ORIGINAL ARTICLE

To Study the Effects of Simvastatin on Lipid Profile in Obese Patients

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ABSTRACT
Simvastatin is a competitive inhibitor of HMG-CoA (3Hydroxy 3Methyl Glutaryl Coenzyme A) reductase. 20 male and 20 female obese patients were selected. The obese patients were re-examined three times i.e. before giving the simvastatin, then after 6 and 12 weeks. The patients were advised to take fat free diet and a morning walk. Serum Cholesterol, serum Triglycerides and serum Lipoprotiens (HDL, LDL) was carried out by Standard kit methods (Merck). This study shows that with use of Simvastatin serum cholesterol, serum triglycerides, and serum LDL-Cholesterol was reduced significantly and serum HDL-Cholesterol increased significantly in both sexes and causes weight reduction which may be due to low calorie diet and physical exercise. It is therefore concluded that Simvastatin shows significant lipid lowering effects and also reduced the body weight, if patients used calorie restricted diet with some morning walk.
Key Words: Simvastatin, Lipid Profile, Obesity.

INTRODUCTION
Simvastatin is a competitive inhibitor of HMG-CoA (3Hydroxy 3Methyl Glutaryl Coenzyme A) reductase. It was isolated from a mould, Penicillium citrinium, and identified as inhibitors of chlesterol biosynthesis in 1976 by Endo and colleagues[1]. Subsequently, it was established that statins act by inhibiting HMG-CoA reductase[2]. Since the approval of Lovastatin by the United States Food And Drug Administration (FDA) in 1987, five other statins have been approved. Two of these Pravastatin and Simvastatin, are chemically modified derivatives of Lovastatin.

HMG-CoA reductase mediates the first commited step in sterol biosynthesis. Simvastatin is structural analog of HMG-CoA intermediate that is formed by HMG-Co A reductase in the synthesis of Mevalonate[3]. HMG-CoA reductase inhibitors are effective in the prevention of cardiovascular events and regression of atherosclerotic lesions evaluated by angiography[4].

Simvastatin is a safe and efficacious lipid lowering drug. It is quite effective in reducing Low Density Lipoprotein (LDL) levels. The lowering of LDL-Cholesterol primarily is due to decrease in LDL particle number, although there also is a slight decrease in the cholesterol content of the LDL particle and a small decrease in VLDL Cholesterol. Triglyceride concentration also decline by 10-30% reflecting the decrease in VLDL levels. Of great importance is the fact that HDL-Cholesterol levels typically rise 8-10%. The most important adverse effects of Simvastatin are increases in hepatic transaminases in serum and myopathy[5].

PATIENTS AND METHODS
The present study of lipid profile was undertaken on 20 male and 20 female obese patients. In each case a detailed personal, past and family history was obtained and physical examination for body weight and blood pressure was recorded. Dose of Simvastatin was 10 mg/day at bed time. The data was collected and analysed by standard statistical methods.

The obese patients were re-examined three times i.e. before giving the simvastatin, then after 6 and 12 weeks. The patients were advised to take fat free diet and a morning walk. They were checked physically for weight and blood pressure and biochemical investigations. Effort was made to minimize the dropouts. Serum Cholesterol, serum Triglycerides and serum Lipoprotiens (HDL, LDL) was carried out by Standard kit methods (Merck).

RESULTS
The mean values of age, body weight and blood pressure at 0 week and after 6 and 12 weeks was noted in both sexes. (Table 1) It was observed that the mean age of the male patients was 32 years and in female patients was 34 years. Mean body weight at 0 week was 203 lbs, after six weeks it was 200 lbs and after 12 weeks of administration of Simvastatin it was 199 lbs in male patients, however in female patients mean body weight at 0

week was 199 lbs, after six weeks was 187 lbs and after 12 weeks of administration of Simvastatin it was 176 lbs. This showed a highly significant decrease in body weight (P<0.001) after use of Simvastatin in female patients. Mean blood pressure at zero week was 125/80 mm/Hg, after six weeks was 125/80 mm/Hg and after twelve weeks it was 120/80 mm/Hg in male patients, while in female patients it was 125/80 mm/Hg, after six weeks was 120/80 mm/Hg and after twelve weeks it was 120/80 mm/Hg.

Table 1: Mean age, body weight and blood pressure in male/female patients before (0 week) and after (6, 12 weeks) taking Simvastatin. Values expressed in mean + s.e.m. No. of cases in (parentheses).

