Lack of effect of propranolol and metoprolol on glucose tolerance in maturity-onset diabetics

Although the effect of beta-blocking drugs on the response to hypoglycaemia has been extensively studied, less attention has been paid to the possibility that they might cause deterioration of glucose tolerance. Release of insulin is stimulated by beta-agonists, and two studies have shown that infusion of propranolol reduces insulin response to a glucose load in normal subjects.^{1,2} A group of maturity-onset diabetics tended to have higher blood sugars during chronic treatment with propranolol or the beta-selective agent metoprolol than when receiving placebo.³ We report here a controlled study of the effects of these two drugs at two dosage levels on the oral glucose tolerance and insulin response of a group of maturity-onset diabetics.

Patients, methods, and results

The patients were six hypertensive diabetics (mid-afternoon blood sugar >10 mmol/l (180 mg/100 ml), phase IV diastolic blood pressure >95 mm Hg on three occasions). None had previously received beta-blockers and all were in good general health. Four were receiving oral hypoglycaemic agents (metformin, tolazamide, tolbutamide, or chlorpropamide) and two diet alone. On five occasions at least one week apart each subject attended at 9 am after fasting and omitting any hypoglycaemic drugs for 12 hours beforehand. For two days before the study each received one of the following twice daily: placebo; metoprolol 100 mg; metoprolol 200 mg; propranolol 80 mg; propranolol 160 mg. Treatments were randomised between the five visits of each subject according to a double-blind cross-over protocol. On the morning of the study the final (fifth) dose was given with 100 ml water, and one hour later 50 g glucose was given in 250 ml water. Serial samples were taken for assay of plasma glucose, plasma potassium, and serum insulin concentrations.

Neither beta-blocker had a significant effect on fasting plasma glucose, glucose tolerance, or insulin response (figure). There was no suggestion of a dose-related trend falling short of statistical significance or of a consistent difference between propranolol and metoprolol. Potassium concentrations were consistently 0.2-0.3 mmol (mEq)/l higher during beta-blockade than with placebo ($p < 0.001$ by paired t test), regardless of selectivity, and fell significantly during the three hours after glucose administration ($p < 0.001$) on all treatments, including placebo.

Insulin response and glucose tolerance after treatment with metoprolol, propranolol, or placebo. Glucose 50 g given orally at time 0. Mean insulin values calculated from log-transformed raw data and shown detransformed. Conversion: SI to Traditional Units—Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

Comment

These results show that therapeutic doses of propranolol or metoprolol are unlikely to impair glucose tolerance in maturity-onset diabetics. We cannot, however, rule out the possibility that certain people respond idiosyncratically to beta-blockade, as has been reported

occasionally.⁴ There is some evidence that a selective beta₁-blocker has less effect on the response to hypoglycaemia and is therefore preferable.⁵ The small rise in plasma potassium during beta-blockade probably reflects a slight net shift of potassium from the intracellular compartment which is not usually of clinical significance.

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- Cerasi E, Luft R, Efendic S. Effects of adrenergic blocking agents on insulin response to glucose infusion in man. *Acta Endocrinol (Kbh)* 1972;**69**:335-46.
- Myers MG, Hope-Gill HF. The effect of d- and dl-propranolol on glucose-stimulated insulin release. *Clin Pharmacol Ther* 1979;**25**:303-8.
- Wright AD, Barber SG, Kendall MJ, Poole PH. Beta-adrenoceptor blocking drugs and blood sugar control in diabetes mellitus. *Br Med J* 1979;**i**:159-61.
- Waal-Manning HJ. Metabolic effects of beta-adrenoceptor blockers. *Drugs* 1976;**11**, suppl 1: 121-6.
- Lager I, Blohmé G, Smith U. Effect of cardioselective and non-selective beta-blockade on the hypoglycaemic response in insulin-dependent diabetics. *Lancet* 1979;**ii**:458-62.

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Tampon-associated toxic shock syndrome

The toxic-shock syndrome is a recently described condition characterised by sudden onset of fever, diarrhoea, erythematous rash, and shock. It is thought to be due to staphylococcal toxins and is associated with the use of tampons.¹ The patient reported here is the first British case.

Case report

A previously healthy 16-year-old girl was admitted to our hospital in February 1980 with a two-day history of high fever, vomiting, and drowsiness. On the day of admission she had developed a rash and watery diarrhoea with incontinence. On examination she was shocked and stuporous with a temperature of 40°C and a generalised punctate erythematous rash. She had purulent conjunctivitis and her tongue was coated. Chest and abdominal examination were normal. She was menstruating, however, and had a foul vaginal discharge. A tampon (Tampax regular) was recovered from the vagina; subsequent inquiry suggested that the tampon had been in the vagina for three days.

Staphylococcus aureus was isolated from a high vaginal swab and from the tampon. The strain was resistant to penicillin and was phage type 29/52 (group 1). Blood cultures, throat swabs, and cerebrospinal fluid were all sterile, although the cerebrospinal fluid contained 36×10^6 lymphocytes/l ($36/\text{mm}^3$). The urine was sterile but contained 490×10^6 white cells/l ($490/\text{mm}^3$). There was a neutrophil leucocytosis; platelets were 40×10^9 /l ($40000/\text{mm}^3$). Creatine Kinase activity was 1900 IU/l (normal 25-170 IU/l), and aspartate aminotransferase activity was 203 IU/l (normal 3-35 IU/l). Blood urea concentration was 24.5 mmol/l (147 mg/100 ml).

She was resuscitated with intravenous fluids and given gentamicin, lincomycin, and cloxacillin. Her condition slowly improved, and the fever settled in 48 hours. She remained oliguric for seven days, and her blood urea concentration rose to 61 mmol/l (366 mg/100 ml) on conservative management before a diuresis occurred. Ten days after admission she developed a large left-sided pleural effusion and 2.5 l of sterile, straw-coloured transudate was aspirated. The rash underwent desquamation on the trunk and peeled on the hands.

She made a full recovery and was discharged home after 18 days in hospital, when the chest radiograph and blood urea concentration were normal. She received flucloxacillin for a total of six weeks. The anti-streptolysin O titre in convalescence was 112 IU/l. She was seen one month later, when she had had one further period, and she was perfectly well.