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A STUDY ON COMPARATIVE EFFICACY OF HYPOLIPIDEMIC DRUGS

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ABSTRACT

A study was carried out on the comparative efficacy of Lopid, Mevacor, Bezalip and Lasona in sixteen hyperlipidemic subjects. All the subjects were on Lopid at least for the last 15 days. Lopid therapy was discontinued after determining blood lipid profile of the subjects on day zero (day of 1st contact). The subjects were divided into three groups and after a washout period of 15 *days,* they were *given* three different drugs for the next 15 days. Subjects in group a (6), b (5) and c (5) received Mevacor, Bezalip and lasona respectively.

In the present study mevacor was found to be the most potent hypolipidemic drug in lowering blood cholesterol and Low density lipoprotein (LDL) while lopid was most effective in keeping blood Triglycerides (TG) and High density lipoproteins (HDL) level within the desired limits. Bezalip and Lasona were also sufficiently effective in changing blood lipid profile, but lasona showed a negligible effect on HDL rise as compared with Bezalip or any other drug used in this study.

Introduction

The increasing incidence of coronary heart disease in our population and its association with hyperlipidemia has made the people cautions about their blood lipid profile (Abbasi et al., 1968; Kannel et al., 1971; and Shahina et al., 1978). Generally the lipids whose level is determined for clinical evaluation of hyperlipdemia in relation to atherosclerosis include cholesterol, TG, LDL and HDL (Gofmen et al., 1956 and Barbir et al., 1988). Present study deals with the comparative efficacy of different hypolipidemic drugs in hyperlipidemic subjects in order to work out the most suitable drug for the type of hyperlipidemia prevalent in D.I. Khan district of North West Frontier Province of Pakistan.

Materials and Methods

Participants

Sixteen hyperlipidemic subjects were selected for this study after their consent. All were within an age range of 50-60 years and the mean value of their body mass index was 25.03 (kg/M^2) with a standard error mean of ± 0.38. All the subjects were already on lopid (600 mg twice daily) at least for the last 15 days. Their blood lipid profile (BLP) was determined on the day of first contact (day -0), after which they were given a wash out period of 15 days during which they did not take any hypolipidemic drug. These subjects were divided on Day Zero into three groups i.e. a, b and c.

At the end of washout period on the day-15, the blood lipid profile of all the subjects was examined and the subjects in group-a were kept on Mevacor (40 mg twice daily), those in group-b were kept on Bezalip (200 mg thrice daily) while the subjects in group-c received lasona (250 mg thrice daily) for the next fifteen days. Blood lipid profile of the subjects in all the groups was again determined on the day 30. All the subjects were on common Pakistani diet but were avoiding excessive fat intake.

Analysis of blood samples:

5 ml blood was drawn by venepuncture from each subject on 3 occasions (day -0, 15, 30) after an over night fasting of 10-12 hours. Serum was obtained from each blood sample by keeping it for 20-30 minutes at room temperature followed by spinning for 10 minutes at 3000 revolutions per minute in ordinary lab. centrifuge. Serum was analyzed for cholesterol, TO, and HDL while LDL was calculated with the help of *for*mula given by Friedewald et al., 1972.

LDL - cholesterol = Total cholesterol - TG/5 - HDL.

For analysis enzymetic methods were employed, using kits obtained from Muslim Scientific traders, 3- Moj-e-Darya road Lahore.

Kits used include: Randox - Cholesterol: Cat. No - Ch. 290, Randox Triglycerides - Cat. No - TR. - 210, and Randox - HDL Cholesterol precipitant. Cat - No - CH. 204 - Randox Laboratories Ltd; Crumlin, C. Antrim, Ireland.

Analytical procedures in all the estimations were based on the production of chromogen by enzymetic reactions and reading the absorbance in spectrophotometer (UV-DEC 5).

Results and Discussion

Blood lipid profile of the subjects (group a, b and c) was determined on three occasions i.e. on the day 0, 15 and 30. All the subjects were already on lopid at least for the last fifteen days when they were contacted for the first time on day-O. They were given a washout period of 15 days from day-0 to 15, at the end of which subjects in group a, b and c received Mevacor, Bezalip and Lasona respectively for the next days i.e. from day - 15 to 30.

On comparison of lipid profile on day -0, 15 and 30 in group a (Table 1), it can be seen that the values of blood cholesterol and TG level on day - 0 (As a result of previous lopid therapy) are significantly lower compared to those seen on day 15 (As a result of drug withdrawal). Similarly some what increase in LDL level and a bit decrease in HDL level was observed as a result of drug withdrawal, but the change in HDI and LDL level was not significant statistically ($P > 0.05$).

