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The Incidence of Plasma Insulin, Blood Sugar and Serum Lipid Abnormalities in Patients with Atherosclerotic Disease

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Summary. The incidence of abnormalities of fasting serum cholesterol and triglyceride levels and blood sugar and plasma insulin response to an oral glucose load have been investigated in a group of 51 male patients with atherosclerotic peripheral vascular disease. These have been compared with an age and sex matched group of 47 healthy controls. Both groups showed a similar degree of obesity. The most common single abnormality was a prolonged and increased plasma insulin response, which was much more frequently seen among patients than controls. Over 75% of the patients showed abnormality of blood sugar or insulin response. Elevation of fasting levels of serum lipids was considerably less common, although the mean serum cholesterol level of the patients was significantly higher than that of the controls. The relevance of these results is discussed.

Fréquence des anomalies de l'insuline plasmatique, de la glycémie et des lipides du sérum chez des patients atteints d'athérosclérose

Résumé. Les auteurs présentent leurs observations sur la fréquence du taux anormal de cholestérol et de triglycérides sériques et sur les réponses anormales du glucose sanguin et de l'insuline provoquées par le test de tolérance au glucose chez 51 patients de sexe masculin présentant des troubles athérosclérotiques des vaisseaux périphériques. La comparaison des résultats relevés dans ce groupe avec ceux d'un groupe de 47 témoins strictement comparables par l'âge et le sexe a été faite. Les deux groupes présentaient un même degré d'obésité. L'anomalie la plus fréquente était une réponse de l'insuline du plasma plus prolongée et plus prononcée. Cette réponse était beaucoup plus fréquente chez les athérosclérotiques que chez les sujets normaux. Plus de 75% des malades ont montré une anomalie du taux de glucose sanguin ou de la réponse de l'insuline. Une augmentation du taux des lipides sanguins à jeûn était beaucoup plus rare bien que le taux moyen de cholestérol sérique ait été nettement supérieur à celui des sujets témoins.

Die Häufigkeit von Anomalien des Plasmainsulins, der Glykämie und der Serumlipide bei Atherosklerotikern

Zusammenfassung. Die Autoren berichten über die Häufigkeit von Anomalien der Nüchternwerte von Serumcholesterin und Serumtriglyzeriden und über anormale Blutzucker- und Plasmainsulinreaktionen nach einem oralen Glucosebelastungstest bei 51 männlichen Patienten mit atherosklerotischen peripheren Gefäßkrankheiten. Sie verglichen diese Befunde mit 47 gesunden Personen in einer nach Alter und Geschlecht vergleichbaren Gruppe. Die beiden Gruppen wiesen einen ähnlichen Grad von Adipositas auf. Die häufigste Anomalie war eine verlängerte und erhöhte Plasmainsulinreaktion, die viel häufiger bei den Atherosklerotikern als bei den Kontrollen vorkam. Über 75% der Patienten zeigten anormale Blutzucker- oder Insulinreaktionen. Eine Erhöhung der Nüchtern-Serumlipidwerte trat viel seltener auf, obwohl die mittleren Serumcholesterinspiegel bei den Atherosklerotikern signifikant höher lagen als bei den Kontrollen.

Key words: Blood sugar response, plasma insulin response, serum cholesterol, serum triglyceride, atherosclerosis.

Introduction

Abnormalities of lipid and carbohydrate metabolism in patients with atherosclerotic disease has been subject to considerable investigation. Kannel *et al.* (1964) showed an association between raised serum cholesterol levels and the incidence of ischaemic heart disease. Juergens *et al.* (1960) noted similar findings in atherosclerotic peripheral vascular disease. Albrink *et al.* (1961) emphasized the association between ischaemic heart disease and raised serum triglyceride levels.

Keen *et al.* (1965) noted the prevalence of atherosclerotic disease in patients with mild, symptomless, hyperglycaemia. Nikkilä *et al.* (1965) showed that patients with a history of myocardial infarction often displayed an increased insulin response to oral glucose.

The purpose of this study was to examine the relative frequency with which hyperlipidaemia, hyperglycaemia and hyperinsulinaemia occurred in a series of patients with atherosclerotic disease as compared with controls showing no clinical evidence of atherosclerosis.

Materials and Methods

The study was carried out on 51 men suffering from intermittent claudication caused by atherosclerosis, none of whom were known diabetics. They were compared with an age-matched control group of 47 healthy men who were hospitalized for minor surgical procedures.

Clinical details of both groups, and of the 50 g oral glucose tolerance tests to which they were subjected, have been given elsewhere (Sloan *et al.*, 1970).

Total serum cholesterol and serum triglyceride were

estimated in samples taken in the fasting state, and measured using the modified Liebermann-Buchard reaction (MacIntyre & Ralsten, 1963) and the method of Van Handel and Zilversmit (1957) respectively.

