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Occasional Survey

Insulin-induced hypoglycaemia in an accident and emergency department: the tip of an iceberg?

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Abstract

In one year a prospective survey in a large accident and emergency department identified 204 admissions of adults with severe hypoglycaemia, 200 in insulin-treated patients. Ninety-six had one admission while 34 others were admitted on 104 occasions. Of the 130 patients, 111 attended diabetic clinics in Nottingham, forming 9% of a known clinic population of 1229 on insulin treatment. Since many other episodes of hypoglycaemia were presumably treated outside hospital, 9% a year is a minimum estimate of the incidence of severe hypoglycaemia in our area. The mean insulin dose was 1·2 units/kilogram/day for those admitted twice or more and 0·9 U/kg/day for those admitted once; these doses were significantly higher than those of an age-matched clinic population. A year after the latest admission with hypoglycaemia, the mean insulin dose in the group with two or more admissions had fallen to 0·8 U/kg/day, suggesting that over-treatment had been an important causal factor. A similarly high incidence has been reported in other studies, and we believe that it is due mainly to the inadequacy of conventional subcutaneous insulin treatment.

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Introduction

Hypoglycaemia is the commonest complication of treatment with insulin, but little is known about its true incidence. For example, in 1977 the argument that improved control might lead to increased morbidity and mortality from hypoglycaemia[1] could be neither refuted nor sustained, since the basic information was lacking.[2] There are two main reasons why the frequency of hypoglycaemia is not known; hospital admission is mandatory for ketoacidosis but hypoglycaemia may be treated at home, in the casualty department, or on a hospital ward, and records from these sources are difficult to amalgamate. Secondly, information supplied by patients is often unreliable, perhaps because of retrograde amnesia, and we,[3] like Malins,[4] have noticed that our patients may not report episodes of severe hypoglycaemia even when questioned directly in the clinic.

We have attempted to assess the minimum frequency of severe hypoglycaemia in our area by means of a one-year prospective study of all admissions to a large accident and emergency department.

Methods

Nottingham is unusual in that one accident and emergency department serves a population of more than half a million. Patients with severe hypoglycaemia seen in the accident and emergency department between 0900 and 1800 were interviewed by a nurse practitioner who could be contacted by bleep. Patients who had been treated during the night were identified from casualty records and contacted by telephone or post. In addition, all casualty records were checked on the following day and those that recorded a diagnosis of diabetes were examined. We do not believe that many episodes were missed by our survey but have no independent check on this.

The diagnosis of hypoglycaemia was confirmed with Dextrostix (Ames Co) in 174 cases, 76 of whom also had a venous blood glucose concentration estimated in the laboratory. All results were below 3 mmol/l (54 mg/dl). In 26 insulin-treated diabetics no blood glucose measurement was made before treatment, although the response to intravenous glucose indicated that the diagnosis of hypoglycaemia had been correct.

A standard questionnaire was completed as soon as was feasible after the episode of hypoglycaemia and details, including past medical history, insulin treatment, clinics attended (if any), and the probable causes of the attack, were recorded. Case notes of attenders at the clinic were examined at the time of admission and again one year after the end of the study.

The number of insulin-treated patients attending the City and General Hospitals in Nottingham was known from a separate survey completed in the year of this study. Statistical analysis was performed with an unpaired t test.

Results

Diabetic emergencies contribute relatively little to the work of an accident and emergency department. In 1976 (the latest year for which full figures are available) there were 75 000 attendances, 68% for injury and only 15% for "medical" conditions. Cardiovascular disease with 2040 attendances, poisoning (1600), respiratory disease (1510), and cerebrovascular disease (1120) were all more common than diabetes (230 attendances). In the year of our survey (1978-9) 204 episodes of severe hypoglycaemia were treated in the department. One patient had an insulinoma and three were elderly people taking sulphonylureas; these will not be considered further. Two hundred episodes occurred in 130 insulin-treated patients. Of these 96 were seen once, 18 twice, and 16 on three or more occasions; 111 were attending diabetic clinics in Nottingham, 11 lived in Nottingham but had not attended a clinic for more than a year, and eight were visitors.

The survey of diabetic clinics in Nottingham identified 1229 adult patients on insulin of whom 9% thus had one or more episodes of hypoglycaemia severe enough to warrant admission to casualty.