Mevacor therapy lead to a decreased level of cholestrol, TG and LDL and slightly raised level of HDL but the change was significant only for cholesterol and LDL.

Almost similar response of lopid withdrawal was shown by the subjects in group b, as was observed for group a. Values of cholesterol, TG and LDL level were found to be low and that of HDL high on the day-0 as compared to those seen on the day 15. Change in the level of all the lipids was significant with the exception of LDL. Bezalip therapy also caused lowering of cholesterol, TG and LDL significantly but rise in HDL was quite small (comparison of BLP on day 15 and 30 in group b). Mild hypolipidemic response was observed in subjects of group c who were administered Lasona for fifteen days. Although the level of cholesterol TG and LDL was found to be low and that of HDL high on day - 0 (As a result of previous therapy with lopid) as compared with that seen on day 15 (as a result of lopid withdrawal) in group c subjects, the level was found to be significantly changed only for TG. lasona too caused significant lowering of TG (comparison of BLP on day 15 and 30 in group c).

Table 2 shows comparative difference in the blood level of different lipids arising as a result of hypolipidemic therapy.In order to judge which of the drug is more effective in keeping blood lipid level with in desired limits, the difference in the concentration of cholesterol, TG, HDL and LDL in blood between i) day - 0 and day 15 and ii) day 15 and day 30 has been calculated for all the groups. All the drugs produced a decrease in the level of cholesterol, TG and LDL and an increase in HDL level to a certain extent but the difference arising as a result of Mevacor therapy (decrease) was significantly greater for the concentration of cholesterol and LDL as compared with that produced as a result of lopid therapy, however for TG the difference was found to be greater as a result of lopid therapy.

In group b subjects, Bezalip also produced significantly greater difference of cholesterol and LDL concentration (decrease) as compared with lopid, although the value of difference in TG and HDL concentration was found to be just comparable to that seen as a result of lopid therapy.

In group c lasona produced much smaller changes in the concentration of blood lipids as compared with lopid.

Since the subjects in all the three groups were already on lopid, we assessed the hypolipidemic effect of lopid by comparing the lipid profile on the day of first contact (day - 0) and on the day 15 at the end of washout period. A sufficient rise in the level of cholesterol, TG and LDL was noted on discontinuing drug for fifteen days. Lopid is a well known hypolipidemic drug that stimulates HDL synthesis and increases the concentration of HDL apolipoprotein that can bind plasma lipids leading to decreased TG level (Samuel 1983 and Thompson 1984).

Bezalip which is also fibric acid derivative like lopid, has also shown hypolipidemic effect comparable to that seen with lopid in our subjects which were on normal Pakistani diet except that they were avoiding excessive fate intake. Our findings on lopid and Mevacor response were not much different from a number of studies conducted on these drugs for the[i]r hypolipidemic action (Faruqui et al., 1988; Havel et al., 1987 and Tikkanen et al., 1988). Although changes in lipid profile were also noted as a result of Mevacor therapy but Mevacor affected greatly the level of LDL and cholesterol in our subjects. Mevacor has been shown to interrupt cholesterol synthesis by inhibiting hydroxy methyl glutaryl Co. A reductase (Grundy 1988).

In this comparative study we have also included an indigenous medicine "Lasona" which is a garlic extract. Garlic is botanically named as Allium Sativum and belongs to family Lilliacae. It has been used in Indopak sub-continent since long as remedy for a number of ailments (Bordia et al., 1975). In human trials garlic has also been shown to have a protective effect against fat induced increases in serum cholesterol (Bordia et al., 1975, Konar and Jain 1978). In the present study hypolipidemic effect of Lasona seemed to be milder as compared with that of lopid, Mevacor and Bezalip, possibly because it was in crude form.

As shown by the level of various lipids at the end of washout period it appears that TG level was more elevated than other lipids in our subjects. Our data indicates that lopid can lower TG and raise HDL level more effectively than any of the drug used in this study, however in individuals with higher cholesterol and LDL level, Mevacor will be more suitable. Lasona can be used as prophylactic agent but its use in extreme con. ditions of hyperlipidemia will not be justified.

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Table 1
Blood lipid profile of the subjects on the day -0, day-15 and day-30

Subjects receiving Lopid atleast for the last fifteen days were given a washout-period of fifteen days at the end of which they were kept on Mevacor (group-a), Bezalip (group-b) and Lasona (group-c) for the next fifteen days. BLP was determined at the start and the end of each regime. Each value is the mean ± s.e.m. of the number of observations shown in parenthsis.

