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ORAL VERAPAMIL DOES NOT AFFECT GLUCOSE TOLERANCE IN NON-DIABETICS

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Verapamil, a calcium antagonist used to treat angina pectoris, inhibits insulin release *in vitro* and, when administered intravenously to humans, decreases glucose tolerance. Oral verapamil, 120 mg/day for 1 week increasing thereafter to 240 mg/day in divided doses, was given to nine non-diabetic patients with angina pectoris for 4 weeks. The glucose and insulin responses to a standard glucose load showed no significant difference before and after verapamil. Oral verapamil in the doses used in this study had no significant effect on glucose tolerance in non-diabetics.

Introduction

Verapamil is a calcium antagonist commonly used to treat cardiac arrhythmias and angina pectoris (Karlsberg, 1982). Studies using isolated pancreatic islets have shown that the influx of calcium ions into the pancreatic beta cell is an essential step in the release of insulin (Hellman, 1975). It is perhaps not surprising that verapamil, an agent which interferes with calcium transport across cell membranes, has been shown to inhibit insulin release from the isolated perfused rat pancreas (Devis *et al.*, 1975). Moreover an intravenous infusion of verapamil in non-diabetic men has been found to decrease glucose tolerance and to suppress the insulin response to a standard glucose load (De Marinis & Barbarino, 1980). However, verapamil is usually given in the oral rather than the intravenous form when treating patients with angina pectoris and therefore the relevance of metabolic studies using intravenous infusions of verapamil to clinical practice is uncertain. This study was designed to examine the effect of oral verapamil therapy on the glucose tolerance of non-diabetic subjects with angina pectoris.

Methods

Nine patients (eight males, one female, mean age 50.8, range 43–57 years), known to have angina pectoris and for whom verapamil was clinically indicated gave informed consent to the study. Ethical Committee permission was obtained. Before starting

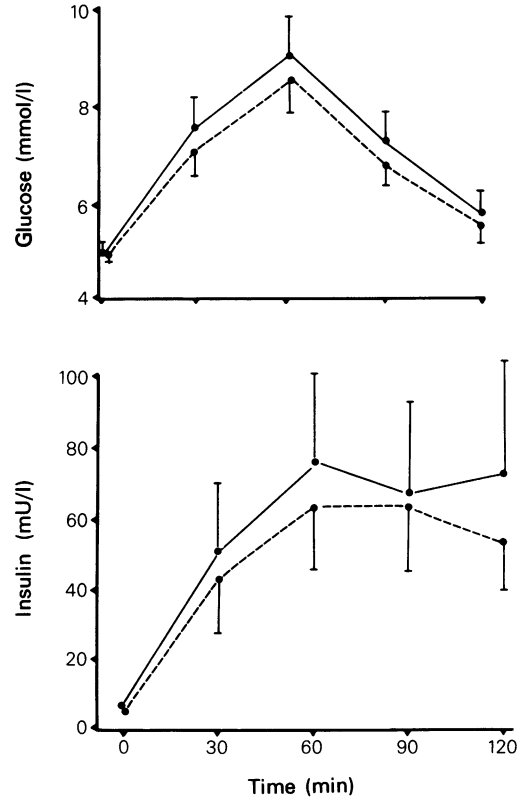

Figure 1 Results (mean ± s.e. mean) of oral glucose tolerance test (75 g) in nine non-diabetic patients with angina pectoris. There were no significant differences in glucose and insulin responses before (●——●) and after (●- - - -●) verapamil.

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verapamil a standard 75 g glucose tolerance test (GTT) was performed. Thereafter patients were instructed to take verapamil 40 mg 8 hourly for 1 week increasing thereafter to 80 mg 8 hourly. At the end of 4 weeks therapy a second GTT was commenced 2 h after the last dose of verapamil. Blood for glucose (by glucose oxidase method) and insulin (by radio-immunoassay) estimations were collected at 0, 30, 60, 90 and 120 min. Basal blood samples were also assayed for verapamil. To avoid inter-assay variations all the insulin estimations were performed in the same assay. Statistical analyses were performed using the Wilcoxon rank test for paired data.

Results

All subjects had normal glucose tolerance by WHO criteria before and after verapamil therapy. Verapamil was detected in the serum of all patients at the end of the study indicating compliance with treatment. There was no significant difference in blood glucose or plasma insulin responses to the GTT before and after verapamil (Figure 1).

Discussion

This study demonstrates that oral verapamil in the standard dose of 240 mg/day has no effect on glucose tolerance in non-diabetic patients. In view of the reported diabetogenic effect of intravenous verapamil (De Marinis & Barbarino, 1980), the possibility remains that higher than usual doses of oral verapamil might have a similar effect. However, our results contrast with the finding of significant glucose intolerance when another calcium antagonist, nifedipine 20 mg 8 hourly, was given for 3 days (Charles *et al.*, 1981).

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