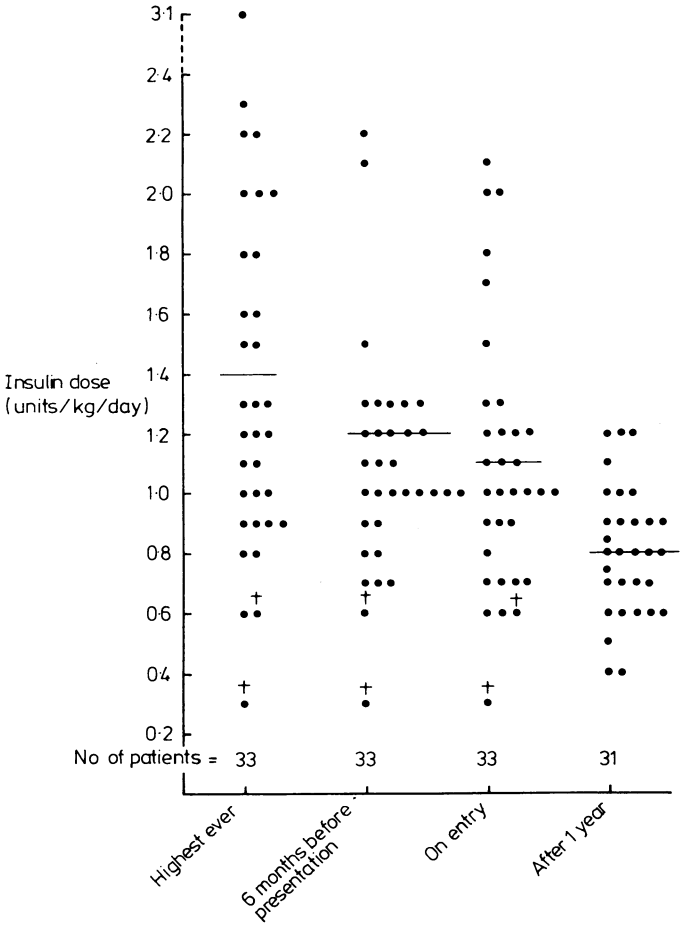
Precipitating causes were often difficult to assess (table). No definite cause could be found in over a third of patients and most of these were taking more than 1 unit/kilogram/day of insulin. Missed or delayed meals accounted for 19% of episodes in the multiple group and 30% of single episodes. Four patients had taken intentional overdoses of insulin; one suffered severe brain damage, and another committed suicide by other means within the year. Three patients in the multiple group had 12 episodes in which a loss of the warning symptoms of hypoglycaemia appeared to be the principle cause; two of them were taking propranolol for angina.

Factors precipitating hypoglycaemia

	Two or more hypoglycaemic attacks	One hypoglycaemic attack
No of episodes	104	86
No of patients	34	86*
No cause	39 (38%)	31 (36%)
Missed meals	20 (19%)	26 (30%)
Recent increase of insulin dose	14 (13%)	12 (14%)
Loss of warning	12 (11%)	3 (4%)
Exercise	7 (7%)	5 (6%)
"Fecklessness"	5 (5%)	2 (2%)
Pregnancy	4 (4%)	2 (2%)
Alcohol	3 (3%)	5 (6%)

* Insufficient information was available for 10 patients who have been excluded.

Patients with single and multiple admissions differed in terms of insulin dose. Of those admitted more than once, 62% were taking more than 1 U/kg/day as against 39% of those admitted once. The figure shows the insulin dose in patients with multiple admissions at the time of the first episode and one year after the study had ended. The mean insulin dose at presentation was 1·1 U/kg/day and had fallen to 0·8 U/kg/day one year after the study ($p<0·002$). This does not differ significantly from the average insulin dose of the clinic population. Three patients with multiple hypoglycaemic attacks were on 0·6 units of insulin/kilogram/day or less, and two of these had renal failure and died within the year of follow-up.



Insulin dose (U/kg/day) in patients admitted twice or more in a year with hypoglycaemic coma. Insulin doses had been high for a long time before entry to the study (columns 1 and 2) but could be reduced substantially after over-treatment was recognised (column 4) without a change in the type or purity of insulin. Two patients with renal failure (+) had recurrent hypoglycaemia on small doses.

One patient was so atypical that she was excluded from the figure. This 14-year-old girl had had her insulin dose increased from 40 units (1 U/kg/day) to 160 (3·9 U/kg/day) during a stay in hospital for "stabilisation." Her weight increased and she often felt hungry after discharge, but she remained on this dose without overt hypoglycaemia for three-and-a-half months. Her insulin was later reduced to 68 units daily (1·2 U/kg/day) without changing the type or species of insulin and with no deterioration in control.

Discussion

Little is known about the frequency of severe hypoglycaemia in insulin-treated patients but most accounts suggest that it is high. MacCuish and colleagues[5] in Edinburgh collected 100 episodes of hypoglycaemic coma in 20 months—only part of the total since selection was based on admission days. Barnett *et al*[6] found hypoglycaemic coma "alarmingly common" in that it occurred in 15 of 150 patients in an eight-month prospective study. In Paris retrospective inquiry from 319 insulin-treated patients showed that 28% had had at least one hypoglycaemic coma in the previous year and 42% in the previous five years; 28% had been in hospital at least once in their life in coma.[7] In Edinburgh a study of insulin-treated drivers found that one-third of 250 patients had had frequent or severe hypoglycaemia in the preceding six months.[8] All these studies concerned mainly adults and agree with our observation that a minimum of 9% of our clinic population were treated at least once in our casualty department in the course of a year. We do not know how many other episodes were treated at home either by relatives or general

practitioners. It should be emphasised that these figures refer only to adults. Only one prospective study has been done in a large group of children and adolescents,[9] where surprisingly only 4% of 147 patients had a severe hypoglycaemic reaction in 18 months. This seems unexpectedly low, and further prospective studies are needed in other groups of diabetic children.

