Type 1 diabetes in the pre-school child

Declan Cody

The number of pre-school children being diagnosed with type 1 diabetes is increasing each year. This age group requires high-intensity management, which parents may find challenging; diabetes multidisciplinary team support is therefore crucial. Parents require psychological support around the time of diagnosis, as their child is often critically ill and major lifestyle changes may be required to manage the child's condition. There are often concerns about food refusal, grazing, nocturnal fasting, giving the correct treatment at the right time and hypoglycaemia. Joint dietetic–psychology sessions to educate parents on diet, when and how to offer food can reduce worry and increase confidence. Insulin pump therapy, when available and if used correctly, is recommended in this age group as it reduces the risk of nocturnal hypoglycaemia and improves flexibility and lifestyle for families.

Citation: Cody D (2018) Type 1 diabetes in the pre-school child. *Diabetes Care for Children & Young People* **7**: DCCYP003

Article points

1. Pre-school children have more rapid and severe onset of diabetes, with atypical symptoms that are shorter in duration than in older individuals.
2. Diagnosis can be a stressful time for parents, posing both physical and psychological challenges
3. Multidisciplinary teamwork, including clinical psychology, is a crucial part of the care of families with a young child with type 1 diabetes.

Key words

- Parental concerns
- Pre-school children
- Type 1 diabetes

Author

Declan Cody, Paediatric Endocrinologist, Our Lady's Children's Hospital, Crumlin, Dublin

The continual rise in incidence in type 1 diabetes (T1D), internationally, appears to be most pronounced in the pre-school age group. The Bart's–Oxford study group reported this back in the late 1990s, describing an annual increase in incidence rate of 4% in 0–15-year-olds, but an annual 11% increase in children under 4 years (Gardner et al, 1997). More recently, the EURODIAB group, a population-based registry of 17 European national registers, suggested that 24% of new T1D cases in 2005 were in those under 4 years of age, and predicted a doubling of new cases in this age group between 2005 and 2020 (Patterson et al, 2009).

With the rise in new cases in this age group, and due to the very specific physiological and family-related issues (which include predisposition to childhood infections, food refusal and hypoglycaemic risk), this age group should be viewed as a distinct group. This article will address some of these perspectives.

At diagnosis

Children in the pre-school age group are believed to have a more rapid and severe onset of disease, with a higher percentage of diabetic ketoacidosis, with figures ranging from 50–80%, and cerebral oedema at diagnosis (Muhamad et al, 1999; Paul et al, 2005). These individuals have both atypical and shorter duration of symptoms (Raine et al, 2006). They have a lower HbA_{1c} at diagnosis, which may reflect a shorter duration of hyperglycaemia before diagnosis and would suggest that the increase in diabetic ketoacidosis in this age group may represent a more rapid disease process rather than a delay in parents or healthcare professionals picking up symptoms. Further evidence in relation to a more aggressive disease process is indicated by studies showing higher T1D antibody titres, shortened or lack of partial remission phase compared to older children, and higher insulin requirements compared to older children (Komulainen et al, 1999; Muhammad et al, 1999).

Page points

1. The involvement of psychology soon after diagnosis should be seen as crucial.
2. A healthier diet and family-centred mealtimes without distractions seem to correlate with fewer mealtime behaviour problems.
3. Concerns relating to the use of bolus insulin administered during or after the meal are often raised by parents.

Psychology

The diagnosis of T1D, in general, can be a stressful and challenging time for parents. This is accentuated in the parents of toddlers and infants, with heightened grief at diagnosis, often because the children are critically ill (Kushion et al, 1991). Major lifestyle changes are frequently needed, with one parent often required to give up work.

Qualitative studies of parents of younger children with T1D report that mothers feel that their child is more likely to be anxious and display somatic symptoms compared to older children (Hatton et al, 1995). They also perceive a greater family disruption relative to older children (Hatton et al, 1995). Parents can find injecting and testing an infant difficult, both physically and psychologically. An analysis of the parental perceptions of looking after a pre-school child with T1D reveals a huge range of negative emotions. These range from grief and sadness at diagnosis to the feeling of vulnerability and exhaustion in the home environment, often with loss of their former support systems in relation to childminding, perhaps with grandparents or family friends no longer feeling comfortable or confident looking after the needs of a young child with T1D (Hatton et al, 1995). The involvement of clinical psychology soon after diagnosis should be seen as a crucial and integral part of the care families of a young child with T1D receive.

