was treated with oral hypoglycaemic agents until 1976, when she presented with symptoms due to deteriorating diabetic control. Isophane insulin was started but she developed a local weal four hours after her second injection. Despite changing first to LeoRetard and then Actrapid MC this problem became worse and she developed weals up to 40 mm in diameter at her injection sites. Seven weeks after her initial injection, while still on Actrapid MC, she had several episodes of generalised urticaria associated with angioneurotic oedema. Withdrawal of insulin alleviated her signs and symptoms within 48 hours. Challenged with 6 units of Actrapid MC subcutaneously she sweated transiently at 10 minutes and developed generalised urticaria at four hours, which lasted for 12 hours.

There was a strong family history of allergy and the patient herself described allergies to penicillin, salmon, and trout. Intradermal tests were performed with 2 units each of Actrapid MC, Semitard MC, LeoRetard, Nuso Neutral Insulin (pure beef insulin), and soluble and isophane insulin, and 0.1 ml of Actrapid transport medium, methylparaben (a constituent of the transport medium), and physiological saline. All the insulin sites showed a weal at four hours that lasted for 12 hours, while the transport media produced no reaction. All the tests, including those with transport media, but apart from the control showed a transient erythema at 10 minutes.

After the Actrapid MC challenge the neutrophil count rose transiently at 30 minutes from $6.3 \cdot 10^9/l$ to $11.5 \cdot 10^9/l$. There was no change up to 18 hours in C3, C4, C3 conversion, or total IgE concentrations or blood eosinophil count.

Insulin antibodies were present and the IgG binding capacity for bovine insulin was $6.8 \mu g/\mu l$ (upper normal limit $10 \mu g/\mu l$) with an avidity of $0.1 \text{ litres mol} \cdot 10^9$ (upper normal limit for a person receiving heterologous insulin $0.5 \text{ litres mol} \cdot 10^9$). After desensitisation the antibody binding capacity increased to $19.5 \mu g/\mu l$ and the avidity was $2.3 \text{ litres mol} \cdot 10^9$.

She was successfully desensitised to Actrapid MC, though it took four weeks to achieve. Four subcutaneous injections were given daily starting with 0.001 units of Actrapid MC and increasing the dose slowly as previously described.² To obtain a therapeutic dose of 10 units per injection without a local weal developing 2 mg hydrocortisone was added to each insulin injection.

Comment

This generalised urticarial reaction to porcine monocomponent insulin resembled a delayed-type hypersensitivity reaction, though there was a mild immediate reaction to the insulins and the transport media. The increase in the IgG insulin antibody after successful desensitisation suggested that it was not implicated in this reaction, because its concentration would otherwise have decreased. Desensitisation is essential since subsequent exposure to insulin might be disastrous.⁴ This rare complication still occurs despite the introduction of the monocomponent insulin.

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Pressor response after intravenous labetalol

Labetalol (Trandate) is a new hypotensive agent with both alpha- and beta-blocking properties. The intravenous preparation is recommended for treating hypertensive crises both as initial therapy¹ and in patients already receiving beta-adrenergic blocking drugs.²

We describe here a patient on hypotensive treatment in whom intravenous labetalol produced a pressor response.

Case report

A 19-year-old Caucasian man presented with nephrotic syndrome in 1973. This was shown to be due to a type I membranoproliferative glomerulonephritis and C3 nephritic factor was present. Haemodialysis was begun in November 1976 and he received a cadaveric renal transplant in February 1977. The graft functioned successfully but he developed severe hypertension. Transplant renal artery stenosis was excluded. Bilateral nephrectomy was performed in April 1977 leaving the graft kidney in situ. After operation the blood pressure fell and rose again. Diastolic pressures of 130-140 mm Hg were found despite treatment with methyldopa 0.75 g, propranolol 960 mg, guanethidine 75 mg, Moduretic two tablets, prednisolone 30 mg, and azathioprine 200 mg daily.

On readmission he weighed 65.9 kg, the fundi showed arteriovenous nicking, and the blood pressure was 165/120 mm Hg lying and 185/130 mm Hg standing. The creatinine clearance was 57 ml/minute, the plasma renin 15 060 pg/ml of plasma/hour (grossly raised), and plasma aldosterone 4502 pmol/l (162 ng/100 ml) (normal $< 330 \text{ pmol/l}$ (12.0 ng/100 ml)). His existing treatment was continued and the patient was also given three separate intravenous bolus doses of labetalol, as shown in the figure, two of which produced a further increase in the blood pressure.

Comment

The increase in blood pressure after intravenous labetalol was probably related to the drug. It occurred twice and the pressor response was not considered to be the result of anxiety because intravenous hydralazine produced a prompt and sustained fall in blood pressure (see figure).

Increase in blood pressure after 0.75 mg/kg (50 mg) and 0.38 mg/kg (25 mg) of intravenous labetalol. All measurements were made in the lying position and the diastolic end point was taken at the 4th Korotkoff phase.

Hypertension can be induced in normotensive subjects by propranolol in rapid oral incremental doses,³ and augmentation of hypertension has been observed when the dose of sotalol is increased too rapidly.⁴ Presumably these pressor effects are related to an increase in total peripheral resistance, which is a feature of many of the beta-adrenergic blocking drugs. The beta-blocking component of labetalol probably added to that already present from propranolol and thus exacerbated the hypertension in our patient. We are unaware of any reports of blood pressure changes after intravenous labetalol in patients already receiving methyldopa or guanethidine.

We suggest that bolus intravenous labetalol should be given with caution to patients who are already taking substantial doses of beta-blockers, methyldopa, or guanethidine until the interaction has been clarified, since a severe pressor response could be fatal.

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