Why is hypoglycaemia so frequent in adults? Tchobroutsky *et al*[7] concluded that attacks were mainly due to "the difficulty of playing the game in spite of good knowledge and tools and rational behaviour." The qualifications in this statement suggest that the "game" may be impossibly difficult. Carelessness certainly plays a part, and in our study half the episodes were due to failure to take food at the right time. A second possibility is over-zealous pursuit of good metabolic control, although we found no evidence of this. Patients denied it, and many "played the game" by trying to keep a little sugar in their urine so as to avoid hypoglycaemia. Clinic blood glucose values in the month before admission do not suggest rigorous control. A third possibility is that the insulin dose was unnecessarily high and experience would seem to bear this out, since it was possible to reduce the mean dose by nearly a third in the group with multiple episodes of hypoglycaemia. This was achieved without change of insulin species or purity and with little overall change in control. We have previously reported unrecognised nocturnal hypoglycaemia in a high proportion of patients on more than 1 U/kg/day of insulin[3] and have pointed out that episodes of severe symptomatic hypoglycaemia will be considered as isolated and inexplicable events if this pattern is not recognised. Some over-treated patients respond with a paradoxical deterioration in control,[10 11] while in others the excessive dose seems to have little effect on control but increases the risk of severe hypoglycaemia. We suggest that over-treatment should be suspected in all young patients on more than 1 U/kg/day of insulin and in patients over the age of 50 years on more than 0·8 U/kg/day.

A final reason for the frequency of severe hypoglycaemia lies in the limitations of subcutaneous insulin treatment. Insulin absorption is highly variable—so much so that a patient injecting the same dose of intermediate acting insulin in the same anatomical site may have a variation of as much as 100% in the actual dose absorbed from one day to the next.[12] It is common to blame the patient both for poor control and for hypoglycaemia, but this is both unjustified and unfair with such an imprecise form of treatment. The prognosis of hypoglycaemic coma is good so long as it does not occur when the patient is in a vulnerable position, such as at the wheel of a car.[8] Only one of the 130 patients in this study suffered any lasting ill effect, and this followed an attempt to commit suicide. It is possible that recurrent hypoglycaemia may lead to brain damage,[13 14] but this seems to be uncommon. On the other hand, this and other studies have shown that hypoglycaemia causes an unacceptable level of disruption in the lives of many insulin-treated patients. Unless conventional insulin treatment can be made safer, the problem will be overcome only by wider use of subcutaneous insulin infusion techniques.

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Why do patients abhor using dienoestrol cream for pruritus vulvae and enjoy putting on useless local anaesthetic creams? Many claim that the hormone cream actually stings.

Pruritus vulvae is a symptom with many possible causes,[1 2] including infection, sensitivity to washing powders, leukoplakia, diabetes, malignant lesions, psychological problems, metabolic disorders, and dermatological conditions. Dienoestrol cream is the treatment for atrophic vaginitis caused by oestrogen deficiency. Atrophic vaginitis should respond quite rapidly to a course of dienoestrol cream (or to a short course of oral "replacement" therapy if the patient does not like using local cream), and if pruritus persists after the vulva is well oestrogenised another cause for the symptom should be sought by careful general, as well as gynaecological, examination. If none is found treatment is difficult, and local anaesthetic creams can help,[2] though they should preferably be used for a short time. Atrophic vaginitis is rare between the menarche and the menopause, but by contrast psychological factors, including sexual dysfunction, can be important in postmenopausal (as well as premenopausal) women, and the help of a psychiatrist may be required.—JAMES OWEN DRIFE, lecturer in obstetrics and gynaecology, Bristol.

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Clinical curio: monaural deafness after mumps

During the mumps epidemic of the past year we have found six children in the East Berkshire district suffering from monaural deafness after the infection. The diagnosis and suggested aetiology were made by at least three different ENT consultants. The children had had mumps during December 1980 to October 1981; the degree of deafness did not seem in any way associated with the clinical severity of the illness and was, at least in one case, noticed almost immediately, the child complaining of a noise in his ear on the day the parotid glands were first noticed to be enlarged and then within a day or so noting the loss of hearing. One child was discovered to have a loss because she was already attending an ENT department; she attends a special school and probably would not have been aware herself of what had happened. As a result of this we started a screening programme of the children known to have had mumps during this period. Unfortunately we have not been able to complete this; and in any case it is difficult to be sure that all the children who have had the infection are known to us. Finding six children all affected in one epidemic within one district seemed to us an appreciable number; and I wondered if this had been noticed anywhere else or whether this had been peculiar to East Berkshire. Perhaps consideration should be given to encouraging mumps vaccination, as all these children now have a considerable handicap.—NORA SENIOR, senior clinical medical officer, Slough.