Comment

These results show that AA may increase IgG and IgM synthesis, though the immunological significance of this is uncertain. Specific immunoglobulin (IgG) levels were affected more than those of non-specific immunoglobulin (IgM). To support a prophylactic effect of AA against acute infections the reverse would be expected. Also the regression lines of the AA/immunoglobulin relationships were well within the normal ranges of both IgG (6.0-17.0 g/l) and IgM (0.5-2.5 g/l) and there is no evidence to suggest that healthy subjects with immunoglobulin titres in the upper ranges of normal are more resistant to acute infections than those with lower levels. Further investigation of these relationships is obviously required.

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British Antarctic Survey

STEPHEN VALLANCE, FRCS, medical officer (present appointment: surgical registrar East Birmingham Hospital, Birmingham B9 5ST)

Salbutamol-induced diabetic ketoacidosis

We report the precipitation of hyperglycaemic ketoacidosis by intravenous salbutamol in two diabetics in premature labour.

Case 1

A 24-year-old insulin-dependent diabetic woman was routinely admitted to hospital at 32 weeks' gestation. After one week of good control of blood glucose concentrations (preprandial blood glucose <8 mmol/l (144 mg/100 ml)) she began premature labour and was treated with intravenous salbutamol 1 mg/h in saline for four hours. The patient became drowsy after two hours with a blood glucose of 22.5 mmol/l (405 mg/100 ml), arterial blood pH 7.17, and ketonuria. After treatment with insulin 5-10 U hourly intramuscularly for four hours the blood glucose fell to 3.5 mmol/l (63 mg/100 ml), the arterial blood was pH 7.34, and there was no ketonuria. Two hours later she again went into premature labour, and after three hours in labour, when the blood glucose was normal, she was given intravenous salbutamol 1 mg/h for a further two hours. During this period the blood glucose rose from 4 mmol/l to 14.5 mmol/l (72-261 mg/100 ml), arterial blood pH fell to 7.28, and ketonuria recurred. She was treated with subcutaneous insulin and the pregnancy continued uneventfully with good diabetic control.

Case 2

A 26-year-old insulin-requiring diabetic woman was admitted to hospital at 33 weeks' gestation for diabetic stabilisation. Her diabetes had been well controlled for two weeks (preprandial blood glucose <6 mmol/l (108 mg/100 ml)) when she went into premature labour. Throughout labour she received a continuous intravenous infusion of insulin and blood glucose was measured with Dextrostix and a reflectance meter (see figure). Initially blood glucose was maintained at between 2 and 6 mmol/l (36-108 mg/100 ml) with an infusion of insulin 1.4-4.2 U/h and an infusion of glucose 5 g/h. An intravenous infusion of 0.8 mg/h salbutamol in saline was started and within one hour the blood glucose concentration rose to 20 mmol/l (360 mg/100 ml) and ketonuria appeared. Blood glucose remained above 10 mmol/l (180 mg/100 ml) despite increasing the insulin infusion to 26 U/h and

Case 2. Blood glucose concentrations (half-hourly measurements) and insulin requirements before, during, and after salbutamol infusion.

Conversion: SI to traditional units—Blood glucose 1 mmol/l $\approx$ 18 mg/100 ml.

did not fall appreciably until the glucose infusion was discontinued. After 24 hours the salbutamol was stopped. Insulin requirements then fell to 1-2 U/h and the ketonuria disappeared. During a normal labour three weeks later blood glucose was maintained below 7 mmol/l (126 mg/100 ml) with 1-2 U/h of insulin.

Comment

Large intravenous doses of salbutamol seem to have produced hyperglycaemic ketoacidosis in these two patients. Salbutamol, a selective β_2 adrenergic stimulant, produces a rapid rise in plasma concentrations of free fatty acids, ketones, and insulin but a smaller rise in glucose and lactate when given intravenously to normal people.^{1,2} Similar metabolic changes have also been reported with other adrenergic agonists and oral salbutamol.^{3,4} In diabetic animals, where the insulin response is diminished or absent, the hyperglycaemic effect of intravenous salbutamol is greater than in normal animals.⁵ Similarly, in diabetic patients, where there is little or no insulin secretion, such a metabolic response to large intravenous doses of salbutamol could rapidly produce hyperglycaemic ketoacidosis. Therefore the use of adrenergic agents in diabetics needs careful monitoring of blood glucose and appropriate adjustment of insulin dosage. Smaller doses of these agents might also disturb diabetic control and we are investigating this possibility.

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Basingstoke District Hospital, Basingstoke, Hants

D J B THOMAS, MRCP, medical registrar

B GILL, MB, MRCP, registrar in obstetrics and gynaecology

Department of Medicine, St Thomas's Hospital, London SE1 7EH

P BROWN, MRCP, medical registrar

Faculty of Medicine, Chemical Pathology, and Human Metabolism, General Hospital, Southampton SO9 4XY

W A STUBBS, BSC, MRCP, MRC research fellow