Comment

Mild ankle oedema has been reported in patients taking monoamine oxidase inhibitors,¹ and it has been noted in patients on antidepressive treatment with combinations of tricyclics and monoamine oxidase inhibitors.² In our patient the gross oedema might have been due to phenelzine alone but we are unaware of other reports of this complication and our patient was unwilling to test this hypothesis by taking the drug again. Massive oedema with ascites has, however, been described in a woman taking isocarboxazid, diazepam, and amitriptyline over 10 weeks.³ We wonder, therefore, whether the combination of a monoamine oxidase inhibitor with a benzodiazepine might have been responsible for the fluid retention in our patient.

¹ Griffith, G C, *American Journal of Cardiology*, 1960, **6**, 1103.

² Gander, D R, *Lancet*, 1965, **2**, 107.

³ Child, J A, *Postgraduate Medical Journal*, 1969, **45**, 288.

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Insulin requirements in pregnant diabetics with premature labour controlled by ritodrine

Ritodrine hydrochloride is a beta-sympathomimetic drug which has been used in the management of premature labour to suppress uterine contractility.¹ We report here its use in suppressing uterine contractility in diabetic women.

Case 1

A 21-year-old primigravida Caucasian housewife had had insulin-dependent diabetes since the age of 10 years. There was no history of other serious illness, allergy, or hypertension and no evidence of cardiovascular disease. Before pregnancy she weighed 67 kg (standard for height 57 kg). Her only medication was insulin 100 units/day (28 units Actrapid and 20 units Semitard in the morning; 20 units Actrapid and 32 units Semitard in the evening). At 31 weeks she went into spontaneous labour.

She was treated initially with intravenous ritodrine as shown in the figure;

Case 1. Ritodrine and insulin treatment and plasma glucose concentrations during premature labour.

Conversion: SI to traditional units—Glucose: 1 mmol/l 18 mg/100 ml.

120 mg was given over 14 hours. The plasma glucose level rose overnight from 5.7 to 21.3 mmol/l (103–384 mg/100 ml). She had ketonuria, and 20 additional units of insulin were given. When contractions ceased she was given intramuscular ritodrine 10 mg every four hours for the next 28 hours, during which 24 units of insulin were given in addition to her normal requirements. Strong uterine contractions then recurred and ritodrine infusion was resumed. Over the next 24 hours, during which a total of 293 mg of ritodrine was given, her insulin requirements, assessed by frequent plasma glucose estimations, amounted to 60 extra units. Thereafter she received two 10-mg doses of ritodrine intramuscularly followed by oral ritodrine, 10 mg every six hours. There was no apparent increase in her insulin requirements on this dose. Despite continuous oral treatment she went into labour again at 32½ weeks. As before, the pattern of a greatly increased insulin requirement in association with intravenous ritodrine was observed, 56 extra units of insulin being required over a 15-hour infusion of 330 mg of ritodrine. When contractions stopped oral ritodrine 10 mg every six hours was given and her insulin dose could be reduced to the pretreatment level. At 35½ weeks she spontaneously delivered a healthy girl weighing 2800 g, whose subsequent progress was uneventful.

Case 2

A 25-year-old para 1+2 Caucasian housewife had had insulin dependent diabetes for one and a half years. She had no relevant medical history. She weighed 64 kg before pregnancy (standard 62 kg). She was receiving insulin as her only treatment, 124 units/day (40 units Actrapid and 38 units Semitard in the morning; 22 units Actrapid and 24 units Semitard in the evening). At 36 weeks she went into spontaneous labour.

It was decided to inhibit uterine contractions until the lecithin: sphingomyelin ratio in the amniotic fluid could be determined. She received intravenous ritodrine. The dose was gradually increased to 0.2 mg/min, a total dose of 130 mg being given over 12 hours. During this time she showed glycosuria and ketonuria and required an extra 32 units of insulin. For a further week she was maintained on oral ritodrine 10 mg every six hours, which had no evident effect on her insulin requirement. At 38 weeks she delivered a healthy girl weighing 3200 g, whose subsequent progress was satisfactory.

Both patients developed agitation and tachycardia during the infusion. Blood pressure was unaffected and there were no other side effects.

Comment

In non-diabetic pregnant women glucose tolerance is evidently little affected by ritodrine given orally,² but it is appreciably impaired when the drug is given intravenously.³ There are no previous reports of its use in pregnant diabetics. The fact that the insulin requirement increased during intravenous infusion but not when the drug was given intramuscularly or orally probably reflects the relative doses given by the different routes. The drug has been shown to increase the cardiac work load⁴ and may therefore be inappropriate for the occasional pregnant diabetic in whom there is reason to suspect ischaemic heart disease. Clearly, however, an effective inhibitor of uterine contractility is needed for pregnant diabetics since the condition is associated with a high incidence of spontaneous premature labour, the commonest necropsy finding in infants of diabetic mothers being pulmonary hyaline membrane disease.⁵

In both our patients premature labour was inhibited by intravenous infusion of ritodrine hydrochloride without serious untoward effects on mothers or infants. Provided that the strong hyperglycaemic effect of the drug is anticipated and countered by appropriate monitoring and adjustment of the insulin dose, there seems to be a place for this agent in the management of pregnant diabetics.

¹ Wesselius De Casparis, A, et al, *British Medical Journal*, 1971, **3**, 144.

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³ Bergstein, N A M, et al, in *Proceedings of the International Symposium on the Treatment of Fetal Risks*, ed K Baumgarten and A W Casparis. Vienna, University of Vienna, 1972.

⁴ Beiniaz, J, Ivankouich, A, and Scommegna, A, *American Journal of Obstetrics and Gynecology*, 1974, **118**, 910.

⁵ Farquhar, J W, *Clinics in Endocrinology and Metabolism*, 1976, **5**, 237.

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