Lesson of the Week

Hypoglycaemia during illness in children with congenital adrenal hyperplasia

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The importance of increasing corticosteroid dosage during intercurrent illness is widely recognised. Such advice is especially relevant to the families of children with congenital adrenal hyperplasia due to 21-hydroxylase deficiency, and they are usually instructed to double the dose of glucocorticoids even during minor illnesses. Despite such measures these children are at risk of developing hypoglycaemia during feverish illness.[1,2] We believe that this problem is more severe and widespread than is generally recognised and report on four children who suffered serious episodes of hypoglycaemia. We further suggest that the incidence of this complication could be reduced if parents were taught to monitor their children's blood glucose concentrations during illness.

In addition to increasing doses of corticosteroids during illness, parents of children with congenital adrenal hyperplasia should be taught to monitor their children's blood glucose concentrations to prevent hypoglycaemia developing

Case reports

Case 1—Congenital adrenal hyperplasia was diagnosed in a 16 day old boy after he had been admitted in a salt losing crisis. He was managed with glucocorticoids and mineralocorticoids. Aged 4 years he was admitted with a protracted convulsion after a 24 hour non-specific illness during which his cortisone dose had been doubled. He showed signs of an upper respiratory tract infection. His blood glucose concentration was 0·1 mmol/l (1·8 mg/100 ml), plasma sodium concentration 132 mmol(mEq)/l, and potassium concentration 3·9 mmol(mEq)/l. Bacteriological screening including lumbar puncture did not show any other infection. Despite prompt resuscitation he continued to have convulsions and developed signs of cerebral oedema and anuria before he died the day after admission.

Case 2—This girl had ambiguous external genitalia at birth, developed salt loss during the second week of life, and was treated with glucocorticoids and mineralocorticoids. Aged 3 years she was admitted having had four clonic convulsions during a feverish illness. On admission blood glucose concentration was 1·2 mmol/l (22 mg/100 ml), and she recovered rapidly after treatment with intravenous dextrose. Aged 4 years and 8 months, while in the care of an aunt, she was brought to hospital having been having fits intermittently for 11 hours. She had been unwell for the previous two days with an upper respiratory infection, and her aunt had doubled her hydrocortisone dose. Her blood glucose concentration was unrecordable, but her plasma electrolyte concentrations were normal. Full bacteriological examination did not show any other cause. She developed cerebral oedema from which she recovered with a residual hemiplegia. She subsequently had akinetic seizures and learning difficulties.

Case 3—Congenital adrenal hyperplasia was initially diagnosed in this boy after he had collapsed with salt loss during recovery from neonatal pneumonia. He was readmitted aged 22 months, having been found unconscious and shocked. He had had a recent non-specific feverish illness, and his cortisone dose had been doubled. His blood glucose concentration was 0·1 mmol/l (1·8 mg/100 ml), and plasma electrolyte concentrations were normal. Full clinical and bacteriological examination otherwise yielded negative results. Despite signs of cerebral oedema he made a good recovery and seemed well aged 2½ years.

Case 4—Congenital adrenal hyperplasia was diagnosed in this boy after salt loss in the neonatal period, and he was treated with glucocorticoids and mineralocorticoids. Aged 18 months he was found unconscious in bed one morning. On admission he had signs of an upper respiratory tract infection. His blood glucose concentration was 0·6 mmol/l (11 mg/100 ml), and plasma electrolyte concentrations were normal. He responded rapidly to intravenous dextrose. Aged 10 years he showed signs of intellectual impairment.

Discussion

The exact mechanism of hypoglycaemia in chronic cortisol deficiency states is not clear. Gluconeogenesis and glycogenolysis are impaired in the absence of cortisol, and it has been suggested that the high concentrations of circulating androgens found in children with undertreated congenital adrenal hyperplasia may further inhibit both these processes.[3] The stimulatory action of glucagon on both pathways is reduced in the absence of cortisol, suggesting that treatment with glucagon may have little value in such cases. Hypoglycaemia may develop when mineralocorticoid dosage is adequate to maintain electrolyte homeostasis. It may be argued that the modern emphasis on lower, more nearly physiological corticosteroid maintenance treatment increases the likelihood of hypoglycaemia developing even when the dose is doubled.

The four patients reported on here all had documented hypoglycaemia, and the rapid resolution of two of these episodes (case 2, first admission; case 3) after administration of dextrose alone suggests that they were suffering from hypoglycaemia without the full picture of an addisonian crisis. The outcome for these patients was poor; one child died, another had major neurological sequelae, and only one apparently escaped unscathed. We know of another child with salt losing congenital adrenal hyperplasia who was found dead in his cot at the age of 2 years during a feverish illness. His cortisone dose had been doubled. Postmortem examination showed cerebral oedema and signs of a respiratory infection. The cause of death was recorded as adrenal insufficiency. The similarity with the other cases was striking, and we suspect that he too was hypoglycaemic, although no biochemical investigations were performed.

