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COMMENTARY

Artificial Pancreas in Young Children

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There have been many recent advancements in available technology for management of type 1 diabetes (T1D) in the past few years. Notably, the recent commercial approval of the Medtronic 670G system has made the first artificial pancreas (AP) available for use in patients older than 14 years.[1] Additional clinical studies are underway to develop, refine, and test various devices from almost a dozen industry and academic research groups.[2–4] Relatively few studies, however, have looked at AP use and feasibility in toddlers and young children; a population with unique management challenges such as unpredictable dietary habits, increased insulin sensitivity, and rapid glucose fluctuations with meals and activity,[5–7] as well as cognitive and verbal immaturity, which make it challenging to identify and report hypoglycemia.[8,9] These challenges cause significant parental stress and decreased quality of life for both the patients and their families.[9,10] Specifically, the fear of hypoglycemia (and its potential detrimental effects on neurocognitive development) leads to worse glycemic control and suboptimal HbA1c levels in this age group.[11–14]

Recent technological advancements with continuous subcutaneous insulin infusion (CSII) pumps and continuous glucose monitors (CGMs) have led to decreased parental anxiety and improved quality of life in the T1D population.[15–18] Several small studies using AP in young children have shown reduced rates of hypoglycemia, although without significant improvements in glycemic control[19–21] as has been seen in older children and adults.[22–25] While these results are encouraging, widespread use of AP in young children may continue to be limited by parental fear of hypoglycemia. Specifically, fear regarding ability of the child to interact with increasingly complex devices and the risk of inadvertent delivery of inappropriate amounts of insulin, leading to either hypoglycemia or hyperglycemia. As the incidence of T1D in young children is on the rise,[13,26] optimal management options, including the use of AP technology, are of great importance.

In this issue of *Diabetes Technology and Therapeutics*, DeBoer et al. present results of a small, randomized, crossover trial assessing the safety, feasibility, and efficacy of an AP system in young children with T1D (age 5–8 years) compared to their usual home regimen of sensor-augmented pump (SAP) therapy.[27] Unique to this study was the use of altered Diabetes Assistant control-platform software, which included child-resistant (password-protected) lock-out screens for pump settings and carbohydrate ingestion; an addition meant specifically to address the potential safety issue of accidental or intentional tampering with the control settings of an AP system. The authors report significantly improved glycemic control with increased time of blood glucose in-range (70–180 mg/dL) within the AP period versus the SAP period (73% vs. 47%; $P < 0.001$) and increased percent time of blood glucose in tight control (80–140 mg/dL; 46% vs. 25%; $P < 0.001$). They also noted decreased rates of hyperglycemia and improved mean blood glucose in the AP group. These observations (mean blood glucose, time in-range 70–180 mg/dL) were even more prominent overnight; a time when many parents have significant worry about hypoglycemia in this age group. Overall, the number of hypoglycemic events was low in both study arms and there were no severe episodes of hypoglycemia. Of note, during the AP portion, the participants remained in closed-loop nearly 97% of the time and no child was observed gaining access to the system.[27]

Few other studies have evaluated AP use specifically in young children. Del Favero et al. recently reported decreased rates of hypoglycemia in 5–9-year olds on an AP system (versus parent-managed SAP) but at the expense of increased mean glucose and decreased time-in-target.[19] In another study, Russell et al. found lower mean glucose and decreased hypoglycemia (including decreased interventions needed for hypoglycemia) in the bihormonal AP group versus the participant's home CSII in a population of children aged 6–11 years.[21] Interestingly, parental satisfaction and trust in the AP system was high in a group of 5–9-year olds (and their parents) taking part in a week-long summer camp,[15] suggesting that this technology may not only be beneficial for glucose control but also helps to improve parental anxiety and burden of disease.

Although promising, many barriers remain in the successful implementation of these systems in young children with T1D. One is the need for very small insulin doses in these patients, creating challenges related to insufficient infusion volumes needed for optimal insulin delivery and available insulin dosing increments.[28] Currently, the Medtronic 670G AP system requires a minimum of 8 units of total daily insulin to operate safely, thus limiting its current use in very small children.[1] Recent articles discussing diluted insulin with CSII suggest improved glucose variability when compared to

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standard U-100 insulin.[28,29] Furthermore, the use of diluted insulin (U-20) as part of closed-loop (AP) therapy was feasible in maintaining overnight glucose control in a study of 11 young children (aged 3–6 years).[30] As many practitioners are not comfortable prescribing diluted insulin, and the need to be diluted by hand (introducing potential dosing error), the widespread use of diluted insulin is likely to be restricted. Additional barriers to AP use in young children include the limited amount of body surface area and adequate sites to wear two devices,[31] as well as frequent skin reactions and site failures in these patients.[32–34] Improved technologies, including a combined insulin infusion set and CGM sensor,[35] show promise and will be of great importance in this population. Finally, the use of AP algorithms that have been designed and tested in adults may not be appropriate for the management of very young children with T1D. However, the few studies evaluating AP use in children, including the featured article by DeBoer et al., do provide evidence that AP systems are feasible.[19,21,27,30]

In summary, DeBoer et al. have shown that AP use in young children results in improved mean blood glucose and time in-range without increased hypoglycemia when compared to conventional SAP use.[27] This study supports the current literature that AP is safe in this population and can improve overall glucose control while decreasing parental and patient burden. In addition, added features such as childproof lock-out screens provide real-world application to address some of the main safety concerns that face parents of young children with T1D. However, additional barriers including the need for small insulin doses, CSII and CGM sensor site availability, skin irritation and site failures, and the potential requirement of algorithms specific to young children persist.

Author Disclosure Statement

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