Time Period	Male (20)			Female (20)		
	Age (Years)	Weight (lbs)	B.P (mmHg)	Age (Years)	Weight (lbs)	B.P (mmHg)
0 weeks	32.35 + 0.88	203.53+11.14	125.75/80.25 +1.16/+0.85	34.52+1.88	199.40+7.58	125.80/80.00 +4.53/+1.00
6 weeks	---	200.50+2.59	125.0/80.40 +1.04/+1.22	---	187.44+7.39	120.20/80.80 +1.33/+1.04
12 weeks	---	199.17+11.05	120.80/80.60 +0.92/+1.23	---	176.66+7.22**	120.80/80.40 +1.27/+0.97

** P< 0.001= Highly significant difference

The levels of serum cholesterol, serum triglyceride and serum lipoprotiens (HDL and LDL) in male obese patients at 0 week and after twelve weeks with Simvastatin was noted. (Table 2) This showed a significant reduction (P<0.001) in levels of Serum cholesterol, Serum LDL-Cholesterol and in serum triglyceride while serum HDL-Cholesterol was significantly increased (P<0.001) in male patients between 0-12 weeks.

Table 2: Level of serum cholesterol, HDL-Cholesterol, LDL-Cholesterol and serum triglyceride in obese male patients before (0 week) and after (12 weeks) with Simvastatin. Values expressed as mean±s.e.m. No of cases in parenthesis.

Parameters	0 Week (n=20)	12 Weeks (n=20)
Serum cholesterol (mg/dl)	240.28±3.55	215.52±4.00**
HDL-cholesterol (mg/dl)	25.55±0.49	35.29±0.71**
LDL-cholesterol (mg/dl)	201.72±3.23	160.86±3.50**
Serum Triglyceride (mg/dl)	170.88±7.72	122.88±5.00**

**P<0.001=Highly significant difference

The levels of serum cholesterol, HDL-Cholesterol, LDL- Cholesterol and serum triglyceride in obese female patients at 0 week and after twelve weeks with Simvastatin was noted. (Table 3) This showed a significant reduction (P<0.001) in levels of Serum cholesterol, Serum LDL-Cholesterol and in serum triglyceride while serum HDL-Cholesterol was significantly increased (P<0.001) between 0-12 weeks.

Table 3: Level of serum cholesterol, HDL-Cholesterol, LDL-Cholesterol and serum triglyceride in obese female patients before (0 week) and after (12 weeks) with Simvastatin. Values expressed as mean±s.e.m. No of cases in parenthesis.

Parameters	0 Week (n=20)	12 Weeks (n=20)
Total cholesterol (mg/dl)	245.50±4.30	225.20±4.90**
HDL-cholesterol (mg/dl)	30.00±0.60	39.90±0.75**
LDL-cholesterol (mg/dl)	200.50±5.20	165.60±5.00**
Serum Triglyceride (mg/dl)	115.50±3.00	93.22±1.50**

**P<0.001=Highly significant difference

DISCUSSION

In this study we assessed the change in lipid profile before and after giving Simvastatin. A no of studies[3,4,5,9] confirmed its inhibitory effect on HMG-CoA reductase.

It is confirmed by group of authors that life style changes are advocated as a first line of treatment for dyslipidaemia and obesity. They observed that with dietary control and exercise, there is 10 % reduction in body weight associated with 7.6 % reduction in LDL Cholesterol. They found that more intense life style intervention may be effective at improving blood lipids and quality of life[6]. Another study also found that a comprehensive life style intervention can substantially lower blood pressure in hypertensive adults[7]. It is reported[8] that daily walking reduces visceral adipose tissue areas and improves insulin resistance in obese subjects. Although Simvastatin is a safe and efficacious lipid lowering drug but it can cause myopathy syndrome[5].

This study shows that with use of Simvastatin serum cholesterol, serum triglycerides, and serum LDL-Cholesterol was reduced significantly and serum HDL-Cholesterol increased significantly in both sexes and is in accord with no of studies[4,10-12]. Reason being that Simvastatin `is a competitive inhibitor of HMG-CoA reductase. which mediates the first committed step in sterol biosynthesis[3].

An association of hyperlipidemia with obesity (increased body weight) was reported by no of studies[12,13]. Body weight was also checked during treating with Simvastatin. It was observed that although body weight was decreased in both sexes but significant difference ($P<0.001$) was observed in female patients. The effect of Simvastatin on reduction of body weight was not reported but it was observed that changes in lipid profile also effects body weight. It may be an insulin distinct resistance related metabolite syndrome characterized by dyslipidemia and obesity in both sexes[14].

Present study also observed the blood pressure of patients taking Simvastatin. It was observed that there is no remarkable change in blood pressure of patients of both sexes. Study is in accord with a study[15] which reported that Simvastatin promotes intracellular oxidant system, restoring endothelial function but not having any effect on blood pressure.

It is therefore concluded that Simvastatin shows significant lipid lowering effects and treatment with Simvastatin also reduced the body weight, if patients used calorie restricted diet with some morning walk. However a further study is needed to reach a better conclusion.

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