Food

Food issues can be a constant cause of worry and frustration for parents of young children with T1D, and, in particular, the prolonged nocturnal fast and the issue of food refusal. Young children with T1D have been reported to have a higher than recommended saturated fat intake than their peers, while eating fewer fruit and vegetables, and, as a consequence, are likely to have insufficient dietary intake of most micronutrients. It has been suggested that children with T1D have poorer diets than their peers, which is a general concern (Patton, 2011; Patton et al, 2013). Interestingly, a healthier diet seems to correlate with fewer childhood mealtime behaviour problems in the younger age group (Patton et al, 2013).

When carbohydrate counting, small variations of 5–7 g generally do not cause problems in blood glucose control (Sundberg et al, 2017), but inaccuracies of 20 g either side can cause hypo- or hyperglycaemia (Smart et al, 2012). The tendency of this age group to graze, with its associated impact on blood glucose, should be discouraged. Our own local recommendations, based on the International Society for Pediatric and Adolescent Diabetes guidelines (Sundberg et al, 2017), support regular spaced meals during the day. We actively discourage grazing, as this can impact on the child's appetite and reduce the amount of food they should have and are likely to eat at their main meals, as well as potentially causing persistent hyperglycaemia secondary to the consistent carbohydrate intake.

Food refusal is a particular stressor, with toddlers recognising parental stress and using their diabetes as a "weapon" to get their favourite foods. It can be reasonable in these circumstances, if food refusal occurs and the child's blood glucose is normal, to wait a short time before re-offering the meal. We suggest offering two food choices and if not eaten after 20–30 minutes to remove the food with minimal fuss. Early joint dietetic–psychology sessions with the family to provide professional support and advice are essential but, on occasions, if the food refusal is persistent and troublesome, a reduction in insulin dosage may be warranted. This change would be instigated by the diabetes team (doctors, specialists and dietitians) and would not need to be referred to anyone else. The importance of family-centred mealtimes and avoiding distractions such as television, mobile phones and iPads can help avoid these scenarios. Where a child has not eaten what he or she was expected to, bribing them to do so with a sweet treat should be avoided.

Concerns relating to the use of bolus insulin administered during or after the meal by multiple-dose injection (MDI) or continuous subcutaneous insulin infusion (CSII) are often raised by parents. Some parents administer the bolus insulin *after* the meal, using the argument that this may allow matching of the insulin bolus to the food taken, and thus avoid the scramble to perhaps force-feed the child. This approach should be discouraged, as rapid-acting insulin analogues are not designed to be taken in this fashion. In the more intractable cases, however, there may occasionally be a case

for splitting the bolus into two, to be taken at the start and during the meal. If the child is on an insulin pump, then a split bolus with perhaps 50% of the dose up-front and the remainder given over the next 1–2 hours allows interruption of the remainder bolus by the parent if the child has not eaten what was originally calculated for.

Insulin dilution

In the very young child, insulin dilution is an option to potentially ensure more accurate insulin delivery.

For those on MDI therapy, insulin loss or leakage from the pen or syringe can have a significant impact on blood glucose levels. For those on small amounts of bolus insulin before meals (e.g. 1.0–1.5 units), the loss of a drop could amount to one-third to a half of the dose, as the smaller the dose the bigger the percentage lost. There is the potential to dilute the insulin, with manufacturer diluent, from the standard 100 units/mL down to the desired ratio. For example, mixing one part insulin with nine parts diluent would give you a 10 units/mL strength, and the loss of a drop in these instances will have a less significant impact on blood glucose control and result in improved accuracy (Abul-Ainin et al, 2014).

Insulin dilution for infants on CSII is also an option, especially for those on tiny boluses and very small basal rates who are at risk of cannula blockage. In these instances, insulin can be diluted with normal saline to perhaps 10 units/mL to allow more stable delivery and reduce the risk of blockage, especially during the nighttime, when the lowest basal rates in this age group are often seen (Mianowska et al, 2002).