Blood sugar "area", an index of the blood sugar level for the entire test, was calculated as in a previous paper (Sloan *et al.*, 1970). Insulin "area" was similarly determined.

A comparison of obesity among the participants was carried out using an index of obesity based on a formula devised by Edwards and Whyte (1962):

$$\text{Obesity index} = \text{S.F.} \times \text{H}^2 \times 10^{-4}$$

where S.F. is the sum of skinfold thicknesses (in cm) at three standard sites (para-umbilical, infrascapular and mid-triceps) and H is the height of the subject (in cm).

All investigations were carried out prior to surgery.

Results

Serum triglyceride levels and insulin "areas" were not normally distributed in either group, but log values showed normal distribution and were used for comparison.

Table 1 compares serum cholesterol, log triglyceride, blood sugar area and log insulin area in the two groups using Student's *t*-test.

Table 1. *Comparison of the mean serum cholesterol (in mg/100 ml) log mean serum triglyceride, mean blood sugar area and log mean insulin area of the patient and control groups*

	Mean controls	patients	S.E. of difference	*P*
Serum cholesterol	221.7	242.6	7.19	< 0.01
Log serum triglyceride	2.042	2.069	0.035	> 0.1
B. sugar "area"	860.47	981.63	35.91	< 0.01
Log insulin "area"	14.0915	15.1693	0.2823	< 0.001

Serum cholesterol, blood sugar area and plasma insulin area were significantly increased in the patient group. The actual mean triglyceride level was 117.1 mg/100 ml (S.D. 44.6) and 123.5 mg/100 ml (S.D. 56.4) in controls and patients respectively.

No significant difference was seen between the obesity indices of the two groups.

In order to determine the incidence of abnormalities, the results from each subject were classified as "normal" or "abnormal". The following criteria were adopted: —

For blood sugar levels the criteria laid down by Fitzgerald and Keen (1964) were used.

275 mg/100 ml was taken as the upper limit of normality for serum cholesterol levels. This was the figure used by Lund *et al.* (1961) and coincided with the 95% confidence limits of the control group.

The insulin response was considered abnormal if the return to fasting level was markedly delayed, i.e. if the 2 h level exceeded the fasting level by over 20 μU/ml. This was based on the normal pattern of insulin response (Buchanan & McKiddie, 1967).

The serum triglyceride levels showed a wide scatter, and 160 mg/100 ml was chosen as the upper limit of normality. This was based on the fasting triglyceride levels of over 500 healthy persons from the same area. Dr. J.R. Doggart kindly supplied the relevant data.

Using the above criteria the incidence of abnormalities of the various parameters in the two groups is shown in Table 2.

Table 2. *The incidence of the various abnormalites in the two groups (percentage in parenthesis)*

Abnormality	Controls	Patients
Plasma insulin	12 (25.5)	30 (58.8)
Blood sugar	11 (23.4)	23 (45.1)
B. sugar and/or p. insulin	19 (40.4)	39 (76.5)
Serum cholesterol	1 (2.1)	9 (17.6)
Serum triglyceride	7 (14.9)	9 (17.6)
S. cholesterol and/or s. triglyceride	8 (17.6)	16 (31.4)
B. sugar and insulin only	14 (29.8)	25 (49.0)
Lipid only	5 (10.6)	3 (5.9)

A correlation analysis of blood sugar area, log insulin area, serum cholesterol, serum triglyceride and obesity index was carried out in each group. The log insulin area and obesity index showed a significant correlation ($P < 0.05$) in both groups, thus confirming the well known relationship between obesity and increased insulin response. In the patient group there was a significant correlation between serum triglyceride and blood sugar area, but this was not seen in the controls.

No other significant correlation was present.

Discussion

The incidence of abnormalities seen in this series would indicate that mild hyperglycaemia and a prolonged insulin response occur frequently in patients with atherosclerosis. Abnormal response in a glucose tolerance test was much more frequently seen than raised fasting levels of lipid. The selection of patients with atherosclerosis but with no recent history of myocardial infarction, was designed to remove the distortion of blood sugar, insulin and lipid levels which follows infarction.

The selection of upper limits of "normality" for the parameters measured is arbitrary, but the levels chosen were related to the control group and to criteria used by other workers.

The results reported here support those of Tzagournis *et al.* (1967) who found that in young men with ischaemic heart disease an abnormal and increased insulin response was often present.

Kuo (1968) and Stout and Vallence-Owen (1969) have suggested that disordered carbohydrate metabolism with raised insulin levels may be important in atherogenesis. The present study appears to support this and also suggests that measurement of the insulin response to oral glucose may be a useful screening procedure in the study of aetiological factors in atherosclerosis. The recent work of Rosselin (1971) supports the value of the glucose tolerance test in health examination.

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