Changes in plasma high-density lipoprotein cholesterol concentration after weight reduction in grossly obese subjects

D A STREJA, E BOYKO, S W RABKIN

Summary and conclusions

Changes in serum lipoproteins associated with weight loss were assessed in 13 grossly obese (relative weight 183%) patients who had participated in an outpatient semi-starvation diet consisting of liquid protein and carbohydrate. At the follow-up examination an average of six and a half months after the start of refeeding the mean weight loss was 16·1±4·5 kg or 15% of initial body weight. Significant increases in high-density lipoprotein (HDL) cholesterol of 0·16±0·05 mmol/l (6±2 mg/100 ml) and decreases in triglycerides (0·8±0·23 mmol/l; 73±20 mg/100 ml) and fasting blood sugar (0·6±0·22 mmol/l; 11±4 mg/100 ml) were observed. Changes in HDL cholesterol correlated significantly with changes in weight (r=0·667) and percentage change in weight. The intercept of the regression equation relating HDL cholesterol to percentage change in weight was −7·3, indicating that a change in HDL cholesterol greater than zero required a weight loss of at least 7·3% of body weight.

Thus, weight loss can significantly increase HDL cholesterol concentrations but a considerable amount of weight must be lost to produce a significant increase in HDL cholesterol concentration.

Introduction

The relation between atherosclerosis and serum cholesterol concentration is a function of the distribution of cholesterol between the different lipoproteins. Atherosclerosis and premature cardiovascular disease are associated with low concentrations of high-density lipoprotein (HDL) cholesterol and increased concentrations of low-density lipoprotein (LDL) cholesterol.[1-4]

A negative association between HDL cholesterol concentrations and indices of obesity have been reported in several population studies.[3 5-8] But there is little data on the extent to which HDL cholesterol concentrations can be modified by weight reduction. We investigated the changes in serum HDL cholesterol concentration in grossly obese patients who had participated in an outpatient programme for weight reduction.

Patients and methods

Longitudinal, follow-up data were obtained from 13 patients, (10 women and 3 men) aged 20 to 36 years, with a mean weight 183·1% of ideal who had been enrolled in a weight-reduction programme using a liquid protein and carbohydrate low energy diet (table I). All patients were informed of the reports of sudden death on diets using liquid protein alone[9] and gave informed written consent to participate. People entered the programme if they were grossly overweight and had no cardiovascular, renal, liver, or thyroid diseases.

TABLE I—*Characteristics of the grossly obese patients. Values are means ± SE*

Characteristic	Value	Characteristic	No of patients
Age (years)	29·0±1·3 (range 20-36)	Onset of obesity:	
Sex	10 F, 3 M	Infancy	7
Relative weight (%)*	183·1±5·1	Childhood	3
Body mass index (kg/m²)	40·6±1·1	Adolescent	2
Serum lipoproteins (mmol/l)		Adult	1
Triglycerides	2·17±0·35	Cigarettes smoked:	
Total cholesterol	4·92±0·36	None	10
LDL cholesterol	3·06±0·23	10 a day	2
HDL cholesterol:	1·01±0·05	20 a day	1
Men	1·04±0·05		
Women	0·96±0·08		
Fasting blood sugar (mmol/l)	6·33±0·78		
Urate (mmol/l)	0·37±0·02		

*Relative weight = body weight/ideal weight × 100 (ideal weight taken from life insurance tables).

Conversion: SI to traditional units—Triglycerides: 1 mmol/l ≈ 88·5 mg/100 ml. Cholesterol: 1 mmol/l ≈ 38·6 mg/100 ml. Blood sugar: 1 mmol/l ≈ 18 mg/100 ml. Urate: 1 mmol/l ≈ 17 mg/100 ml.

At enrolment all patients underwent a medical interview, physical examination, blood biochemistry estimations (fasting blood glucose, urea nitrogen, creatinine, aspartate aminotransferase, alkaline phosphatase, serum albumin and globulin, and thyroxine concentrations), chest *x*-ray examination, and electrocardiography. Because of our concern about cardiac complications from the diet, patients also had to complete satisfactorily an exercise electrocardiographic stress test and six-hour ambulatory electrocardiographic monitoring.

After completion of the programme the participants returned for remeasurement of body weight, serum lipoproteins, fasting blood glucose, and urate. Many had regained weight lost during the programme so that the change in weight did not represent the maximum weight loss attained.

At reassessment the patients' body weight were basically stable with little recent change. Detailed dietary histories were not obtained, but most patients reported that the major dietary change was a reduction in calories consumed, though some also indicated a reduction in the percentage of carbohydrate consumed.

