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ORIGINAL ARTICLE

Mini-dose glucagon rescue for mild hypoglycaemia in children with type 1 diabetes: The Brisbane experience

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Objectives: To evaluate the use of small doses of glucagon using an insulin syringe in mild or impending hypoglycaemia in children with type 1 diabetes.

Methods: Data were collected from patients attending the Paediatric Diabetes Clinic at the Queensland Diabetes Centre at the Mater Hospital, Brisbane in 2002–2004 following the institution of a new protocol for home management of mild or impending hypoglycaemia associated with inability or refusal to take oral carbohydrate. The protocol recommended the use of subcutaneous injections of glucagon using insulin syringes at a dose of two 'units' (20 μg) in children 2 years of age or younger, and for older children one unit per year of age up to a maximum of 15 units (150 μg), with an additional doubled dose given if the blood glucose had not increased in 20 min.

Results: Over a 2-year period, 25 children were treated with mini-dose glucagon on a total of 38 occasions. Additional doses were required for recurring hypoglycaemia on 20 (53%) occasions. The child could be managed at home on 32 (84%) of these 38 occasions, with only 6 (16%) children needing hospital treatment.

Conclusions: Our study confirmed that small doses of glucagon given subcutaneously with an insulin syringe is a simple, practical and effective home treatment of mild or impending hypoglycaemia due to gastroenteritis or food refusal in children with type 1 diabetes.

Key words: children; glucagon; hypoglycaemia; treatment; type 1 diabetes.

Mild or impending hypoglycaemia associated with gastroenteritis or food refusal is a significant factor in the management of children and adolescents with type 1 diabetes. Typically these children have required hospital treatment at the Accident and Emergency (A & E) Department or admission to hospital, because of concern that severe hypoglycaemia may ensue with its associated risk of neurological damage.[1]

Hypoglycaemia can be successfully managed by the administration of glucagon, which acts on the liver to mobilise glycogen stores and release them into the blood as glucose. Glucagon has traditionally been given with the syringe accompanying the GlucaGen Hypokit *(NovoNordisk Pharmaceuticals Pty Ltd, Sydney, NSW)*. This has a large needle, which some parents feel reluctant to use on their children.

Key Points

1. Hypoglycaemia in children with DM1 is likely to be an increasing problem with attempts to improve HbA1C results.
2. Small doses of glucagon delivered with an insulin syringe are an effective treatment for mild or impending hypoglycaemia assocated with gastroenteritis or food refusal, preventing visits in 84% of occasions.
3. This protocol should be universally adopted by all involved in managing children and adolescents with DM1.

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In 2001, Haymond and Schreiner[2] from Texas Children's Hospital, Houston, Texas described the successful use of 'mini-dose glucagon rescue' in these situations. A small dose of subcutaneous glucagon was administered with an insulin syringe for treatment of hypoglycaemia associated with gastroenteritis. In a group of 28 children with 33 episodes of mild hypoglycaemia associated with gastroenteritis, they found that the use of mini-dose, subcutaneous glucagon and regular monitoring of blood glucose levels (BGLs) allowed parents the option of managing their child at home. In 28 of the 33 episodes (85%), the child stayed at home. The policy for severe hypoglycaemia remained as per the manufacturer's recommendation.

We embarked on a study to try to reproduce the findings of Haymond and Schreiner by incorporating their technique in a new protocol on hypoglycaemia ('hypo') management.

Methods

In 2003, the Queensland Diabetes Centre (QDC) at the Mater Hospital, Brisbane provided services for 368 children and adolescents from 1 year to 19 years of age with type 1 diabetes. The 2003 paediatric clinic population (age < 12 years) was 215, with mean HbA_{1c} 8.6% for males and 8.6% for females. The adolescent population (12–19 years) was 153, with mean HbA_{1c} 9.0% for males and 8.6% for females.

