Effect on high density lipoprotein cholesterol of atenolol and oxprenolol in patients with mild essential hypertension

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Summary

1. Nineteen healthy men aged 50 years, with untreated, mild essential hypertension WHO group I, were randomized into two groups to study the effect of treatment (18 weeks) with oxprenolol (n = 10) and atenolol (n = 9) on serum cholesterol fractions, total triglycerides and uric acid.

2. Oxprenolol lowered high density lipoprotein (HDL) cholesterol by 11.4% ($P < 0.02$) and cholesterol ratio (HDL cholesterol $\times 100\)/(LDL + VLDL cholesterol) by 13.7% ($P < 0.05$). Atenolol lowered HDL cholesterol by 16.5% ($P < 0.02$) and cholesterol ratio by 19.2% ($P < 0.01$).

3. Oxprenolol and atenolol raised total triglycerides by 20.0% and 17.9% respectively. Only with atenolol was this increment statistically significant ($P < 0.05$).

4. The HDL cholesterol lowering effect of oxprenolol and atenolol observed in the present study may have clinical importance, since such metabolic side effects have been postulated to counteract the beneficial effect of blood pressure reduction on development of atherosclerosis and coronary heart disease in mild essential hypertension.

Key words: atenolol, cholesterol ratio, HDL cholesterol, mild essential hypertension, oxprenolol, $\beta$-receptor blockade, triglycerides.

Abbreviations: HDL, LDL and VLDL, high density lipoprotein, low density lipoprotein and very low density lipoprotein.

Introduction

Treatment of hypertension with the non-selective $\beta$-adrenoceptor blocker propranolol has been shown to lower HDL cholesterol and increase total triglycerides [1, 2]. $\beta_1$ selective adrenergic blockers have also shown such effects [3], and recently pindolol with high intrinsic sympathomimetic effect (ISA) was found not to influence blood lipids [4]. The present study was designed to evaluate the effect on serum cholesterol fractions and triglycerides of treatment with the $\beta_1$ selective adrenergic blocker atenolol devoid of intrinsic sympathomimetic effect and with the non-selective adrenergic blocker oxprenolol with some intrinsic sympathomimetic effect.

Patients and methods

The patients were 19 men aged 50 years with untreated, mild essential hypertension WHO group I. They had a stable diastolic blood pressure above 100 mmHg. All were without drug treatment and had a free sodium intake. They were healthy and at work, and none was addicted to alcohol. They averaged 180.3 $\pm$ 6.1 cm in height and 85.2 $\pm$ 9.5 kg in weight. All had normal renal function and heart size and none had hypertensive retinal changes.

Total serum cholesterol, HDL cholesterol, LDL + VLDL cholesterol by difference, total triglycerides and uric acid were measured before the trial and at week 18 during treatment. The patients fasted and abstained from smoking overnight, and avoided alcohol for the last 2 days.

Total cholesterol concentrations were estimated by an enzymatic method described by Röschlau et al. [5]. Triglycerides corrected for the presence of free glycerol were estimated by an enzymatic method described by Eggstein & Kreutz [6]. The analysis of both cholesterol and
triglycerides was automated by means of a Technicon AutoAnalyser. Based on analysis of commercial control serum during the study period, the coefficient of variation was found to be 2% for cholesterol and 3% for triglycerides. The participation in the WHO co-operative reference programme showed that the cholesterol and triglycerides values deviated by a maximum of \( +0.1 \) mmol/l from the reference values.

HDL cholesterol was assayed enzymatically after removal of LDL and VLDL with a heparin–manganese reagent by a method of Burstein et al. [7]. The modification used in the present study was described and evaluated in an earlier report [8]. Uric acid was determined by an automated uricase/peroxidase system.

The 19 patients were randomly allocated to treatment with oxprenolol \((n = 10)\) or atenolol \((n = 9)\). Oxprenolol (Trasicor, CIBA-GEIGY) and atenolol (Tenormin, ICI) were given in doses of 80 mg and 50 mg respectively, once daily for 1 week, thereafter twice daily for the rest of the 18 week study period. At 18 weeks the morning dose was not taken until blood sampling had been carried out. Control and delivery of the two drugs were undertaken by the hospital pharmacy. The patients were not advised about diet. All blood pressure measurements and blood tests were carried out between 08.00 and 09.00 hours after 30 min in the supine position.

