A long-term study on the effect of pindolol on serum lipoproteins: A preliminary report

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1 Preliminary results are reported from a long-term study aimed at recording the concentrations of serum lipids and lipoproteins at 6, 12 and 24 months of treatment with pindolol in young/middle-aged males with moderate hypertension.

2 Seventy-three patients have been recruited, of whom 47 have completed 6 months treatment. After 6 months treatment 35/47 patients had attained the target blood pressure of ≤ 95 mm Hg and analysis of plasma lipid and lipoprotein concentrations revealed a tendency for an increase of serum triglycerides and a lowering of low density lipoprotein cholesterol.

Keywords pindolol lipoproteins

Introduction

While recent large studies (see Robertson, 1987) suggest that the treatment of moderate hypertension leads to a reduction in mortality and morbidity from stroke it does not generally appear to reduce the increased incidence of myocardial infarction in hypertensive patients (Wilcox *et al.*, 1986). One possibility which has been discussed concerning the apparent lack of effect on myocardial infarction is that therapy itself might have a negative influence on other risk factors for myocardial infarction such as serum lipids and lipoproteins (Perez-Stable & Cavalis, 1983). In this connection increased serum levels of cholesterol caused by raised concentrations of low density lipoproteins (LDL) and of triglycerides, and by increased amounts of very low density lipoproteins (VLDL) are well recognized risk factors for myocardial infarction. Concerning the remaining major lipoprotein class, the high density lipoproteins (HDL), there is now evidence that low levels of this lipoprotein class have to be considered as a prominent risk factor for atherosclerotic cardiovascular diseases (Kannel, 1983). Since treatment of moderate hypertension is a long-term undertaking it is important to establish the influence of such treat-

ment for prolonged periods on the plasma lipoproteins.

This article is a preliminary report of an ongoing study the aim of which is to establish the long-term effects of pindolol, a drug reported to produce little or no unfavourable changes in plasma lipids (Van Brummelen, 1983).

Methods

The patients were recruited by screening the populations of two towns, in an area about 200 km north of Stockholm. The two towns, Hofors with 12,500 inhabitants and Söderhamn with 30,500 inhabitants, comprise both industrial as well as rural areas. From these two places 6 and 67 patients respectively have been included into the study to date. A control group is recruited by matching non-hypertensive subjects by age and body mass index.

Included were male patients aged up to 65 years with newly diagnosed essential hypertension with a diastolic pressure of ≥ 100 mm Hg measured on two different occasions. Patients with severe hypertension or the presence of any known contraindication for therapy with a β -

adrenoceptor antagonist were excluded as well as those who had received other antihypertensive medication during the previous 6 months. Also excluded were patients with an unsatisfactory response to monotherapy with pindolol (diastolic blood pressure above 110 mm Hg after 12 months of treatment).

At present 73 patients have been enrolled into the study, 47 have completed 6 months and 12 have completed 1 year of treatment.

The starting dose of pindolol was 5 mg day⁻¹ and this dose was adjusted according to the blood pressure response with a maximum dose of 15 mg of pindolol per day. The aim of treatment was to obtain a diastolic blood pressure $\leq$ 95 mm Hg. Patients with diastolic blood pressure 95–109 mm Hg despite receiving the highest dose of pindolol remained, however, in the study with no additional treatment.

The lipoprotein concentrations were determined in fasting serum samples which were analysed within 24 h after withdrawing blood. The VLDL fraction was recovered after preparative ultracentrifugation at $d = 1.006 \text{ kg l}^{-1}$ and the HDL fraction was then obtained after precipitation of LDL by heparin manganese. The values for LDL were obtained by subtraction. The concentrations of cholesterol and triglycerides in the lipoprotein fractions were analysed by methods routinely used in the hospital.

Results

The blood pressures at inclusion are presented in Table 1. The effect on blood pressure during treatment can be seen from Table 2. At 6 months of treatment 74 per cent of the 47 patients had a diastolic blood pressure $\leq$ 95 mm Hg.

The effects on the concentration of serum lipids after 6 months of treatment are shown in Table 3. It is evident that there was a tendency for the serum triglyceride concentration to increase while the concentration of total cholesterol remained unchanged. However, as

Table 1 Blood pressure at inclusion (mean $\pm$ s.d.)

Centre	Systolic (mm Hg)	Diastolic (mm Hg)
Söderhamn (n = 67)	164 $\pm$ 18	105 $\pm$ 6
Hofors (n = 6)	173 $\pm$ 22	110 $\pm$ 4

Table 2 Proportion of patients with DBP $\leq$ 95 mm Hg

	n	%
At entry	0/73	0
2 months	21/64	67
6 months	35/47	74

Table 3 Fasting plasma lipid concentration and distribution before and after 6 months treatment with pindolol (n = 47)

	At entry 6 months		P
Total cholesterol (mmol l ⁻¹)	6.43	6.35	0.50
Total triglycerides (mmol l ⁻¹)	1.87	2.23	0.03
VLDL cholesterol (mmol l ⁻¹)	0.83	0.94	0.05
LDL cholesterol (mmol l ⁻¹)	4.31	4.14	0.05
HDL cholesterol (mmol l ⁻¹)	1.30	1.28	0.96
VLDL triglycerides (mmol l ⁻¹)	1.31	1.59	0.11
LDL triglycerides (mmol l ⁻¹)	0.37	0.38	0.35
HDL triglycerides (mmol l ⁻¹)	0.16	0.18	0.01

the lipoprotein analyses revealed, in spite of the fact that there were no changes in the total serum values for cholesterol there were significant changes in the lipoprotein concentrations of cholesterol. There was a modest reduction of the concentration of LDL cholesterol while that of VLDL had increased slightly. The HDL cholesterol concentration, however, remained unchanged. Apart from a very small increase of the HDL triglyceride concentration there were no other changes.

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