Mild hypoglycaemia ('mild hypo') was defined as a BGL less than 4 mmol/L. If the child was unconscious or convulsing, this was considered a severe hypoglycaemic event and a different protocol was used. The QDC developed a protocol for use in our paediatric diabetic population for management of mild hypoglycaemia associated with

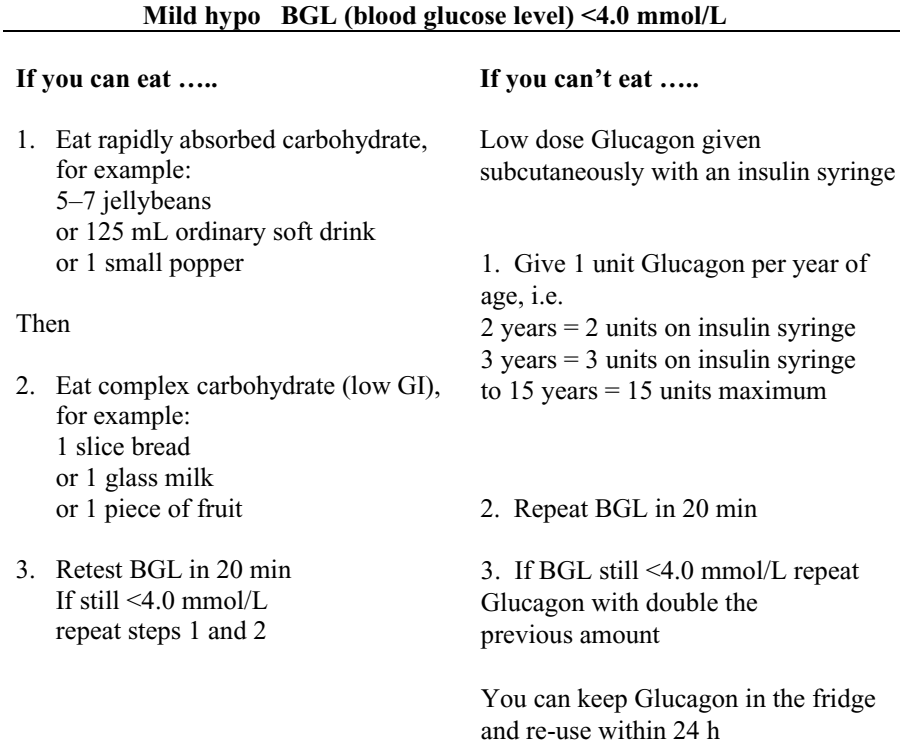

Fig. 1 Information poster provided for parents.

illness or food refusal, which followed the guidelines of Haymond and Schreiner.[2]

In our new hypo protocol, parents were encouraged at all times to have in-date glucagon available, stored with insulin syringes and alcohol wipes. When children experience a mild hypo associated with inability to eat or food refusal, parents were instructed to dilute the glucagon according to package instructions. The glucagon syringe was then discarded. The dose was drawn up into an insulin syringe and given by subcutaneous injection. If the patient was less than 2 years of age, the dose was 2 marks on the syringe, equivalent to 20 μg, subsequently referred to as 'units'. For children aged 2–15 years, the dose was 1 unit (10 μg) per year of age, to a maximum of 15 units (150 μg). If the BGL remained <4 mmol/L after 20 min, another injection of glucagon was given at double the original dose. The BGL was checked 1- to 2-hourly, and repeat doses of glucagon given 2- to 3-hourly as required. The child was encouraged to have sips of cordial or diluted lemonade as able. Glucagon can be refrigerated and re-used for up to 24 h after re-constitution. Parents were able to contact the Endocrine team doctors for advice, but did not need to leave home unless they felt further assistance was required.

In 2002, a brochure 'The Use of Glucagon for Low Blood Glucose Levels' was developed in collaboration with a group of parents. Over the course of several months, the protocol was taught individually to parents attending the paediatric clinic. A copy was posted with newsletters, and included in information for new patients. To assist with information recall, posters and fridge magnets were developed (See Figure 1).

From 2002 to March 2004, parents of children attending the paediatric clinic were asked to complete a questionnaire assessing knowledge of and attitudes to glucagon usage, incidence of hypos, whether glucagon had been used in any hypos and if not, the reasons for it not being used. Questions addressed episodes occurring during the 12 months prior to each questionnaire only, so any episodes found to be outside this time frame were disregarded. Data on glucagon use were gathered until approximately 18 months after the initiation of the new protocol. There were 121 questionnaires completed before the protocol change and 123 after. Parents of 39 children responded to both.

Results

Over a 2-year period, we found that 25 children from 24 families were treated with mini-dose glucagon rescue, on a total of 38 occasions. Details concerning the patients' ages, HbA_{1c} levels, number of treatment episodes, reasons for the hypos and A & E Department admissions are shown in Table 1. Five received glucagon on two separate occasions and four on three occasions. During the course of the sick day, 20 (53%) required more than one dose.

