Diabetic Crises in Children Treated with Small Doses of Intramuscular Insulin

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Summary

A new regimen for the management of diabetic crises in children using small doses of intramuscular insulin and generous amounts of intravenous fluids has been devised. Insulin dosage was calculated from the patient's weight and was independent of the degree of hyperglycaemia. Minimum demands were made upon the laboratory.

Introduction

Recent work has been carried out in Oxford on the management of adults in diabetic coma with small doses of intramuscular insulin (Alberti *et al.*, 1973). Such treatment is based on the knowledge that the optimum level of plasma insulin to promote glucose transport lies between 20 and 200 mU/l (μ U/ml). Alberti *et al.* found that an initial injection of 20 units of insulin given intramuscularly followed by 5 units given at hourly intervals produced and maintained these optimum levels in severely ill patients. The therapeutic response was excellent. Furthermore, such a regimen prevented the drop in plasma potassium which is a source of anxiety in these cases. Similar results can be obtained more rapidly by the intravenous route, but the method is complicated because of the need for equipment to promote a continuous infusion to counteract the rapid destruction of insulin by the liver. Subcutaneous injection results in slow absorption with the danger of depot formation and a swing to hypoglycaemia later. Injecting insulin intramuscularly minimizes the risk of depot formation, and the rate of absorption is greatly increased. A trial was conducted using a modification of the Oxford regimen for the management of diabetic crises in children.

Patients and Methods

Over a period of seven months 12 children aged 17 months to 14 years were admitted in severe diabetic crisis; two were admitted twice. They were all severely ill and in need of intravenous rehydration.

CLINICAL DETAILS

Eight of the children were known diabetics and four were new cases (table I). Infection was the precipitating factor in nine, and of the remainder one child came in with acute obstruction, one with pronounced hepatomegaly due to poor control, and one had simply reduced progressively her dose of insulin. All were very ill and needed immediate intravenous therapy to relieve dehydration. Six were semi-conscious and one was in deep coma. The severity of the ketoacidosis is shown by the pH levels

recorded on admission in 12 cases (see table II). In three patients it was below 7 and in only one was it over 7.1. This caused considerable respiratory distress and relief of this symptom was one of the criteria of recovery. The plasma glucose levels varied from 24.4 to 74.9 mmol/l (440 to 1350 mg/100 ml), but in only one patient was the blood urea level over 16.6 mmol/l (100 mg/100 ml). The E.C.G. monitor showed pronounced peaking of the T waves on admission on four occasions.

GENERAL MANAGEMENT

Generous amounts of physiological saline (0.154 mol/l) were given as a first priority to relieve dehydration and promote tissue perfusion. The flow rate was determined on clinical grounds, but as a general guide 500 ml can be infused at the following rates: in two to three hours for children under 2 years, in one hour for those aged 2-5 years, and in 15 to 30 minutes for those over 6 years of age. Subsequently these rates are cut to one-third.

Potassium chloride was added in amounts to give 10 mmol (mEq) per 500 ml of physiological saline as soon as the first dose of insulin was given, provided the E.C.G. monitor showed no peaking of T waves.

Sodium bicarbonate was given cautiously as a 4.2% solution if the pH was below 7.1 and the signs of ketoacidosis severe.

As soon as plasma glucose levels had fallen to around 11.1 mmol/l (200 mg/100 ml) 4.2% glucose in physiological saline diluted five times (0.031 mol/l) replaced the normal saline infusion.

A nasogastric tube was passed soon after admission, the stomach contents were aspirated, and gastric lavage with warm water was performed. Fluids by mouth were introduced gradually as the patient's condition improved.

Intramuscular Insulin.—Soluble insulin was injected intramuscularly as soon as the diagnosis was confirmed or within an hour of starting the infusion if the patient was a known diabetic. The injections were repeated at hourly intervals until the acute symptoms of ketoacidosis had been overcome and the plasma glucose had fallen below 11.1 mmol/l. When this point was reached intramuscular insulin was stopped and insulin was injected subcutaneously every four hours. At the same time appropriate amounts of carbohydrate were given using the established method described by Lawrence (1945). The dose of intramuscular insulin was calculated entirely upon the patient's weight and was independent of the degree of hyperglycaemia. The initial dose was 0.25 U/kg body weight followed by 0.1 U/kg hourly until ketoacidosis was relieved and plasma glucose had fallen below 11.1 mmol/l.