Subjects	Therapy	Day of BLP determination	(mg/d.l) Cholesterol	Triglycerides	H.D.L.	L.D.L.
Group a	Lopid (Previous drug)	0	265.16* ± 3.55 (6)	164.66* ± 9.66 (6)	49 ± 2.03 (6)	183.16 ± 5.74 (6)
"	No. drug (washout period)	15	291.83 ± 7.45 (6)	229.83 ± 16.48 (6)	46.16 ± 2.16 (6)	199.63 ± 7.43 (6)
"	Mevacor	30	210.16* ± 6.60 (6)	192.50 ± 10.60 (6)	48.50 ± 1.90 (6)	123.16* ± 6.76 (6)
Group b	Lopid (Previous drug)	0	228.40* ± 6.83 (5)	175.20* ± 10.02 (5)	44.80* ± 0.58 (5)	148.60 ± 7.90 (5)
"	No. drug (washout period)	15	259.00 ± 6.35 (5)	240 ± 16.69 (5)	41.60 ± 1.29 (5)	169.36 ± 8.20 (5)

Table continue . . .

Subjects	Therapy	Day of BLP determination	(mg/d.l) Cholesterol	Triglycerides	H.D.L.	L.D.L.
Group b	Bezalip	30	197* ± 8.33 (5)	184* ± 9.94 (5)	43.60 ± 1.07 (5)	116.36* ± 9.24 (5)
Group c	Lopid (Previous drug)	0	257.20 ± 7.3 (5)	142.20* ± 2.13 (5)	49.80 ± 1.56 (5)	178.80 ± 7.70 (5)
"	No. drug (washout period)	15	270 ± 7.06 (5)	187 ± 5.52 (5)	46.60 ± 1.63 (5)	185.96 ± 7.54 (5)
"	Lasona	30	248 ± 8.24 (5)	158* ± 5.22 (5)	47 ± 1.52 (5)	169.52 ± 8.84 (5)

*P < 0.05 As compared with the day-15 in each group of the subjects.
Day-0 = day of Ist contact/star of washout-period.
Day-15 = end of washout-period/start of Mevacor/Bezalip/Lasona therapy
Day 30 = end of Mevacor/Bezalip/Lasona therapy.
BLP = blood lipid profile.

Tabl 2
Change in the blood lipid profile of the hyperlipidemic subjects observed as a result of switch over from lopid to Mevacor Bezalip and Lasona

Subjects receiving Lopid atleast for the last fifteen days were given washout-period of fifteen days at the end of which they were kept on Mevacor (group-a), Bezalip (group-b) and Lasona (group-c) for the next fifteen days. Each value is the mean ± s.e.m. of the difference of blood-lipid profile observed as a result of hypolipidemic therapy. The number of observations is given in parenthesis.

Subjects	Drug Therapy	Day of BLP determination	(mg/d.l) Cholesterol (-)	Triglycerides (-)	H.D.L. (+)	L.D.L. (-)
Group a	Lopid (atleast fifteen days back from day-0)	day-0 & day-15	26.60 ± 3.45 (6)	65.16 ± 7.22 (6)	2.83 ± 0.31 (6)	16.50 ± 3.20 (6)
Group b	"	"	30.60 ± 2.87 (5)	65.20 ± 7.19 (5)	3.20 ± 0.86 (5)	20.80 ± 2.81 (5)
Group c	"	"	29.20 ± 3.99 (5)	45 ± 3.74 (5)	3.20 ± 0.37 (5)	26.40 ± 6.04 (5)
Group a	Mevacor (from day-15 to day-30)	day-15 & day-30	81.66* ± 4.38 (6)	37.33 ± 6.87 (6)	2.33 ± 0.33 (6)	76.50* ± 4.84 (6)
Group b	Bezalip (from day-15 to day-30)		62* ± 3.48 (5)	56.00 ± 7.24 (5)	2.00 ± 0.54 (5)	53.00* ± 2.50 (5)

Table continue . . .

Subjects	Drug Therapy	Day of BLP determination	(mg/d.l) Cholesterol (-)	Triglycerides (-)	H.D.L. (+)	L.D.L. (-)
Group c	Lasona (from day-15 today-30)		22 ± 1.78 (5)	29.60 ± 1.03 (5)	0.40 ± 0.24 (5)	16.80 ± 1.71 (5)

*P < 0.05 As compared with Lopid.
Day-0 = day of Ist contact/start of washout-period,
day-15 = end of washout-period/start of Mevacor/Bezalip/Lasona therapy,
day-30 = end of Mevacor/Bezalip/Lasona therapy.
BLP = blood lipid profile.
(-) = Difference resulting from decrease in the level.
(+) = Difference resulting from increase in the level.

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