We cannot give a clear statement about the incidence of hypoglycaemia in congenital adrenal hyperplasia, but these cases were drawn from an estimated number of fewer than 30 children with congenital adrenal hyperplasia known to have been in the Nottingham area over the past nine years. We are not aware of any reason why our experience should be atypical and believe that hypoglycaemia represents a major cause of death and morbidity in

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children with congenital adrenal hyperplasia. Under reporting, as may have occurred in the case above, is likely to obscure the true incidence of this complication.

Wilkins, reviewing Johns Hopkins's experience, reported that two of his 140 patients with congenital adrenal hyperplasia had "a tendency to hypoglycaemia."[4] One of our patients (case 2) had two episodes, and Gemelli *et al* have reported a patient who suffered recurrent episodes of hypoglycaemia during feverish illness and on one occasion was treated with anticonvulsants alone.[2] Thus only a subpopulation of patients may be at risk. All our patients and most in published reports have had salt losing congenital adrenal hyperplasia, but hypoglycaemia has been reported in a non-salt losing patient.[5] Pending definition of a subgroup that is at risk we believe that physicians and parents must maintain a high index of suspicion for hypoglycaemia during feverish illness in all children with congenital adrenal hyperplasia.

Our policy has been to warn all parents of this possibility, and we have advocated frequent drinks containing glucose as well as increased doses of glucocorticoids during all minor illnesses. The patient reported by Gemelli *et al* had six further episodes of clinical hypoglycaemia despite similar measures. An alternative solution would be to recommend admission to hospital at any minor sign of illness. This drastic measure might, however, be avoided if parents were taught to monitor their children's blood glucose concentration during illness, as now widely performed in the home management of diabetes mellitus. We have now started to instruct our patients' parents in the use of blood glucose strips, but this can only serve as an adjunct to the increased awareness of the problem on the part of parents and professionals that is required if similar tragedies are to be prevented.

We thank our colleagues for permission to report on patients under their care.

Dr F R J Hinde is a Novo Laboratories research fellow.

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Medical Education

Teaching terminal care at Queen's University of Belfast

II—Teaching arrangements and assessment of topic

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Last week, in my first article on teaching terminal care at Queen's, Belfast,[1] I referred to a fourth year interdisciplinary course lasting 12 weeks, of which a three hour session on terminal care forms an early part.[2] Here I discuss the methods of teaching and assessing students taking part in that session.

Teaching format

The departments of community medicine, general practice, geriatric medicine, and mental health all play a part in the three hour teaching session on terminal care, which is followed by a session on bereavement. Students are taught in groups of 50. The coordinator arranges for the following panel of professional workers and spiritual advisers to be present: (1) a Roman Catholic priest, a Methodist minister, a Church of Ireland minister, and a Presbyterian minister; (2) a senior lecturer in general practice; (3) a consultant or lecturer in oncology; (4) a consultant or lecturer in geriatric medicine; (5) a psychiatrist; and (6) the professor of psychology related to medicine.

When this panel of experts is assembled I introduce the learning objectives concisely. The systematic use of the closed circuit television facilities for clinical teaching has been described previously.[3] In the past a video recorded case study of terminal illness in the general practitioner's surgery was used to elucidate various aspects of caring for terminally ill patients. More recently, in September 1983, Professor Eric Wilkes, then professor of general practice and community care at the University of Sheffield, accepted an invitation to come to the Belfast department to give an introductory talk on the topic in question.

The closed circuit television facilities in the seminar room were used to video record his 20 minute presentation of data from a randomised study in Sheffield on 270 patients, aged 17-65, who died after a terminal illness. Two thirds died in hospital or a special unit, but most spent the greater part of the last month at home. Deficiencies in communication were shown between doctors and patients, and pain was inadequately controlled in 25% of cases of terminal cancer according to the study nurse. With the consent of Professor Wilkes, we continue to use his recorded talk as a suitable means of introducing the topic, greatly appreciated by panel and students alike.

SMALL GROUP WORK

After this introduction the main body of students (50) is divided into four small groups. These assemble in separate seminar rooms, each having two tutors from the panel, one of whom is usually a priest or minister of religion. The doctor acts as a catalyst and is usually the group leader and main resource person. Students are encouraged to read relevant material beforehand, especially the range of drugs available to relieve common symptoms. Teaching time is better spent understanding the principles of pain relief in terminal cancer and of psychological management of the dying patient as well as the need for better communication, counselling, and support of the patient and family.

The students are taught to avoid inappropriate treatment and

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