Original Article

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

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ABSTRACT

Simvastatin is a competitive inhibitor of HMG-CoA (3-hydroxy 3-Methyl glutaryl Coenzyme A) reductase.

Objective: Present study proposed that the lipid lowering effect of simvastatin may be enhanced, if it was taken with fat free diet and morning walk.

Study Design: Cross Sectional Study.

Place and Duration of Study: This study was conducted at Fatima Jinnah Medical College, Lahore for a period of six months from December 2009 to May 2010.

Patients and Methods: 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) were determined.

Results: 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. It was also observed that the fat free diet and some exercise causes weight reduction.

Conclusion: It is therefore concluded that simvastatin shows significant lipid lowering effects augment process of body weight reduction, if patients used calorie restricted diet with some morning walk.

Key Words: Simvastatin, Lipid Profile, Obesity.

INTRODUCTION

Simvastatin is lipophilic statin with a short half-life that is primarily metabolized by Cytochrome P450[1] (Robinson 2007). It is a competitive inhibitor of HMG-CoA (3Hydroxy 3Methyl Glutaryl Coenzyme A) reductase. The gene of HMG-CoA reductase may serve as a modifier gene for hypercholesterolemia in diabetic patients.[2](Ying).

HMG-CoA reductase mediates the first committed 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]. It is reported that HMG-CoA reductase inhibitors are effective in the prevention of cardiovascular events and regression of atherosclerotic lesions evaluated by angiography[4].

Simvastatin treatment significantly reduced circulating conjugated diene level and led to an increase in glutathione peroxidase activity. These effects were more pronounced in patients with combined hyperlipidemia than in hypercholesterolemia. The results suggest that simvastatin possesses certain antioxidant properties, which may contribute to its beneficial cardiovascular effect [5](Molka).

Simvastatin is a safe and efficacious lipid lowering drug. It is quite effective in reducing Low Density Lipoprotein (LDL) levels. It appears to be twice as effective as Lovastatin at doses of 40 mgs/day.[6] 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.

Simvastatin also inhibit intestinal cholesterol absorption and appears to offer significant therapeutic value. It is anticipated that this option will allow clinicians to optimize the management of dyslipidemia in high-risk patients, thereby further reducing the morbidity and mortality of cardiac disease[7] (Stein et).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%. However, the most important adverse effects of Simvastatin are increases in hepatic transaminases in serum and myopathy[8].

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. A singly dose therapy of Simvastatin 10 mg/day at bed time was taken by patients.

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).

Statistical Analysis: The data was collected and analysed by standard statistical methods using SPSS Computer Soft ware Program Version 9.

RESULTS

The mean value 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, 6 & 12 week was 203 lbs, 200 lbs and 199 lbs. However in female patients, mean body weight at 0, 6 & 12 weeks was 199 lbs, 187 lbs & 176 lbs respectively. This showed a highly significant decrease in body weight (P<0.001) after use of Simvastatin in female patients. Mean blood pressure at 0, 6, 12 weeks 125/80,125/80 & 120/80 mm/Hg in male patients respectively, while in female patients the mean blood pressure was 125/80, 120/80 & 120/80 mm/Hg respectively.

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..

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 were 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 week.

Table No. 1: Mean age, body weight and blood pressure in male/female patients before (0 week) and after (6, 12 weeks) taking Simvastatin+ changing life style.

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**

Table No. 2: Level of serum chol, HDL-Chol, LDL-Chol and serum triglyceride in obese male patients before (0 week) and after (12 weeks) with Simvastatin + changing life style.

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

Table No. 3: Level of serum chol, HDL-Chol, LDL-Chol and serum triglyceride in obese female patients before (0 week) and after (12 weeks) with Simvastatin + changing life style.

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 number of studies[3,4] confirmed its inhibitory effect on HMG-CoA reductase. An association of hyperlipidemia with obesity (increased body weight) was also reported by studies[9,10].

Present study tried to find out the effect of simvastatin in obese patients without instructing any fat free diet or changing of life style (routine morning work). It is found that although simvastatin showed a lipid lowering effect but there is a mild effect on body weight (data not shown). This study was a pilot study.

Later, study was designed to find out the lipid lowering effect of simvastatin along with the instructions of fat free diet and morning walk of 20-30 min. Present study was observed that although body weight was decreased in both sexes but significant difference ($P<0.001$) was only observed in female patients. It is confirmed by group of authors[11] 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. Another study[12] also found that a comprehensive life style intervention can substantially lower blood pressure in hypertensive adults. It is reported[13] that daily walking reduces visceral adipose tissue areas and improves insulin resistance in obese subjects. However, the effect of Simvastatin on reduction of body weight was not reported[14] 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[15]. This study shows that with the 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[4,5,10-16]. A lipid lowering effect of simvastatin also reportrd by a group of workers[17]. Reason being that Simvastatin `is a competitive inhibitor of HMG-CoA reductase. which mediates the first commited step in sterol biosynthesis[3]. On the other, a study[18] found that simvastatin reduced lipoprotein lipase and endothelial lipase expression, mechanism independent of HMG-CoA reductase inhibition. However a contradictory study found that monotherapy of statin fail to achieve cholesterol goal[19].

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[16] which reported that Simvastatin promotes intracellular oxidant any effect on blood pressure. Another study also found that the use of simvastatin did not incrementally lower blood pressure.[20]

CONCLUSION

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. However a further study is needed to reach a better conclusion.

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