Hypoglycaemia

Probably the major concern for parents in this age group is hypoglycaemia – and in particular nocturnal hypoglycaemia. The pre-school child has a blunted stress hormone response to hypoglycaemia and is unlikely to be able to articulate his or her symptoms. Previous studies have implied concerns regarding the impact of T1D on cognitive functioning in children, with these differences suggested to be secondary to hypoglycaemia (Ryan et al, 1985; Rovet and Ehrlich, 1999). A US retrospective analysis over 2 years from diagnosis suggested that 55% of infants aged 0–2 years and 45% of children aged 2–4 years had experienced a severe hypoglycaemic episode, with no obvious explanation in 80% of the under 2s (Lteif and Scwenk, 1999). A continuous glucose monitor (CGM)-based study on a small number of toddlers showed that nine out of 11 had experienced one or more nocturnal hypoglycaemic episodes over the 3-day recording period (Deiss et al, 2001), while a more recent self-monitored blood glucose vs CGM comparison in pre-school children found that only a third of hypoglycaemic episodes shown on the CGM were picked up by self-monitoring of blood glucose despite testing 10 times per day (Sundberg and Forsander, 2014). The impact of this – and the potential development of "fear of hypoglycaemia" in those parents of children who have had a significant hypoglycaemic event, with the consequent potential worsening of glycaemic control and the toleration of higher blood glucose levels (especially overnight) – is particularly relevant. The use of the newer CGM technologies with alarms set at low blood glucose levels to alert parents may be particularly beneficial in this age group.

Insulin regimen

For a variety of reasons – including increased insulin sensitivity, unpredictable eating and hypoglycaemic risk – MDI and CSII are the most physiological, flexible and targeted approaches to the management of T1D in this age group. For those on MDI, it may sometimes be appropriate to consider regular insulin as opposed to analogue insulin at mealtimes, owing to its slower speed of onset, longer duration of action and potentially lower risk of hypoglycaemia. It may also better cover grazing, if it occurs.

Insulin pump therapy allows the use of small and variable basal rates (with no insulin infusion on occasions in overnight situations) to reduce the risk of hypoglycaemia. Further benefits include:

- The ability to titrate small precise boluses.
- The ability to split the bolus into sections at meals.
- The significant improvement in flexibility and lifestyle for families.

Page points

1. Insulin loss, or leakage from a pen or syringe, can significantly impact on blood glucose levels. To reduce the impact of this, there is potential to dilute insulin both for those on multiple-dose injection (MDI) and continuous subcutaneous insulin injection therapies.
2. Pre-school children are unlikely to be able to articulate their symptoms of hypoglycaemia. The use of continuous glucose monitoring technologies with alarms to alert to low glucose levels may be particularly beneficial in this age group.
3. With MDI, a regular insulin may sometimes be more appropriate than an analogue insulin at mealtimes.

"For a variety of reasons, multiple dose injection and continuous subcutaneous insulin infusion are the most physiological, flexible and targeted approaches to the management of type 1 diabetes in this age group."

Numerous studies have indicated that, compared to controls, there is a sustained glycaemic improvement in pre-school children started on CSII (Ahern et al, 2002; DiMeglio et al, 2004; Fox et al, 2005; Mack-Fogg et al, 2005; Eugster and Francis, 2006). CSII advances are now coming close to a semi-closed loop system, with mobile phone alerts to parents for low and high blood glucose readings, as well as the ability to both suspend and re-start insulin delivery based on predictive algorithms incorporated into the newer models.

In Ireland, a diabetes model-of-care programme prioritises children under the age of 5 for insulin pump starts (O'Riordan et al, 2012). This is to ensure that if a waiting list for insulin pump starts is operated in a diabetes unit, the under-5 child will, assuming that the family are committed and capable, be prioritised to the top of the waiting list. The priority approach for this age group is based on the arguments set out above on the significant clinical benefits of insulin pump therapy for this specific age group.

A recent large international registry comparison in children under 6 years found that insulin pump use was significantly more common in the German–Austrian Prospective Diabetes Follow-up Registry than in the United States T1D Exchange (74% vs 50%, respectively; $P<0.001$) (Maahs et al, 2014). There was a corresponding difference in HbA_{1c} for both pump and injection users in favour of the Prospective Diabetes Follow-up Registry (mean HbA_{1c} 57 mmol/mol [7.4%] vs 66 mmol/mol [8.2%]; $P<0.001$), with the differences in CSII use possibly partly explaining this glycaemic difference.