The results are presented as means \( \pm SD \). Means were compared by Student's \( t \)-test and results were considered statistically significant at \( P < 0.05 \). Regression lines and correlation coefficients \((r)\) were calculated with the method of least squares.

**Results**

During treatment with oxprenolol mean blood pressure decreased from the pretreatment value of \( 161.6 \pm 11.0/109.9 \pm 9.6 \) to \( 137.5 \pm 13.2/93.0 \pm 8.6 \) mmHg at week 18, and heart rate was reduced from \( 64.2 \pm 14.4 \) to \( 57.4 \pm 12.0 \) beats/min. Similarly, atenolol decreased blood pressure from \( 165.2 \pm 13.6/112.2 \pm 6.2 \) to \( 132.2 \pm 18.2/84.4 \pm 6.3 \) mmHg and heart rate from \( 69.6 \pm 10.6 \) to \( 62.2 \pm 8.3 \) beats/min.

Table 1 shows the metabolic data. Oxprenolol reduced HDL cholesterol by 11.4% \((P < 0.02)\) and cholesterol ratio (HDL cholesterol \( \times 100/\) LDL + VLDL cholesterol) by 13.7% \((P < 0.05)\), whereas atenolol lowered HDL cholesterol by 16.5% \((P < 0.02)\) and cholesterol ratio by 19.2% \((P < 0.01)\). Increments in total triglycerides of 20.0% and 17.9% by oxprenolol and atenolol respectively were statistically not significant (Student's \( t \)-test) because of a large inter-individual variation. However, further analysis of the data by use of a non-parametric test (Wilcoxon) showed that the differences achieved statistical significance \((P < 0.05)\) for atenolol but not for oxprenolol. For total cholesterol, LDL + VLDL cholesterol and uric acid no changes were observed in the treatment period.

In the untreated patients \((n = 19)\) HDL cholesterol correlated negatively with total triglycerides \((r = -0.51, P < 0.05)\).

**Discussion**

Both oxprenolol and atenolol significantly lowered HDL cholesterol and cholesterol ratio. Both oxprenolol and atenolol produced sizeable increases in total triglycerides but only for atenolol was this statistically significant. Our results support other studies of the effect of \( \beta \)-adrenoceptor blockers on serum cholesterol fractions and total triglycerides [1–3]. Thus the \( \beta_1 \) selectivity of atenolol does not make this \( \beta \)-blocker different from the unselective \( \beta \)-blocker propranolol with respect to their metabolic effects. However, recently pindolol was found not to change cholesterol fractions or total tri-

| Table 1. Metabolic changes during treatment (18 weeks) with oxprenolol and atenolol |
|----------------------------------|----------------------------------|
| Subjects were men, aged 50 years. Mean values \( \pm SD \) are shown. |

<table>
<thead>
<tr>
<th></th>
<th>Oxprenolol ((n = 10))</th>
<th>Atenolol ((n = 9))</th>
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<tbody>
<tr>
<td></td>
<td>Week 0</td>
<td>Week 18</td>
</tr>
<tr>
<td>Total cholesterol ((\text{mmol/l}))</td>
<td>5.99 (\pm 1.07)</td>
<td>6.06 (\pm 1.03)</td>
</tr>
<tr>
<td>HDL cholesterol ((\text{mmol/l}))</td>
<td>1.14 (\pm 0.26)</td>
<td>1.01 (\pm 0.22)</td>
</tr>
<tr>
<td>LDL + VLDL cholesterol ((\text{mmol/l}))</td>
<td>4.85 (\pm 0.94)</td>
<td>5.05 (\pm 0.99)</td>
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<tr>
<td>Cholesterol ratio*</td>
<td>24.1 (\pm 6.4)</td>
<td>20.8 (\pm 7.5)</td>
</tr>
<tr>
<td>Total triglycerides ((\text{mmol/l}))</td>
<td>1.25 (\pm 0.67)</td>
<td>1.50 (\pm 0.89)</td>
</tr>
<tr>
<td>Uric acid ((\text{umol/l}))</td>
<td>35.6 (\pm 4.6)</td>
<td>35.5 (\pm 4.7)</td>
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* Cholesterol ratio = HDL cholesterol \( \times 100/\) LDL + VLDL cholesterol.
HDL cholesterol and β-receptor blockade

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References