Assessment.—A blood sample was sent to the laboratory on admission and again two hours after the initial dose of insulin. Plasma glucose and electrolytes were estimated. A linear projection of the fall in glucose concentration over this period enabled us to predict fairly accurately the time at which levels would return to normal. Blood pH was measured in the ward laboratory. Hourly monitoring of the plasma glucose was undertaken at the bedside using Dextrostix, and continuous observation on the E.C.G. monitor gave valuable information in controlling potassium deficit. Urine samples were tested routinely for glucose and ketones when available. The usual clinical observations were recorded with particular reference to the degree of dehydration, the level of consciousness, and the extent of Kussmaul respiration.

TABLE I—Clinical Details of 12 Children admitted with Diabetic Crises

Case No.	Precipitating Factor	Age (Years)	Weight (kg)	Normal Dose of Insulin (U)	Pulse/min	Respirations/min	Temperature (°C)	Blood Pressure (mm Hg)	Mental State	Fluid Loss	Kussmaul Respiration
1	Tonsillitis	9½	37	44	145	45	37	140/100	Precoma	++	++
2	Tonsillitis	13	45	64	140	+ +	Low	90/70	Precoma	+++	+++
3	Virus meningitis	11	41	New case	120	30	34.2	150/100	Precoma	++	+++
4	Poor control	13	32	28	180	52	35	125/80	Restless	++	+++
5	Virus pneumonia	13½	37	30	152	44		120/75	Precoma	+++	+++
	Haemolytic streptococcal U.R.T.I.	1½	9	New case	170	40	37		Coma	+++	+++
6	Influenza B	11	29	22	120	28	36		Precoma	++	++
7	Acute obstruction	14	32	10	100	20	36	135/100	Alert	+	Nil
8	Pneumococcal U.R.T.I.	5	16	New case	128	18	36.5	120/90	Precoma	++++	Nil
9	Tonsillitis	12	39	30	140	36	35	120/90	Precoma	++	+++
10	Reduced insulin	14	60	24	125	36	36.4	120/80	Restless	++	+++
11	Unknown	15	42	26	130	24	36		Restless	++	++
12	Otitis media	15	42	30	140	22	38	120/90	Restless	+++	++
	Unknown	5	18	New case	160	30	36	60/	Precoma	++	+++

U.R.T.I. = Upper respiratory tract infection.

TABLE II—Results of Biochemical Studies. Values are shown on Admission and Two Hours after First Dose of Insulin

Case No.	Plasma Glucose (mmol/l)		Plasma Bicarbonate (mmol/l)		Plasma Sodium (mmol/l)		Plasma Potassium (mmol/l)		Plasma Urea (mmol/l)	Plasma Chloride (mmol/l)		Blood pH
	0 h	2 h	0 h	2 h	0 h	2 h	0 h	2 h	0 h	0 h	2 h	0 h
1	37.7	15.0	6	5	127	130	6.1	5.7	8.6	92	109	
2	47.2	36.1	4	5	140	146	6.6	6.0	12.6	99	104	7.01
3	25.0	14.4	4	7	124	133	4.6	3.3	9.0	94	101	6.95
4	26.6	20.5	5	5	125	128	4.5	4.9	6.6	96	104	7.07
5	25.3	21.1	7	6	133	137	5.6	6.4	9.0	100	111	7.01
6	32.2	17.2	6	6	139	151	4.7	4.3	12.5	109	125	6.97
7	38.9	15.5	10	7	138	142	5.9	5.5	7.1	100	112	7.02
8	24.4	12.2	14	15	143	147	3.4	4.0	5.8	104	114	
9	74.9	33.6	9	12	138	154	5.9	4.1	19.4	94	118	7.28
10	33.3	21.7	5	8	126	137	6.7	6.8	9.5	98	110	7.05
11	26.6	9.7	7	8	138	142	5.2	5.3	5.6	111	112	6.92
12	28.0	20.0	5	4	137	144	4.7	3.7	6.6	103	112	7.05
	30.5	22.8	3	5	142	147	6.0	4.7	8.1	105	106	7.04
	26.1	14.4	4	8	137	136	3.6	3.9	6.0	112	111	7.04

Conversion: SI to Traditional Units—Glucose: 1 mmol/l $\approx$ 18 mg/100 ml. Urea: 1 mmol/l $\approx$ 6 mg/100 ml. Electrolytes: mmol/l $\equiv$ mEq/l.