The programme had three stages. The first or preparatory stage consisted of six visits to the nutritionist and two to the doctor. Some basic concepts of nutrition and self-control strategies were discussed. The patient was told what the diet entailed and his resolve was ascertained. The second phase, during which the patients followed the diet, lasted two to eight months. During this time they visited the doctor once a week for six weeks and once every two weeks thereafter. At every visit blood was drawn for electrolyte estimation. Electrocardiography was done if bradycardia (< 50 beats/min) or an irregular pulse was detected on clinical examination or a history of palpitations was obtained. During the third phase of the programme, when food was gradually reintroduced, the patients visited a nutritionist each week. The diet was 2·5 MJ (600 kcal) for women and 3·8 MJ (900 kcal) for men. It consisted of equal parts of protein and carbohydrate taken by reconstituting a powder. The protein was a combination of equal parts of milk and soya-bean protein. Daily vitamin and mineral supplementation throughout the programme included the following: a minimum of 35 mmol (mEq) potassium chloride, magnesium hydroxide 300 mg, zinc 10 mg, vitamin B_1 75 mg, vitamin B_2 45 mg, niacinamide 45 mg, vitamin B_6 3 mg, vitamin B_{12} 14 mg, calcium D-pantothenate 15 mg, folic acid 100 µg, vitamin C 150 mg, vitamin A 10 000 IU, vitamin D 400 IU, calcium 125 mg, phosphorus 125 mg, iron 10 mg, magnesium 50 mg, and copper 1 mg.

Lipoprotein assessment—A sample of blood was obtained after a

Departments of Medicine and Social and Preventive Medicine, University of Manitoba, Winnipeg, Manitoba, Canada

D A STREJA, MD, FRCP(C), assistant professor, department of medicine
E BOYKO, RD, health sciences centre
S W RABKIN, MD, FRCP(C), associate professor, departments of medicine and social and preventive medicine

14-hour overnight fast. The serum was separated and assayed for triglycerides by the method of Kessler and Lederer,[10] for total cholesterol and LDL cholesterol by the method of Bronzert and Brewer[11] using the Beckman lipoprotein profiling system (Beckman Co, Palo Alto, California), and for HDL cholesterol using the cholesterol method after precipitating with manganese-heparin.[12] Biochemical analysis was done on blood obtained before patients entered the programme and an average of 202·7±(SEM) 34·4 days after refeeding had been started.

Results

At the follow-up examination one patient had lost more than 40 kg, three 30-40 kg, two 20-30 kg, two 10-20 kg, and two 1-10 kg and three patients had gained 0·5-5 kg. The group as a whole had a significant weight loss of 16·1 kg or 15% of body weight (table II). A significant increase in HDL cholesterol and decrease in triglyceride and fasting blood sugar concentrations were noted. There were no significant changes in total cholesterol, LDL cholesterol, or urate concentrations.

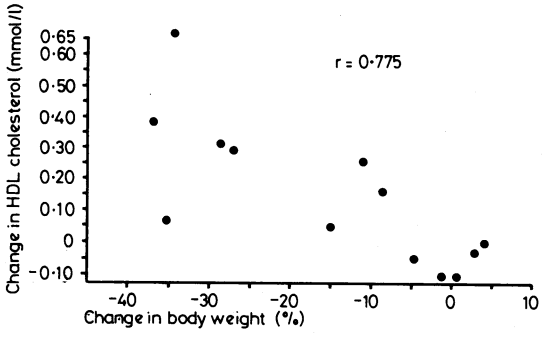
TABLE II—*Changes in body weight and biochemical data between entry into the programme and after return to regular diet.*

	Change in value	p Value
Body weight (kg)	16·1±4·5	<0·001
Triglycerides (mmol/l)	−0·83±0·23	<0·005
Total cholesterol (mmol/l)	−0·16±0·31	NS
LDL cholesterol (mmol/l)	+0·23±0·26	NS
HDL cholesterol (mmol/l)	+0·16±0·52	<0·01
Fasting blood sugar (mmol/l)	−0·61±0·22	<0·01
Urate (mmol/l)	−0·02±0·018	NS

TABLE III—*Correlation between change in weight and change in biochemical data.*

Change in:	Cholesterol			Triglycerides	Fasting blood sugar	Urate
	Total	HDL	LDL			
Change in weight:	0·348	−0·667*	0·265	0·308	0·120	0·321

*p<0·01



Relation of change in serum HDL cholesterol to percentage change in body weight.

Conversion: SI to traditional units—HDL cholesterol: 1 mmol/l≈38·6 mg/100 ml.

There was significant negative association (r= −0·667, p<0·01) between weight loss and change in HDL cholesterol but not between weight loss and the other biochemical data (table III). The correlation between change in HDL cholesterol concentration and weight loss was stronger when weight loss was considered as a percentage of initial body weight (r=0·775, p<0·005). The regression equation relating change in HDL cholesterol concentration to percentage change in weight indicated that zero change in HDL cholesterol concentration was associated with a 7·3% change in body weight (see figure).

Change in serum triglyceride concentration correlated significantly with changes in HDL cholesterol concentration (r= −0·546, p=0·03) and LDL cholesterol concentration (r=0·513, p=0·04).