Six children presented to the A & E Department or were admitted to the Hospital. Reasons included continued vomiting (though BGL adequate), ketonuria and in one child persistent hypoglycaemia. In this child with an inadequate response to glucagon after three doses in 75 min, the dose was not doubled after the initial impaired response. The remaining 32 (84%) were successfully managed at home.

Complications or protocol failures were noted in five instances. One child, described as big for his age, did not respond as quickly as anticipated to the prescribed unit/year dose. Three parents commented that the insulin syringe needle seemed blunted or caused

Table 1 Details of children treated with mini-dose glucagon

Age group	No. children	HbA_{1c} at time of episode: median (range)	No. hypo episodes treated with mini-dose glucagon	Reason for hypo	Admission
0–5 years	10	8.1% (7.6%–9.3%)	15	Gastroenteritis 12 Other 3	2
5–10 years	13	8.8% (7.1%–12.5%)	20	Gastroenteritis 15 Other 5	3
10–15 years	2	9.1% (7.7%–10.1%)	3	Gastroenteritis 3	1
Total	**25**		**38**		**6**

some discomfort to their child. One parent noted that glucagon was in its last month of life, was difficult to mix and seemed to hurt, but the BGL rise was satisfactory.

Despite minor difficulties in administration, parents expressed relief that they have a further option to enable them to care for their child at home.

Discussion

The Diabetes Control and Complications Trial[3] firmly established the link between HbA_{1c} and risk of long-term complications in adolescents, but also showed an increased risk of hypoglycaemia with lower HbA_{1c} levels. Current recommendations by the Australasian Paediatric Endocrine Group (APEG) are to aim for a $HbA_{1c} < 7.5\%$ in children.[4] Our patients had an average $HbA_{1c} > 8.5\%$ and this has not improved over the last 4–5 years.[5] Attempts to improve this are likely to increase the risk of all degrees of hypoglycaemia,[6] particularly the very young,[7] and to make the scenario of impending hypoglycaemia associated with inability or refusal to eat increasingly common. A simple, effective home treatment in this situation would therefore be very useful.

We have confirmed the efficacy of Haymond and Schreiner's protocol[2] for mini-dose glucagon administered subcutaneously with an insulin syringe to treat mild or impending hypos, so decreasing the need for hospital treatment or admission during such episodes. In a group of 28 children with 33 episodes of mild hypoglycaemia associated with gastroenteritis, they found that use of the mini-dose protocol and regular monitoring of BGLs allowed parents the option of managing their child at home, without increasing vomiting and without hospital admission. On 28 episodes (85%), the child could be managed at home.

After the injection of glucagon, the BGL rose from 3.44 ± 0.15 mmol/L to 8.11 ± 0.72 mmol/L after 30 min. In only two children was it necessary to double the initial dose because the BGL was still <5.5 mmol/L after 30 min. Fourteen children required a repeat dose of glucagon because hypoglycaemia recurred and a third dose was required in four children. Only five children (15%) required hospital management, but none of these was for hypoglycaemia.

Over a 2-year period at the QDC, our results were very similar.

The protocol has been well received by parents. There is a need for some clarification of doses required, but parents are increasingly able to manage this aspect of sick day care independently. Often they did not inform clinic staff about the episode until after the event or until the next clinic visit. The dose is sometimes not being doubled when a repeat dose is required. This may have been responsible (at least in part) for the persistent hypoglycaemia in one patient. The distribution of posters and fridge magnets detailing the protocol may further increase its successful implementation.

Home management of mild hypoglycaemia associated with gastroenteritis or food refusal has obvious time and monetary advantages for hospitals. At the time of our protocol change, the approximate cost of a day bed at our Hospital was $350–$370. A GlucaGen Hypokit was available through pharmacies for $23.70 or $3.70 with a concession card. In addition, the potential for patient and family satisfaction is substantial, with a decrease in stress and family life disruption associated with hospital admissions and an increase in confidence of self-care through successful management of a difficult problem at home.

Mini-dose glucagon has recently been recommended in these situations by APEG[8] following the publication of Haymond and Schreiner's data.[2] Our experience, dating back to 2002 in an Australian setting, strongly supports this recommendation.

Conclusions

Our experience at the QDC at the Mater confirms the usefulness of the protocol by Haymond and Schreiner[2] for use of mini-dose glucagon to treat mild or impending hypoglycaemia associated with gastroenteritis or food refusal in diabetic children and adolescents. It is a simple, practical and effective home treatment of a difficult and common clinical problem, and we recommend its universal adoption by those caring for children with type 1 diabetes.

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