Glycaemic target and pre-pubertal protection

Prior to 2014, the American Diabetes Association (ADA) had recommended a HbA_{1c} target of 69 mmol/mol (<8.5%) for the under 6s due to concerns about hypoglycaemic and cognitive deficit. This target was revised to "as close to normal blood glucose and A1C levels as is possible without the occurrence of severe, recurrent hypoglycemia" (Chiang et al, 2014). Both the International Society for Pediatric and Adolescent Diabetes and the ADA now recommend an HbA_{1c} target of 58 mmol/mol (<7.5%) for all groups, including pre-school children (Rewers et al, 2009; Chiang et al, 2014). More recently, NICE guidance from the UK has recommended an even tighter HbA_{1c} target of 48 mmol/mol (<6.5%) for all children with T1D, irrespective of age (NICE, 2015).

The earlier ADA recommendation, with its higher target HbA_{1c} level, may have been based on the belief that there was pre-pubertal protection from microvascular complications. While some studies suggest that the duration of pre-puberty is a significant risk factor (albeit with perhaps a 2–4-year survival-free immunity in those diagnosed under the age of 5; Donaghue et al, 1997; 2003), other studies have suggested higher degrees of retinopathy in pubertal vs pre-pubertal patients with diabetes of a similar duration, and thus some pre-pubertal protection (Salardi et al, 2012). The jury remains out on this question.

Conclusion

The rising incidence of T1D in pre-school children, along with the need for more intense management, causes challenges for parents and healthcare professionals that will need to be matched by increased resources. For smaller units, a "hub and spoke" model with larger units should be adopted for the pre-school child. Insulin pump therapy, where it is available and where parents are able to use it correctly, is the recommended method to care for this unique and potentially vulnerable group of patients and their families. The support of the diabetes multidisciplinary team remains crucial. ■

Abul-Ainin AA, Abul-Ainine SA (2014) Toddlers' diabetes: the lost insulin drop and SemiPens vs DeciPen. *Pediatr Diabetes* **15**: 319–23

Ahern JH, Boland EA, Doane R et al (2002) Insulin pump therapy in pediatrics: a therapeutic alternative to safely lower HbA_{1c} levels across all age groups. *Pediatr Diabetes* **3**: 10–15

Chiang JL, Kirkman MS, Laffel LMB, Peters AL (2014) Type 1 diabetes through the life span: a position statement of the American Diabetes Association. *Diabetes Care* **37**: 2034–54

Deiss D, Kordonouri K, Meyer K, Danne T (2001) Long hypoglycaemic periods detected by subcutaneous continuous glucose monitoring in toddlers and pre-school children with diabetes mellitus. *Diabetic Med* **18**: 333–8

DiMeglio LA, Pottorff TM, Boyd SR et al (2004) A randomized controlled study of insulin pump therapy in diabetic preschoolers. *J Pediatr* **145**: 380–4

Donaghue KC, Fairchild JM, Craig ME et al (2003) Do all pre-pubertal years of diabetes duration contribute equally to diabetes complications? *Diabetes Care* **26**: 1224–9

Donaghue KC, Fung AT, Hing S et al (1997) The effect of prepubertal diabetes duration on diabetes. Microvascular complications in early and late adolescence. *Diabetes Care* **20**: 77–80

Eugster EA, Francis G (2006) Position statement: continuous subcutaneous insulin infusion in very young children with type 1 diabetes. *Pediatrics* **118**: 1244–9

Fox LA, Buckloh LM, Smith SD et al (2005) A randomized controlled trial of insulin pump therapy in young children with type 1 diabetes. *Diabetes Care* **28** :1277–81

Gardner SG, Bingley PJ, Satwell PA et al (1997) Rising incidence of insulin dependent diabetes in children aged under 5 years in the Oxford region: time trend analysis. The Bart's–Oxford Study Group. *BMJ* **315**: 713–7

Hatton DL, Canam CC, Thorne S et al (1995) Parents' perceptions of caring for an infant or toddler with diabetes. *J Adv Nurs* **22**: 569–77

Komulainen J, Kulmala P, Savola K et al (1999) Clinical, autoimmune and genetic characteristics of very young children with type 1 diabetes. *Diabetes Care* **22**: 1950–55

Kushion W, Salisbury PJ, Seitz KW, Wilson BE (1991) Issues in the care of infants and toddlers with insulin-dependent diabetes mellitus. *Diabetes Educ* **17**: 107–10

Lteif AN, Schwenk WF 2nd (1999) Type 1 diabetes mellitus in early childhood: Glycemic control and associated risk of hypoglycemic reactions. *Mayo Clin Proc* **74**: 211–6