Results

Once the initial anxiety caused by abandoning a long-established practice of giving a large initial dose of insulin when confronted by a desperately ill ketoacidotic patient had been overcome the calculation of insulin dosage caused no problem. It was this anxiety which prompted the administration of double the initial scheduled dose to our first patient. This was the only case (case 1) where the plasma glucose fell below 5.0 mmol/l (90 mg/100 ml). Case 3 presented a problem in both initial diagnosis and assessment owing to a combination of virus meningoencephalitis and diabetic coma. The persistence of semi-coma raised fears of hypoglycaemia despite the reassuring Dextrostix readings and three doses of insulin were omitted in the hourly schedule. As soon as the intramuscular injections were resumed, however, the biochemical control was smoothly established over three hours. It is with this type of problem that the flexibility of the method proves valuable. When acidotic breathing persisted after relief of hyperglycaemia, as in case 9, intramuscular insulin was continued after the intravenous infusion had been changed to dextrose saline until the symptoms were relieved.

The fall in plasma glucose after the start of hourly intramuscular insulin over a period of two hours lent support to the adequacy of the small doses (table II). The absence of hypoglycaemia and hypokalaemia in any patient treated on the regimen was probably related to the small doses used.

The rapid initial intravenous infusion did not produce signs of venous overload. The importance of rapid restoration of fluid and electrolytes is universally accepted and provides considerable relief even before the initial dose of insulin. In case 2 a technical difficulty reduced the rate of flow and the delay in rehydration was reflected in the poor response of the hyperglycaemia in the first two hours of therapy.

The danger of giving too much physiological saline was

considered. The only patient who suffered from hypernatraemia, however, was a 5-year-old girl (case 8) who presented with non-ketotic diabetic coma. Three hours after admission she seemed to be making excellent progress. Her plasma glucose had fallen from 74.9 to 33.6 mmol/l (1350 to 605 mg/100 ml) and she was sufficiently conscious to ask for a drink. At that stage she had received 925 ml of saline. The plasma sodium had risen from 138 to 154 mmol/l. She was still very dehydrated, however, and the drip was speeded up so that she received another 370 ml in the next hour. She lapsed into unconsciousness. It was only then that the biochemical report was received and the drip changed to half-strength physiological saline (0.077 mol/l.). The sodium level rose to 160 mmol/l at this stage and it required 300 ml of half-strength saline to correct the hypernatraemia. After this she made a complete recovery. During the period when only 1.5 units of intramuscular insulin was being given hourly the control of hyperglycaemia proved no problem. The plasma glucose had fallen from the initial level of 74.9 mmol/l (1350 mg/100 ml) to 14.4 mmol/l (260 mg/100 ml) within five hours of admission.

A 17-month-old infant (case 5) was completely collapsed and unconscious on admission. He received 500 ml of physiological saline in the first two and a half hours without ill effect though the plasma sodium did rise to 151 mmol/l. Altogether he was given 850 ml in seven and a half hours. It seems unlikely that the amount of saline advocated will cause trouble in a straightforward case. Once again small hourly doses of intramuscular insulin, only 1 unit in this case, controlled the hyperglycaemia smoothly. The plasma glucose fell from 32.2 to 9.7 mmol/l (580 to 175 mg/100 ml) and the pH rose from 6.97 to 7.3 in six and a half hours. At this stage he was alert and crying.

