups (except Xanthelasma, Xanthomata and premature arcus cornea both drugs has no effect on this parameter). While comparing to the test group v/s standard group, improvement of subjective parameters did not differ significantly. Its shows both drugs are equally effective on clinical symptoms and signs.

Objective parameters

Both drugs are very effective on all objective parameters like BMI, WHR, Total Cholesterol, HDLc, LDLc, VLDLc, and Triglycerides. The "P" value of each intervention groups on all parameters is P= 0.001.

Table 1. Comparison of BMI between two intervention groups.

Title	Test Drug DF 0-90 days	Standard Drug DF 0-90 days
Mean	2.836	2.21
SD	0.515	0.566
SE of Mean	0.0941	0.103
"t" Value (Unpaired)	-4.652 with 58 df	
P Value	0.01 Significant	

WHR: In test group, mean reduction in WHR is 0.1007±0.0421 and standard group, mean reduction WHR is 0.1233±0.0352. The "t" unpaired value is 2.286 with 58 df P=0.026 that is statistically very significant.

Table 2. Comparison of WHR between two intervention groups.

Title	Test Drug DF 0-90 days	Standard Drug DF 0-90 days
Mean	0.1007	0.1233
SD	0.0421	0.0352
SE of Mean	0.0077	0.0064
"t" Value (Unpaired)	2.286 with 58 df	
P Value	0.026 Significant	

Total Cholesterol: In test group, mean reduction in Total Cholesterol is 64.07±22.71 and standard group, mean reduction Total Cholesterol is 55.17±22.47. The "t" unpaired value is -1.654 with 58 df, P=0.103 which statistically did not differ significantly in both groups.

Table 3. Comparison of total cholesterol between two intervention groups.

Title	Test Drug DF 0-90 days	Standard Drug DF 0-90 days
Mean	64.07	55.17
SD	22.71	22.47
SE of Mean	4.14	4.10
"t" Value (Unpaired)	-1.654 with 58 df	
P Value	0.103 Non Significant	

HDLc: In test group, mean difference in HDLc is 10.07±3.039 and standard group, mean difference HDLc is 6.93±2.982. The "t" unpaired value is 3.757 with 58 df, P= 0.001 that is statistically very significant.

Table 4. Comparison of HDL cholesterol between two intervention groups.

Title	Test Drug DF 0-90 days	Standard Drug DF 0-90 days
Mean	10.07	6.93
SD	3.039	2.982
SE of Mean	0.555	0.544
"t" Value (Unpaired)	3.757 with 58 df	
P Value	0.001 Significant	

LDLc: In test group, mean reduction in LDLc is 59.53±22.40 and standard group, mean reduction LDLc is 49.50±24.386. The "t" unpaired value is -1.853 with 58 df P=0.069 that is statistically did not differ significantly in both groups.

Table 5. Comparison of LDL cholesterol between two intervention groups.

Title	Test Drug DF0-90 days	Standard Drug DF 0-90 days
Mean	59.53	49.50
SD	22.40	24.386
SE of Mean	4.09	4.45
"t" Value (Unpaired)	-1.853 with 58 df	
P Value	0.069 Non Significant	

VLDLc: In test group, mean reduction in VLDLc is 13.13±6.219 and standard group, mean reduction VLDLc is 12.97±5.997. The "t" unpaired value is -0.588 with 58 df P=0.599 that is statistically did not differ significantly in both groups.

Table 6. Comparison of VLDL cholesterol between two intervention groups.

Title	Test Drug Df 0-90 days	Standard Drug Df 0-90 days
Mean	13.13	12.97
SD	6.219	5.997
SE of Mean	1.135	1.095
"t" Value (Unpaired)	-0.588 with 58 df	
P Value	0.559 Non Significant	

Triglycerides: In test group, mean reduction in Tg is 65.80±30.920 and standard group, mean reduction Tg is 65.60±31.363. The "t" unpaired value is -0.515 with 58 df P=0.609 that is statistically did not differ significantly in both groups.

Table 7. Comparison of triglycerides between two intervention groups.

Title	Test Drug Df 0-90 days	Standard Drug Df 0-90 days
Mean	65.80	65.60
SD	30.920	31.363
SE of Mean	5.645	5.726
"t" Value (Unpaired)	-0.515 with 58 df	
P Value	0.609 Non Significant	

Abbreviations: BMI = Body mass index; Df = Difference; HDL = High Density Lipoprotein; LDLc = Low Density Lipoprotein; P = probability; SD=Standard Deviation; S.E. Mean= Standard Error of Mean; VLDL = Very Low Density Lipoprotein; WHR= Waist Hip Ratio.

While comparing to the test group v/s standard group improvement of drugs as follows:

BMI: In the test group, the mean reduction in BMI is 2.836±0.515 and standard group, mean reduction BMI is 2.21±0.566. The "t" unpaired value is -4.652 with 58 df P= 0.001 that is statistically very significant.

