A COMPARATIVE STUDY ON THE EFFECTS OF GEMFIBROZIL, DILTIAZEM AND ISOSORBIDE DINITRATE ON LIPID PROFILE IN PATIENTS OF ISCHEMIC HEART DISEASE IN INDIA

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ABSTRACT

Effects of three drugs, Gemfibrozil, Diltiazem and Isosorbide dinitrate (ISDN) on various lipid parameters were studied in patients with ischemic heart disease (IHD) with positive treadmill stress response. Gemfibrozil and diltiazem significantly lowered the levels of serum total lipids (TL), triglycerides (TG), phospholipids (PL), total cholesterol (TC), low density lipoprotein cholesterol (LDL-C) and very low density lipoprotein cholesterol (VLDL-C), and increased the levels of serum high density lipoprotein cholesterol (HDL-C) significantly. However, patients administered with ISDN showed a significant increase in all the lipid parameters except HDL-C, which showed a significant decrease.

KEY WORDS: Ischemic heart disease, Lipid profile, Gemfibrozil, Diltiazem, Isosorbide dinitrate.

INTRODUCTION

The syndrome of ischemic heart disease (IHD) includes angina pectoris, acute myocardial infarction (fatal and non-fatal), and sudden cardiac death. With regard to progression, the prime pathological cause of IHD is coronary atheroma (1). The elevated lipid levels lead towards the development of atherosclerosis. The lipid research clinics conducted coronary primary prevention trial and demonstrated that reduction in plasma cholesterol, specially LDL-C decreased the risk of development of coronary artery disease (2).

Various drugs are available for the treatment of atherosclerosis and ischemic heart disease. Patients with ischemic heart disease are administered either beta-blockers, calcium channel blockers or nitrates or a combined drug therapy. Gemfibrozil, is considered the most effective antiatherosclerotic drug. Several studies have established the adverse effects of beta-blockers on lipid profile (3). But very little or no work has been done on calcium channel blockers or ni-

trates on lipid profile.

Keeping in view the lacunae and contradictory observations reported by earlier workers and the condition of patients in India, a comparative study on the effects of gemfibrozil, diltiazem and isosorbide dinitrate on lipid profile have been investigated in the present study.

MATERIALS AND METHODS

75 patients of ischemic heart disease were selected for the study after confirmation by computerized treadmill test (positive C.T.M.T. responses) carried out in C.T.M.T. lab, at Bangur Medical Research Centre, S.M.S. Hospital, Jaipur. The subjects of the study were divided into three groups, consisting of 25 patients each. Group-I was administered gemfibrozil (600 mg, twice daily), Group-II was administered diltiazem (30 mg, thrice daily) and Group-III was administered ISDN (10 mg thrice daily). All the groups received medication for three months. Fasting blood samples were drawn and collected in dry plain vials. Serum was separated and was analyzed for lipid profile. The lipid profile was estimated for each patient before and after treatment. Lipid profile was also studied in 25 normal healthy subjects

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Table 1: Levels of serum lipids in control and IHD patients.

Lipid profile	Control group	Gemfibrozil group	Diltiazem group	ISDN group
TL	538.0 ± 48.4	730.0 ± 52.5	607.3 ± 65.7	622.4 ± 44.3
PL	169.9 ± 15.1	231.2 ± 23.5	188.4 ± 24.1	192.3 ± 15.8
TG	120.8 ± 27.9	201.1 ± 57.8	145.2 ± 25.7	147.0 ± 15.5
TC	180.6 ± 16.7	275.0 ± 29.0	214.2 ± 24.5	211.0 ± 14.1
HDL-C	49.8 ± 10.1	37.4 ± 8.1	44.6 ± 8.9	41.4 ± 7.1
LDL-C	105.2 ± 17.5	197.4 ± 34.2	140.4 ± 23.6	140.5 ± 18.2
VLDL-C	24.4 ± 5.7	40.2 ± 11.5	29.1 ± 5.0	29.3 ± 3.0

Values as Mean ± S.D. in mg%.

free from any disease in order to establish normal levels.

Estimations for various lipid parameters viz. total lipids (TL), phospholipids (PL), triglycerides (TG), total cholesterol (TC) and high density lipoprotein cholesterol (HDL-C) were done as per methods given in Varley (4). Low density and very low density lipoprotein cholesterol (LDL-C and VLDL-C) were calculated by Friedewald-Levy-Fredrickson formula (5).

