SHORT COMMUNICATION

Associations between sex hormones, thyroid hormones and lipoproteins

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Summary

1. A study of 150 middle-aged male industrial employees has shown significant positive correlations between plasma levels of high-density-lipoprotein (HDL) cholesterol and both serum testosterone and alcohol intake, and significant negative correlations between HDL cholesterol and both serum thyroxine and obesity. These associations persist when examined by multiple linear regression, indicating their independence.

2. Significant positive correlations are also shown between plasma triglyceride levels and both obesity and serum thyrotropic hormone (TSH) levels.

3. There are no evident relationships between serum oestrone or oestradiol and either HDL cholesterol or triglyceride levels, nor between any of the hormones and either total or low-density-lipoprotein (LDL) cholesterol.

4. Because of the potential importance in relation to coronary heart disease prevention, further studies are needed to try and understand the mechanisms of the associations between HDL cholesterol and obesity, alcohol intake and thyroid and sex hormone levels.

Key words: lipoproteins, sex hormones, thyroid hormones.

Abbreviations: HDL, high-density-lipoprotein; LDL, low-density-lipoprotein; TSH, thyrotropic hormone.

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Introduction

After a suggestion that testosterone might be a risk factor for coronary heart disease in men [1], a case-control study indicated that men with coronary heart disease had slightly higher testosterone levels than control subjects (although the difference was not significant) [2]. Previous studies had shown that injections of synthetic androgens alter plasma lipid levels, producing a reduction in high-density-lipoprotein (HDL) cholesterol [3]. Since low HDL cholesterol levels are associated with a high risk of coronary heart disease [4] we considered the possibility that any adverse influence of testosterone on coronary heart disease might be mediated through an effect on HDL cholesterol. The present study was set up to explore any relationship between sex hormone levels and lipid levels in a sample of middle-aged men. Measurements were also made of thyroid function, in view of evidence that patients with both hypo- and hyper-thyroidism have altered lipoprotein metabolism [5].

Methods

Participants in one of the industrial groups in a study of the prevention of coronary heart disease [6] were eligible to take part if they were still in employment (8 years after the start) and if they had attended a cardiovascular screening examination 2 years before the present study. Those who were free of coronary heart disease at this examination (having no past history or chest pain symptoms and a normal ECG) were asked to visit the factory medical department in the...
morning after having either fasted or had a breakfast free of fat and dairy produce. A blood sample was taken, spun and separated the same day; 5 ml of serum was stored at -20°C until total testosterone, oestrone, oestradiol, thyrotropic hormone (TSH) and thyroxine measurements were made by radioimmunoassay as described previously [7-10]. A 5 ml sample of plasma was stored at 4°C until total cholesterol, HDL cholesterol, low-density-lipoprotein (LDL) cholesterol and triglycerides were measured (within a week of venepuncture) as described previously [11]. A self-administered questionnaire, completed before venepuncture, included a question about the amount of alcoholic drinks consumed during the previous week; this was converted to grams of alcohol.

Statistical analyses involved simple regression techniques to assess the relationships between the different variables measured. In addition, multiple linear-regression models were fitted to the data, with the GLIM package programme [12], to assess the independence of the relationships between the different measured variables.

Results

Of the 253 men who had attended the screening examination 2 years previously, 38 had died or left employment by the time of this survey and 150 men attended (70% of the possible attenders). Those who attended this survey were significantly lighter, less likely to be cigarette smokers and less likely to come from social classes IV and V than those who were still in employment but did not participate.

Over the age-range represented by the study participants (47-64 years) there is no significant association between age and any of the hormone or lipid levels, nor is there any suggestion of an effect on hormone or lipid levels of cigarette smoking or social class. There are, however, associations between obesity (measured by body-mass index, weight/height$^2$) and serum testosterone, oestradiol, HDL cholesterol and triglyceride concentrations (Table 1). Fatter people have higher levels of oestradiol and triglycerides and lower levels of testosterone and HDL cholesterol. Table 1 also shows that increasing alcohol intake is associated with high HDL cholesterol and low thyroxine levels. Those consuming an average of more than 60 g of alcohol/day (9% of these men) also have raised plasma triglyceride levels, but a relationship is not seen over the whole range of alcohol intake.

The crude correlations between lipid and hormone levels (Table 1) indicate a positive association between testosterone and HDL cholesterol levels and a negative association between thyroxine and HDL cholesterol. TSH also shows a negative correlation with HDL cholesterol, but this does not reach statistical significance. In each case there is a correlation between hormone and triglyceride levels which is in the opposite direction to that with HDL cholesterol, but significance is reached only in the case of TSH.

Entering each of the hormones, age, body-mass index and alcohol intake into a multiple linear-regression model, with each of the lipids in turn as the dependent variable, confirms that body-mass index, alcohol intake and testosterone and thyroxine levels each have a significant and independent association with HDL cholesterol, whereas body-mass index and TSH have an independent association with triglyceride levels.

Oestrone and oestradiol do not show an association with HDL cholesterol or triglycerides; nor do they affect the association with testosterone. None of the hormones appears to be correlated with total or LDL cholesterol levels. Nearly half of the variance in HDL cholesterol (42%) and nearly a third of the variance in

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triglycerides (32%) can be explained by the eight variables entered into the multiple regression model.

Discussion
The results of the present study relate to male middle-aged industrial employees, working in the same factory for at least 8 years, who were thought to be free of coronary heart disease. Under-represented in this study are smokers, the overweight and those of social classes IV and V, and the possibility of generalizing from these results should be influenced by this. Smoking and social class do not influence any other measured variables, but obesity is strongly related to many of the measured lipids and hormones: in the statistical analyses we have tried to take account of this.

We confirm previous observations on the relationship of obesity with HDL cholesterol [4] and triglyceride levels [13], and of alcohol intake with HDL cholesterol [14] (and with triglycerides at high alcohol intake). We also find an inverse association between plasma thyroxine and both alcohol intake and HDL cholesterol. Neither of these relationships with thyroxine were predicted before the study and both need independent confirmation.

The positive association between testosterone and HDL cholesterol is in the opposite direction to the one predicted, but has been found elsewhere [15]. This finding weakens the original hypothesis that the serum testosterone concentration is a risk factor for coronary heart disease [1] in view of the 'protective' effect of high HDL cholesterol levels [4]. It is also surprising in view of the higher HDL levels in women than in men [4]; in this male population oestrogens had no influence on HDL cholesterol nor on the testosterone/HDL relationship.

These cross-sectional associations do not allow an understanding of any possible mechanisms; nor of whether a change in any of the variables would be followed by a change in lipid levels within individuals. HDL cholesterol does, however, appear to have a close association with obesity, alcohol intake, and thyroid and sex hormone levels. Further studies are indicated to elucidate the metabolic mechanisms underlying these associations, in view of their potential importance in relation to coronary heart disease prevention.

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References