

ORIGINAL ARTICLE

Study of Lipid Profile in Obese Individuals and the Effect of Cholesterol Lowering Agents on Them

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Abstract: *Objectives:* To study the effect of cholesterol lowering agents on lipid profile in obese patients. *Background:* Obesity leads to morbidity as well as mortality. There is usually increased level of total cholesterol, LDL- cholesterol, VLDL- cholesterol, triglycerides and decreased level of HDL- cholesterol in obesity. These are the risk factors for cardiovascular disease, hypertension, diabetes mellitus, pulmonary disorder and gall stones. *Method:* Thirty obese patients received treatment with Lovastatin along with dietary measures, compared with age and sex matched controls- before and after 6 weeks of therapy, presented in a table and results were analysed using student's "t" test (both paired and unpaired). *Result:* There was significant reduction in total cholesterol as well as LDL- cholesterol; HDL- cholesterol was also increased significantly. But triglycerides and VLDL- cholesterol showed small but significant increase. *Conclusion:* Cholesterol lowering agents like Lovastatin was quite effective when used long-term in dyslipidaemia in obesity towards reduction of risk factors for cardiovascular diseases, strokes, etc. Hypertriglyceridaemia should also be treated adequately.

Key Words: Obesity, Dyslipidaemia, Lovastatin therapy, Risk reduction.

Introduction

Obesity refers to excess of body-fat. It is due to greater energy intake compared with energy expenditure. Despite inbuilt feed back system, how energy intake becomes chronically disproportionate is not properly understood. It is difficult to study obesity because the abnormality is not a single disease and because the result of long-term follow up in large scale is not available in the existing literature. The knowledge that is available today is only a cross-sectional survey in the population. These reports indicate that fat content is greater in women than in men, and that a gradual increase in fat content of body occurs from the pre-pubertal age till the 6th or 7th decade of life after which there is decrement in fat content of the body. Available data also suggest that fat infants are more prone to become obese in adulthood in comparison with lean infants and also that obesity is not inevitable for those having higher body weight in relation to height, age and sex in the early years of life [1].

To consider complications, they may be due to obesity per se or due to metabolic defects. Obesity is second only to cigarette smoking as the leading cause of preventable death in the United States [2]. It has also been reported that with massive obesity there is an increased prevalence of cardiovascular disease, hypertension, diabetes mellitus, pulmonary disorder and Gall stones [1].

The metabolic defects that ensue in obesity include increased levels of free fatty acids resulting from insulin resistance, increased LDL-cholesterol, VLDL and triglycerides and decrease in HDL-cholesterol. It is most likely that presentation of increased free fatty acids to liver as a function of obesity is primarily responsible for over production of VLDL and this is probably the key to increased LDL via the sequence: VLDL → intermediate density lipoprotein (IDL) → LDL [3]. VLDL production has also been shown to be directly related to insulin levels [4] and per cent body fat [5].

Aims and Objectives: Apart from achieving durable weight loss an attempt should be made for safe and efficacious drug therapy to combat risks associated with obesity. Recent reports, Blankenhorn et al [6] & Jukema et al [7] indicate that the statin group of drugs such as Lovastatin, Pravastatin and Simvastatin may be useful for this purpose. Out of them Lovastatin has been found to be well tolerated in the elderly patients as well as in postmenopausal women [8]. It is possible that by reducing serum cholesterol level, Lovastatin is likely to bring back lipid profile of an individual towards normalcy, thereby reductions in the risks related to obesity.

Material and Methods

The present study of the effect of Lovastatin, a cholesterol lowering agent, on serum lipid profile (viz. cholesterol, TG, HDL, LDL and VLDL) was carried out on obese patients who attended the Endocrinology out patient department of SSKM Hospital, Kolkata. Control individuals were collected from the neighbourhood. The selection of the cases was at random aged between 40 and 60 years (both male and female), some of them having uncontrolled hypercholesterolaemia with or without any cardiovascular disease. Prior screening of the hypercholesterolaemic subject was done from the Biochemistry laboratory of the said hospital. Similar number of age-matched controls without any systemic disease was chosen. Subjects of this experiment were comprised of 30 obese individuals and same number of control. Each case was offered 20 mg of Lovastatin tablet daily with evening meal for a period of six weeks and the controls received only placebo therapy for the same period during that hour.

Criteria for selection of cases: Body weight more than 20% of the standard as determined by Broca's Index (Height in cm. minus 100) having serum cholesterol more than 200mg/dl. despite conventional measures like dietary restrictions and regular physical exercise.

Sample collection, preparation and general procedures:

Criteria and precautions-

- Fasting serum was collected because after meal FFA and triglycerides might increase.
- Rest for 30 minutes, since exercise might affect lipid concentrations.
- Prolonged tourniquette application was avoided, because it might increase plasma lipid concentration.

About 8.0 ml. of venous blood was collected in a glass tube without additives which was then allowed to clot at room temperature. Serum fraction was separated after centrifugation, kept in the deep freeze at -20°C for longer storage. Estimations were carried out on those sera by enzymatic assays, and optical densities were measured with the help of spectrophotometer with appropriate filter. Highly lipaemic or haemolysed sample was discarded altogether. Repeated freezing and thawing was avoided as far as practicable. For analysis student's 't' test (both paired and unpaired) was applied. Fisher's Table gave the values of 't' which were exceeded with the given probabilities of different degrees of freedom. Probability of 0.05(5%) was considered as the critical level of significance.

Results

The results of the study have been presented in the following table.