RESULTS AND DISCUSSION

As evident from table 1, the values of serum lipids (mean ± S.D.) were elevated (except HDL-C) in IHD patients in all the three treatment groups as compared to normal healthy subjects. Levels of serum HDL-C were decreased in the IHD patients as compared to normal healthy subjects. This clearly suggests the role of elevated lipid levels in IHD. It is well established that patients with low levels of HDL-C

and increased levels of other lipids like LDL-C and VLDL-C are at a higher risk of development of atherosclerosis. High levels of HDL-C are reported to be protective against atherosclerosis (6) and indicate an efficient catabolism of VLDL & LDL. On the other hand when HDL-C is low, catabolism of VLDL and LDL may be abnormal and may help in susceptibility to atherosclerosis.

As evident from table 2, gemfibrozil is an effective lipid lowering drug, because after administration of gemfibrozil, for three months, levels of serum TG, TC, TL, PL, LDL-C and VLDL-C decreased significantly, whereas a significant increase in the levels of HDL-C was also observed. IHD patients before treatment were hypertriglyceridemic (201 ± 57.8 mg%, range 145 to 259 mg%). Gemfibrozil administration significantly lowered the serum TG levels in these patients causing a mean percentage decrease of 25.5%.

Table 2. Effect of Gemfibrozil, diltiazem and ISDN on serum lipids in patients with IHD (As expressed in % decrease/increase).

Lipid profile	Gemfibrozil group	Diltiazem group	ISDN group
TL	8.7 (D)	2.6 (D)	3.8 (I)
PL	8.2 (D)	2.6 (D)	4.9 (I)
TG	25.5 (D)	4.3 (D)	6.3 (I)
TC	21.2 (D)	7.3 (D)	5.5 (I)
LDL-C	28.7 (D)	12.1 (D)	8.1 (I)
VLDL-C	25.0 (D)	5.1 (D)	6.5 (I)
HDL-C	26.3 (I)	6.7 (I)	4.2 (D)*

(D) = Decrease and (I) = Increase, Values in mg %

*P<0.05 (Significant),

for all other (D) and (I) the P value is P<0.01 (highly significant).

Fenderson et al (7) observed that all the patients studied by him showed decrease in serum TG after gemfibrozil administration (statistically significant in 15 out of 22). Mean serum TG was decreased by 45.6% ($P < 0.001$). Two investigators (8,9) reported a decrease of TG by 44.6% and 43% respectively. The decrease observed in the present study is in agreement with that observed by the above workers. In the present study it is observed that gemfibrozil administration decreased the mean serum TC by 21.2%, whereas Kesaniemi and Grundy (10) reported that gemfibrozil did not change the concentration of total cholesterol.

The possible mechanism by which gemfibrozil produces hypolipidemic effect is due to the reduction in circulating TG through the suppression of free fatty acid mobilization from adipose tissue. It also decreases the synthesis of VLDL carrier protein, apolipoprotein B. Saku et al (11) suggested that gemfibrozil causes a rise in HDL-C carrier apolipoprotein apo A-I and A-II. Thus it enhances the HDL-C transport which increases the removal of tissue cholesterol.

Levels of serum TG, TC, TL, PL, LDL-C and VLDL-C decreased after diltiazem administration for three months. The decrease in these lipid parameters are statistically significant. A significant increase in serum HDL-C level was also observed after diltiazem administration. Pool et al (12) reported that administration of diltiazem is associated with a significant increase in levels of HDL-C, whereas other lipid parameters viz. TG, TC, VLDL-C and LDL-C did not show a decrease greater than 5% in magnitude. Our present results confirm the above study. The decrease in blood lipids is probably related to an interference of calcium channel blocker with lipid metabo-

lism in the arterial wall (13).

After ISDN administration for three months, IHD patients showed a significant increase in levels of serum TL, PL, TC, TG, LDL-C and VLDL-C, whereas the level of HDL-C decreased. Loaldi et al (14) reported that administration of ISDN increased the lipid values between 4 to 8% in the IHD patients and concluded that ISDN is not protective against atherosclerosis. Thus the results of present study confirm the observation of Loaldi et al (14).

The present study concludes that as observed by earlier coworkers gemfibrozil is a very effective lipid lowering agent and it is effective in the treatment of hypertriglyceridemia and acts as an antiatherosclerotic agent. Of the two, diltiazem and isosorbide dinitrate only diltiazem possesses lipid lowering properties while isosorbide dinitrate adversely affected the lipid profile. Thus administration of diltiazem is also beneficial to ischemic heart disease patients. It is observed that ISDN administration increased significantly the levels of serum LDL-C, which is atherogenic in nature and its elevated level may cause further atherosclerosis in IHD patients, suggesting constant monitoring of lipid profile in IHD patients receiving ISDN.

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