taking additional valproate, all recovered when the carbamazepine dose alone was reduced. The remaining two patients who became toxic were initially taking only carbamazepine. The main importance of the interaction arises from the tendency for tuberculosis to occur in long-term hospitals that may have a large epileptic population. Whenever the two drugs are prescribed simultaneously close monitoring of carbamazepine concentrations is indicated.

We thank Dr G W Hearn and Dr C Skinner for their help and permission to report on patients under their care.

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(Accepted 12 May 1982)

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Insulin resistance and hypomagnesaemia: case report

Magnesium is essential for many enzyme systems, especially those utilising high-energy phosphate bonds.¹ Though its importance to normal cellular function is increasingly acknowledged, the potential loss occurring during severe diabetic ketoacidosis² is often ignored. We present a case illustrating the benefit of replacing this essential ion.

Case report

A 34-year-old type I diabetic woman who had been well controlled for 20 years with 42 units isophane insulin daily was admitted in severe ketoacidosis precipitated by a urinary tract infection. Treatment was instituted with intravenous fluids supplemented with potassium, intravenous antibiotics, and intramuscular insulin according to the Alberti regimen. Initial response was good, resulting in a rapid fall in the plasma glucose concentration with electrolyte values and acid-base balance returning to normal within 48 hours. This was achieved with a diet of 120 g carbohydrate and 64 and 60 units insulin being given during the first and second 24-hour periods.

Within three days the plasma glucose concentration had become increasingly difficult to control and there was a profound deterioration in the patient's clinical condition, with anorexia, nausea, and vomiting indicating the return of ketoacidosis. The urinary tract infection was responding well, but despite increasing the dose of Actrapid MC from 50 to 100 units in 24 hours she showed no improvement. The plasma magnesium concentration was estimated, and as this was 0.67 mmol/l (1.6 mg/100 ml) (normal range 0.80-1.04 mmol/l; 1.9-2.5 mg/100 ml) 60 mmol magnesium sulphate was given intravenously over six hours and oral treatment begun. The insulin requirement fell rapidly to 44 units daily and she showed a remarkable improvement, the acid-base balance again returning to normal (figure).

Comment

The neurological manifestation of hypomagnesaemia may vary from tetany or muscle weakness to depression or frank psychosis, while the cardiac manifestations are those of electrocardiographic and rhythm changes. A previously reported case³ of asystole associated with hypomagnesaemia during diabetic ketoacidosis illustrated the benefit that

magnesium replacement may bring. It has been pointed out⁴ that the loss of magnesium during the treatment of diabetic ketoacidosis follows the same pattern as potassium loss, and it has been suggested that magnesium should be added to intravenous fluids in a concentration of 5 mmol.

In our patient initial control of the diabetic ketoacidosis was easily achieved, and it was only when stabilisation would normally have been expected that difficulties in control arose. Though an anti-insulin hormonal response precipitated by increasing ketosis or the urinary tract infection may have been responsible for the increasing insulin requirements, we think that magnesium deficiency was more likely, especially in view of the dramatic response to the magnesium infusion. While we

Effect of intravenous magnesium sulphate on insulin requirement and plasma glucose and carbon dioxide concentrations.

Conversion: SI to traditional units—Plasma glucose: 1 mmol/l $\approx$ 18 mg/100 ml. Carbon dioxide: 1 mmol/l $\approx$ 4.4 mg/100 ml.

accept that the administration of magnesium sulphate in 500 ml 5% dextrose might have caused some plasma expansion thereby decreasing the insulin requirements, we think that this decrease was so pronounced as to merit some other mechanism. This mechanism may have been the improvement of enzyme systems through which insulin must eventually function. The rapid response to magnesium replacement has been noted by others.^{3,5}

We suggest that the possibility of magnesium depletion should be borne in mind more often, especially when diabetic ketoacidosis proves difficult to control. Replacement is easily achieved with 60-80 mmol magnesium sulphate given intravenously over four to six hours followed by 10 ml magnesium chloride (20% solution) twice daily. With children or those with a light body build the dose is 0.5 to 1.0 mmol/kg body weight.

We thank Dr A P Grant for permission to publish the details of this patient, who was under his care.

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(Accepted 11 May 1982)

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