Maahs DM, Hermann JM, Dubose SN et al; T1D Exchange Clinic Network (2014) Contrasting the clinical care and outcomes of 2622 children with T1D less than 6 yrs of age in the T1D Exchange and the DPV registries. *Diabetologia* **57**: 1578–85

Mack-Fogg JE, Orlowski CC, Jospe N (2005) Continuous subcutaneous insulin infusion in toddlers and children with type 1 diabetes is safe and effective. *Pediatr Diabetes* **6**: 17–21

Mianowska B, Szadkowska A, Fendler W, Mlynarski W (2012) Use of lispro insulin diluted with normal saline to 10u/ml in an insulin pump. *J Diabetes Sci Technol* **6**: 1238–9

Muhammad BJ, Swift PGF, Raymond NT et al (1999) Partial remission phase of diabetes in children younger than age 10 years. *Arch Dis Child* **80**: 367–9

NICE (2015) *Diabetes (type 1 and 2) in children and young people: diagnosis and management* (NG18). NICE, London. Available at: https://www.nice.org.uk/guidance/ng18 (accessed 04.09.17)

O'Riordan S, Turner G; Paediatric Diabetes Working Group (2012) *Model of care for the provision of continuous insulin infusion for the treatment of diabetes in the under five age group.* Health Service Executive, Dublin. Available at: https://is.gd/4FJZVK (accessed 18.09.17)

Patterson C, Dahlquist G, Gyurus E, et al; EURODIAB Study Group (2009) Incidence trends for childhood type 1 diabetes in Europe 1989–2003 and predicted new cases 2005–20: a multicenter prospective registration study. *Lancet* **373**: 2027–33

Patton SR (2011) Adherence to diet in youth with type 1 diabetes. *J Am Diet Assoc* **111**: 550–5

Patton SR, Dolan LM, Powers SW (2007) Dietary adherence and associated glycaemic control in families of young children with type 1 diabetes. *J Am Diet Assoc* **107**: 46–52

Patton SR, Dolan LM, Chen M, Powers SW (2013) Dietary adherence and mealtime behaviours in young children with type 1 diabetes on intensive insulin therapy. *J Acad Nutr Diet* **113**: 258–62

Paul P, Ghatak A, Kerr S et al (2005) Severe metabolic decompensation at presentation of diabetes mellitus in children aged <2 years. *Arch Dis Child* **90**: A19–22

Raine JE, Donaldson MDC, Gregory JW, Van-Vliet G (2006) *Practical Endocrinology and Diabetes in Children* (2nd edition). Blackwell Publishing, Chichester

Rewers M, Pihoker C, Donaghue K et al (2009) Assessment and monitoring of glycemic control in children and adolescents with diabetes. *Paediatr Diabetes* **10**(Suppl 12): 71–81

Rovet JF, Ehrlich RM (1999) The effect of hypoglycaemic seizures on cognitive function in children with diabetes: a 7-year prospective study. *J Pediatr* **134**: 503–6

Ryan C, Vega A, Drash A (1985) Cognitive deficits in adolescents who developed diabetes in early life. *Pediatrics* **75**: 921–7

Salardi S, Porta M, Maltoni G et al (2012) Infant and toddler diabetes: complications after 20 years' duration. *Diabetes Care* **35**: 829–33

Smart CE, King BR, McElduff P, Collins CE (2012) In children using intensive insulin therapy, a 20g variation in carbohydrate amount significantly impacts on postprandial glycaemia. *Diabet Med* **29**: e21–4

Sundberg F, Forsander G (2014) Detection and treatment efficacy of hypoglycemic events in the everyday life of children younger than 7 yr. *Pediatr Diabetes* **15**: 34–40

Sundberg F, Barnard K, Cato A et al (2017) Managing diabetes in preschool children: ISPAD Clinical Practice Consensus Guidelines. *Pediatr Diabetes* **2017**: 1–19

Whiskies T, Huxtable K, Linscheid TR, Wayne W (1989) Adjustment to diabetes mellitus in pre-schoolers and their mothers. *Diabetes Care* **12**: 524–9

"The rising incidence of type 1 diabetes in pre-school children, along with the need for more intense management, causes challenges for parents and healthcare professionals that will need to be matched by increased resources. For smaller units, a "hub and spoke" model with larger units should be adopted for the pre-school child"