Table: Effect of Lovastatin treatment on serum Cholesterol, Triglyceride, LDL, VLDL and HDL levels in obese patients (Mean \pm SE)

SL. No.	Experimental situations	Serum Cholesterol (mg/dl.)	Serum Triglyceride (mg/dl.)	LDL (mg/dl)	VLDL (mg/dl.)	HDL (mg/dl)
I	Control	190.16 \pm 11.04	160 \pm 8.97	112.66 \pm 11.70	32 \pm 1.82	45.50 \pm 6.41
II	Lovastatin treatment before therapy	231.20 \pm 5.60	189.90 \pm 7.93	162.36 \pm 5.18	37.90 \pm 1.59	30.90 \pm 1.89
III	Lovastatin treatment after 6 weeks of therapy	193.70 \pm 8.80	193.80 \pm 8.79	111.18 \pm 10.99	38.70 \pm 1.97	44.18 \pm 0.30

Statistical Analysis- 't' Value

SL. No.	Situations	't' value and probability (P)	't' value and probability (P)	't' value and probability (P)	't' value and probability (P)	't' value and probability (P)
I	Between control and Lovastatin treatment before therapy	t = 18.07 P < 0.001	t = 13.60 P < 0.001	t = 2.14 P < 0.001	t = 5.95 P < 0.001	t = 8.69 P < 0.001
II	Between control and Lovastatin treatment after 6 weeks of therapy	t = 1.46 P > 0.10; NS	t = 14.80 P < 0.001	t = 0.57 P > 0.10; NS	t = 6.44 P < 0.001	t = 0.53 P > 0.10; NS
III	Between Lovastatin before therapy and 6 weeks after therapy	t = 2.34 P < 0.05	t = 2.66 P < 0.05	t = 2.41 P < 0.05	t = 2.65 P < 0.05	t = 2.25 P < 0.05

In the Table serum cholesterol, serum Triglyceride, LDL, VLDL and HDL levels have been shown in control and in obese patients (both men and women), before Lovastatin and after 6 weeks of Lovastatin therapy.

Discussion

In view of hyperlipidaemia and hypercholesterolaemia that occur in obesity, it is a risk factor for atherosclerosis. In fact, obesity is associated with an increase in the incidence of coronary heart disease, congestive heart failure and strokes [9]. In the present experiment an attempt has been made to study the effect of Lovastatin on lipid profile in clinically obese patients. It can be seen that total serum cholesterol level in clinically obese people (both men and women) could be reduced by Lovastatin therapy over a period of 6 weeks. However, serum triglyceride level did show a little but significant increase following Lovastatin treatment. These changes have been compared with the serum cholesterol and serum triglyceride levels in non-obese control people (both men and women) of identical age group. It is interesting to note that the reduction in total cholesterol level has a tailing effect on LDL cholesterol because following Lovastatin therapy for 6 weeks in clinically obese individuals the LDL cholesterol has come down to a large extent and the value is almost identical with the serum LDL cholesterol level in non-obese normal individuals. On the other hand, serum HDL fraction which was low in obese individuals in comparison with the non-obese persons has gone up almost to the level of serum HDL concentration in non-obese individuals. Serum VLDL concentration, however, had increased to a small but significant extent.

The National Cholesterol Education Program (USA) has suggested that total cholesterol less than 200 mg/dl and LDL cholesterol less than 130 mg/dl are desirable levels for any individual. In our case mean serum cholesterol level was found to be 231.20 mg/dl in clinically obese people and serum LDL cholesterol was found to be 162.36 mg/dl. The HDL level in these obese individuals was 30.90 mg/dl which was quite low in comparison with the level of serum HDL concentration in non-obese control individuals. While following Lovastatin treatment the serum HDL concentration had almost reached to the level as in non-obese control individuals. As stated before, liver secretes cholesterol involving endogenous pathway and carried in VLDL which is then converted to LDL by capillary enzymes. In our case VLDL concentration in obese individuals was found to be more in comparison with the non-obese control persons. Whereas following Lovastatin treatment it had increased further to a small but significant extent. However, LDL cholesterol declined significantly. All these observations indicate that the obese individuals were at risks for development of atherosclerosis and coronary heart disease. Following Lovastatin treatment the alteration in serum total cholesterol, triglyceride, LDL, HDL and VLDL levels were mostly suggestive of reaching beyond risk line. Furthermore, the role of total cholesterol, LDL and HDL has been well described in the initiation and propagation of atherosclerosis. Epidemiologic data link diets high in saturated fat to the development of dyslipidaemia and CAD. Conversely, therapy with statins simultaneously reduces both plasma LDL and cardiac event rates [10].

Unlike other risk factors for heart disease, LDL is found both within atherosclerotic plaque and in plasma as oxidised LDL, a form which stimulates macrophages and initiates inflammatory events within the vessel intima [11]. Current NCEP guidelines, therefore, recommend the therapeutic manipulations of LDL to levels below 100 mg/dl and preferentially to levels of 70 mg/dl in patients at high risk of cardiac events. It is important to note that a recent study confirmed that pure reduction of LDL is insufficient for the amelioration of CAD; rather, obesity and hypertriglyceridaemia must also be adequately and concurrently treated to prevent cardiac events [12]. Similarly, lifestyle changes regarding diet and exercise are important cornerstones for the control of LDL [13]. What is evident from the study is that Lovastatin treatment for a minimum period of 6 weeks could alter the lipid profile of both men and women so much that they were converted from high risk group prone to develop coronary heart disease to a low risk one. Of course, larger trials will throw more light to strengthen this view.

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