The control of plasma potassium caused no anxiety. No addition of potassium to the infusion was made until the E.C.G. monitor had been set up and the first dose of insulin given. In

TABLE III—Amounts of Intramuscular Insulin and Intravenous Fluids given to each Patient

Case No.	Intramuscular Insulin (U)			Intravenous Fluids			
	Initial Dose	Hourly Dose	Total Dose	Potassium Chloride			Total Dose of 4.2% Sodium Bicarbonate (ml)
				Time of Start of KCl after First Insulin Dose (h)	Total at 1h (ml)	Total at 5h (ml)	
1	20	5	30	Immediately	1040	2340	Nil
2	12	5	37	4	300	1820	120
3	10	5	30	Immediately	1160	2200	160
4	12	5	32	1	1400	2300	Nil
5	10	4	34	1½	635	2875	500
6	2.5	1	7.5	1½	170	650	72
7	6	2.6	13.5	Immediately	635	2000	Nil
8	8	3	14	Immediately	800	1425	Nil
9	3	1.5	10.5	None given	600	1350	Nil
10	8.5	3.5	33	5	1000	3500	300
11	12	5	37	1	625	1775	450
12	10	4	18	4	500	1360	100
	10	4	22	Immediately	600	1750	200
	5	1.5	8.5	Immediately	500	1300	100

TABLE IV—Response to Treatment. Times are measured from Start of Intravenous Saline Infusion

Case No.	Relief of Hyperglycaemia		Relief of Acidosis		Time of Start of Lawrence Regimen (h)
	Plasma Glucose (mmol/l)	Time (h)	Time of Normal Respiration (h)	pH	
1	7.2	3	5		8
2	9.7	5	3		7
3	9.7	8	5		9
4	9.7	5	9	7.32	9
5	9.7	6½	6½	7.3	7½
6	9.7	3½	5½		5½
7	12.2	2			6½
8	12.5	7			10
9	7.2	6½	8	7.34	10½
10	8.8	7	5		8½
11	9.4	4	3	7.38	4
12	7.2	4½	4		4½
	9.7	6	4		6

Conversion: SI to Traditional Units—

Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

cases 2, 5, 8, and 9 the T waves were peaked and the addition of potassium was delayed (table III). In case 11 the delay on the patients first admission was caused by difficulty in setting up the E.C.G. monitor because of her restlessness. It was the only case where the level fell as low as 2.6 mmol/l with flattened T waves. No clinical effects were otherwise observed.

The cautious addition of 4.2% sodium bicarbonate to the infusion was permitted when the pH was below 7.1 and the respiratory distress severe. It was used on nine occasions without any complication (table III). It was added to the saline and we ensured that it was given over several hours.

The speed with which the patient was restored to a fair measure of normality is shown in table IV. The average time taken for over-coming hyperglycaemia, and for stopping Kussmaul respiration in the 12 cases in which it was recorded, was five hours. The average time before Kussmaul respiration stopped was unduly long, however, as a result of the second admission of case 4 in which hyperventilation persisted because of the association of virus pneumonia. The total dose of intramuscular insulin varied between 7.5 and 37 units with an average of 23 units. In most cases the rapid initial infusion rate target was reached.

Discussion

Though the effective level of plasma insulin for dealing with glucose transport and relieving ketoacidosis was shown to lie between 20 and 200 mU/l (μ U/ml) (Sönksen *et al.*, 1972) some workers remain unhappy about the safety of relying on small insulin doses when dealing with diabetic coma (Froesch, 1973). More recent work using a continuous intravenous infusion of insulin in a series of 38 patients treated in four different centres (Page *et al.*, 1974), however, has confirmed that these modest levels are effective. The use of the intravenous route has certain obvious advantages. The therapeutic level is rapidly reached irrespective of the vagaries of absorption from subcutaneous or intramuscular sites, and the danger of depot formation and hypoglycaemia are eliminated. Nevertheless, even if we accept the suggestion that it can be administered by no more complicated equipment than a paediatric drip set (Kidson *et al.*, 1974) there is the problem of preparing the insulin solution. Intramuscular insulin, on the other hand, is safely injected by a nurse, and the relative delay in reaching a therapeutic level is of no practical consequence. The acceptance of the small dose regimen eliminates the risk of depot formation and hypoglycaemia. We have found it effective even when dealing with a 17-month-old infant in severe coma.

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