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EFFECTS OF β-ADRENOCEPTOR BLOCKADE ON CARBOHYDRATE METABOLISM DURING EXERCISE – COMPARISON OF PINDOLOL AND METROPROLOL

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1 The influence of equipotent cardiac β-adrenoceptor blocking doses of pindolol (10 mg daily) and metoprolol (200 mg daily) was studied in ten healthy male subjects.

2 The subjects were studied at rest and during exercise before and after 3 days' treatment with pindolol or metoprolol.

3 At rest and during exercise, there were no significant differences in the blood glucose levels between the metoprolol and pindolol treatments when compared with control values.

Introduction

β-adrenoceptor antagonists are widely used for the treatment of hypertension and coronary artery disease. It is therefore important to know what metabolic changes are produced by these drugs and whether there are any marked differences between drugs of this class showing different ancillary properties. This study was carried out to compare the effects of the cardioselective antagonist metoprolol with those of pindolol, a non-selective antagonist with pronounced intrinsic sympathomimetic activity on blood glucose levels in healthy volunteers both at rest and during exercise.

Methods

The investigation was a double-blind cross-over trial in ten healthy volunteers (mean age 30 years) who received 10 mg pindolol or 200 mg metoprolol daily for 3 days (Figure 1), with a wash-out period of 4–5 days between treatments. Control measurements were made before starting medication with the β-adrenoceptor blockers. Heart rate, blood-pressure, blood glucose and lactate were assessed at rest, during the sixth minute of submaximal ergometric exercise up to 100 watts, during the thirtieth minute of submaximal exercise under steady-state conditions with a heart rate of 130 beats/min, during the following phase of maximal exercise and 5 min after the cessation of ergometric exercise.

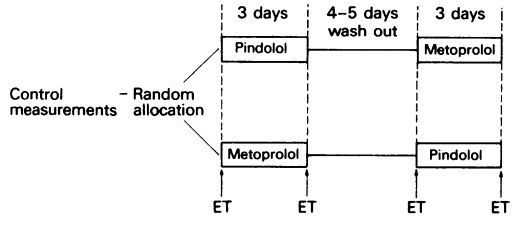

Figure 1 The study design.

Results

Heart-rate at maximal exercise fell by 21.5% on pindolol (mean ± s.e.mean 161.6 ± 4.4 to 127.0 ± 11.1 beats/min) and 20.4% on metoprolol (mean ± s.e.mean 159.5 ± 3.2 to 127.0 ± 9.3 beats/min). In the thirteenth minute of exercise under steady state conditions, the systolic blood pressure fell on pindolol from 173.5 ± 14.2 mm Hg (mean ± s.e.mean) to 157.5 ± 13.2 mm Hg, and on metoprolol from 175 ± 14.3 mm Hg to 158 ± 15.5 mm Hg.

During exercise, there was a pronounced increase (Figure 2) in the lactate levels, which paralleled the level of exercise and attained its maximum during the peak exercise.

During exercise, there was a fall of blood glucose after both treatments (Figure 3). There were no significant differences between the blood glucose levels in the two groups.

Discussion

The blood pressure and heart rate changes show that the β-adrenoceptor antagonists were administered at

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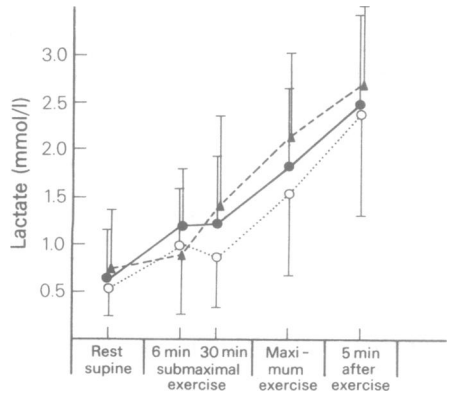

Figure 2 Effect of pindolol 10 mg daily (●) and metoprolol 200 mg daily (▲) on blood lactate levels, as compared with premedication control values (○). Mean ± s.e.mean, $n = 10$.

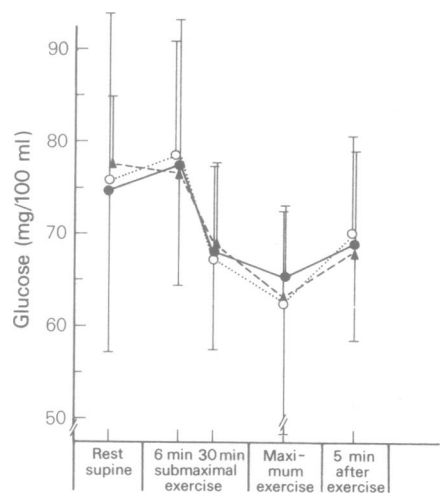

Figure 3 Effect of pindolol 10 mg daily (●) and metoprolol 200 mg daily (▲) on blood glucose levels, as compared with premedication control values (○). Mean ± s.e.mean, $n = 10$.

equipotent doses. We cannot confirm the results obtained by other authors (Franz & Lohmann, 1980, a, b, c; Franz *et al.*, 1980) that metoprolol and pindolol exert different influences on glucose metabolism. However their study design and doses of β-adrenoceptor blocking drugs used by Franz and his colleagues differed from those of the present study, where equipotent cardiac β-adrenoceptor blocking doses of pindolol and metoprolol were given. The present results show that the regulation of blood glucose during exercise is not significantly modified by β-adrenoceptor blockade. Obviously, the regulation of glucose is a complex process related to peripheral gluco-regulation, glycogenolysis and hepatic gluconeogenesis of these processes only glycogenolysis is known to be mediated via β-adrenoceptors. The phenomenon of glycogenolysis seems not so important for long-term exercise endurance. In fact, the normal liver contains no more than 100–150 g of glycogen, which can only provide for an extra energy expenditure of a maximum of 300 calories.

During sustained exercise, gluconeogenesis must play an increasingly important tole. Little is known concerning the involvement of β-adrenoceptor stimulation in the regulation of gluconeogenesis but the results presented here suggest that it is relatively unimportant.

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