DISCUSSION

Hyperlipidemia is a major health problem throughout the world. It is a pathological condition in which lipid level is increased above the normal level. In the Unani system of medicine, Fart-e-Tadassum Fid-Dam is not mentioned in the classical Unani literature but we study the clinical features and complications of Saman-e-Mufrit are very resemblance to the Hyperlipidemia. Therefore, the concept of Fart-e-Tadassum Fid-Dam is relatively newer. The various types of hypolipidemic agents are being used for management of Hyperlipidemia and reduce the risk of IHD and other complication. Although these drugs are effective and possess important role of reducing the raised lipid level, they leads their adverse effect on the long term used (Sever et al. 2003). In the Unani system of medicine also claimed the number of single and compound drugs to cure the Saman-e-Mufrit without causing any side effects. Therefore, it is an important need to provide safe and effective drug from a Unani system of medicine for the long-term management of Hyperlipidaemia. So keeping the fact in mind, the study entitled "A Prospective open-label randomized clinical study of Safoof-e-Mohazzil in the cases of Primary Hyperlipidaemia (Fart-e-Tadassum-Fid-Dam)." All patients were randomly divided into two groups (test group and standard group). The patients of test groups were received Safoof-e-Mohazzil 05 gram OD in morning and the standard group were received Atorvastatin (Atorva) 10 mg OD (HS). As evidence of observation result and discussion of the study following conclusion can be drawn;

All the baseline parameters were patients divided did not differ significantly between two intervention groups. This ensures that two intervention groups are properly randomized.

After Intervention, most of the subjective parameters improved significantly in both interventional groups (except Xanthelasma, Xanthomata, and premature arcus cornea). While comparing to the test group v/s standard group, improvement of subjective parameters did not differ significantly. It shows both drugs are equally effective on clinical symptoms and signs.

On objective parameters, improvement is very significant in both groups. All the biochemical parameters in each intervention groups P=0.001. On the comparison between test group v/s standard group by using unpaired "t" test. In BMI "t" = -4.652 with 58 df "P"= 0.001, In WHR "t"=2.286 with 58df "P"= 0.026 that is extremely significant. This result suggesting the effect of test drug and the standard drug is not equally effective test drug is more effective than standard drug on the lowering of BMI and WHR. In Total Cholesterol "t"= -1.654 with 58df "P"= 0.103. In LDLc "t" test "t"= -1.853 with 58df "P"=0.069. In VLDLc unpaired "t" test "t"= 0.588 with 58df "P"=0.559. In Triglycerides "t" test "t"=0.515 with 58df "P"= 0.609. This result suggesting the effect of test drug and the standard drug is equally effective on the lowering of Total Cholesterol, LDLc, VLDLc and Triglycerides. In HDL Cholesterol, "t"= 3.757 with 58df "P"= 0.001. This result suggesting the effect of test drug and the standard drug is not equally effective. Test drug is more effective than control drug for the increment on HDLc. The HDL Cholesterols considered as good Cholesterols, so this is also the beneficial effect of the test drug. So the results are very resemblance to many clinical study such as Saman-e-Mufrit me Khilt-e-Dum me Shamiyaat ki Kasrat par Luk Magsool Ki Asraat ka Tahqeeqi Muqala, Clinical Study of Farte Tadassum Fiddam and Evaluation Of Efficacy of Unani Formulation in its Management. Clinical Study of Samane Mufrat Ibtedai and Efficacy of Unani Formulation in its Management.

Therefore it can be concluded that the test drug is safe and effective in the cases of Hyperlipidaemia. As literature shows, primary Hyperlipidaemia is a metabolic disorder & genetically inherited the disease, therefore the long-term study is needed to explore other pharmacological action of test drug, and not only this its specific ingredients or extracts' possibly give better comparable impact on Hyperlipidaemia than its crude form. Finally, as with any analysis, the potential for publication bias is of concern. Visual inspection of our analysis funnel plot could not rule out for publication bias

CONCLUSION

The present study shows that Safoof-e-Mohazzil has a hypolipidaemic and weight reducing (lipolytic) properties in its crude form. There is a need to evaluate which active ingredient is effective on hyperlipidemia. Probably that ingredient is more effective in the management of hyperlipidemia and other related disorder without causing any side effects which seen with other available lipid-lowering agents on long-term use.

Therefore it can be concluded that the test drug is safe and effective in the cases of Hyperlipidaemia. As literature shows, primary hyperlipidemia is a metabolic disorder & genetically inherited the disease, therefore the long-term study is needed to explore other pharmacological action of test drug, and not only this its specific ingredients or extracts' possibly give better comparable impact on hyperlipidemia than its crude form. Finally, as with

any analysis, the potential for publication bias is of concern. Visual inspection of our analysis funnel plot could not rule out for publication bias.

CONFLICT OF INTEREST

None declared.

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