Discussion

The increased incidence of cardiovascular disease and mortality in obese people[13 14] is accentuated in the massively obese.[15] This has stimulated the use of new, sometimes radical, approaches to the treatment of "morbid" obesity. A low-energy protein diet became popular because it is an effective method of losing weight,[16 17] though the sudden deaths of some people on this diet[9 18] have limited its usefulness. The diet we used consisted of a mixture of protein and carbohydrate. This kind of mixed diet has recently been shown to be as effective in reducing weight as a pure protein diet but is much safer in that there is less depletion of body sodium and much less derangement in the activity of the sympathetic nervous system.[19]

What little data there is on the effect of weight loss on serum HDL cholesterol concentration is inconclusive, partly because of differences in the patients studied, the programmes used, and the weight loss obtained. The multiple risk factor intervention trial in the United States reported that the intervention group showed an inverse correlation between change in body weight and change in HDL cholesterol concentration.[20] The correlation was small (r= −0·12) but significant, perhaps because of the large size of the sample (1084 men). The intervention group, however, in addition to recommendations for weight reduction, also received recommendations to change the proportion of saturated to polyunsaturated fats in the diet, to stop smoking, and to use drugs and diet to counter hypertension. Thus, the results of this study cannot be used to evaluate the hypothesis that weight loss alone can change HDL cholesterol concentration. One of the participating centres in this trial reported no significant difference between the change in HDL cholesterol concentration in its intervention (n=154) and control (n=147) groups and no significant correlation between change in weight and change in cholesterol concentration.[21]

Wilson and Lees[22] studied five obese men with type IV hyperlipoproteinaemia with a pronounced reduction in HDL cholesterol concentration and reported that a 12% weight loss was associated with a significant increase in HDL cholesterol concentration. We have reported that a 5·8% decrease in body weight in 65 mildly obese subjects (relative weight 125%) was not associated with a significant increase in HDL cholesterol concentration.[23] Our present study, however, showed that a considerable weight loss, 15% of body weight, in grossly obese subjects was associated with a significant increase in HDL cholesterol concentration. Furthermore, weight had to fall by more than 7% of body weight before concentrations of HDL cholesterol rose. This feature may explain our previous findings[23] as well as those of Wilson and Lees.[22]

It may be difficult to extrapolate our present findings to people with more moderate obesity using conventional reducing diets because they do not have as great a proportion of their body weight consisting of adipose tissue and they seldom experience such a large weight loss. If moderately obese subjects do lose a lot of weight, however, we believe that similar changes in lipoprotein concentrations would ensue. Thus our findings suggest that if reduction in body weight is being used as a single strategy to change HDL cholesterol concentrations then the subjects will have to lose a considerable amount of weight to produce a significant increase.

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Primary biliary cirrhosis: an epidemiological study

DAVID R TRIGER

Summary and conclusions

A three-year study (1977-9) of primary biliary cirrhosis in the city of Sheffield disclosed 34 cases, a point prevalence of 54 per million population. Closer inspection showed an apparent clustering of cases, and the prevalence in relation to one water reservoir appeared to be more than ten times that of the other reservoirs. Nevertheless, analyses of the water showed no significant relevant differences between the reservoir serving areas with a high prevalence of cirrhosis and other reservoirs.

Despite the inconclusive results of the water analyses, these findings do suggest that an environmental agent may be a cause of primary biliary cirrhosis and that further epidemiological studies may help to elucidate the cause.

Introduction

Primary biliary cirrhosis is a rare disorder of unknown cause. Although large series of patients with the disease have been reported,[1 2] these have come from major referral centres and have been based on the experience of many years. Little information, however, has been published on the epidemiology of this disease. This paper reports a study on the prevalence of the disorder in the city of Sheffield and also examines factors which may contribute to the cause of primary biliary cirrhosis.

Department of Medicine and Gastrointestinal Unit, Royal Hallamshire Hospital, Sheffield S10 2JF

DAVID R TRIGER, DPHIL, FRCP, senior lecturer in medicine

Patients and methods

All physicians in Sheffield's two major hospitals (the Royal Hallamshire and Northern General Hospitals) were asked to report any patients with proved or suspected primary biliary cirrhosis who were alive at any time from 1 January 1977 to 31 December 1979. In addition all cases in which antimitochondrial antibodies had been reported by the immunology department at the Royal Hallamshire Hospital (the sole immunology laboratory for the city) were followed up by reference to the clinical records. The diagnosis of primary biliary cirrhosis was established on a combination of clinical, biochemical, serological, and histological criteria as defined by Klatskin and Kantor.[1] Liver biopsy results were available for all patients except two elderly women in whom the procedure could not have been ethically justified but in whom all other features were entirely consistent with the diagnosis. Three patients died before the histological diagnosis was established, but necropsy material was available. All the other data in this paper were derived from interviewing the remaining patients, specifically for this project.

The interview was to confirm that the clinical spectrum of the patients under study was comparable with that reported elsewhere for primary biliary cirrhosis and also to examine any possible environmental, genetic, and social characteristics. The study was restricted to patients living within the city boundary since areas adjacent to the city lay within the catchment areas of other hospitals.

Information on the population distribution within the city was obtained from the 1971 census. Data on the water supply to domestic households was provided by the Yorkshire Water Authority (Southern Division), which also provided information on the water analysis of the reservoirs supplying the city, based on regular routine checks. Further analysis of reservoir water for specific trace elements was carried out by Dr D R Ineson of the Department of Geology, Sheffield University, by atomic absorption spectrophotometry using both flame and heated