Diabetes Technology and Therapy in the Pediatric Age Group

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Abstract

Recent data from the Type 1 Diabetes Exchange has highlighted the urgent need for better glycemic control in the pediatric age group. Fortunately, ongoing research on insulin pumps, continuous glucose monitors, and artificial pancreas systems continues to improve our ability to manage type 1 diabetes in all age groups, while reducing the burden of care at the same time. Here we discuss the status of diabetes technology research as well as future directions and goals of these projects.

Keywords

Type 1 diabetes, pediatrics, insulin pump, continuous glucose monitoring (CGM), artificial pancreas

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Recent developments in diabetes technology—CSII, AP and CGM

We are currently in an extremely exciting time for diabetes technology which holds near-term promise to substantially improve the lives of children with type 1 diabetes (T1D). Recent data published by the Type 1 Diabetes Exchange confirms what clinical experience has shown for years, that diabetes control among adolescents and young adults is suboptimal and better tools are needed to improve care in this age group.[1,2] Continuous subcutaneous insulin infusion (CSII) pump therapy has emerged over the past decade as a vital tool for improved diabetes care with usage rates approaching 50% of pediatric T1D patients in the US and numerous studies showing improved quality of life, decreased rates of severe hypoglycemia, improved glycated hemoglobin (A_{1c}) values and decreased incidence of diabetic ketoacidosis (DKA) in patients using CSII.[3–8] Continuous glucose monitoring (CMG) has also seen dramatic improvements in the past three years, with increased sensor accuracy, decreased alarm fatigue and development of remote cell phone-based monitoring all contributing to a likely inflection point in patient uptake and use of this technology.[9–11]

The ultimate goal of this line of research, however, is integration of CGM and continuous insulin delivery into a closed-loop artificial pancreas (AP) system. In such a system, insulin delivery is controlled by an automated closed-loop control algorithm. Systems may be hybrid-closed loop systems, which still require meal announcement from the patient, or fully closed loop with minimal user input required. These systems may also be either insulin only or dual-hormone, with a second counter-regulatory agent included such as glucagon. The past two years have shown dramatic progress on the pathway towards commercially available AP systems.[12–14] Studies have been published for three-day to three-month periods in adults, adolescents, and children in clinical, camp, and at-home settings.[15–23] These studies demonstrate that AP technology does not simply lower glycemic targets but rather tightens glycemia, thereby producing lower average glucose values with decreased time in the hypoglycemic range. Use of these devices can thus be seen to improve glycemic control while at the same time increasing safety for patients with T1D.

Upcoming diabetes technology studies

The next phase of AP development involves moving from small, short term, highly supervised studies to real-world trials where several hundred participants wear these devices for three to six months in an outpatient setting. Kropoff and DeVries recently published an excellent update on these upcoming studies.[12] Among these pivotal, safety, and efficacy phase II and III studies are one industry pivotal study by Medtronic and multiple academic studies with systems under development at University of Cambridge, University of Virginia, Boston University, Stanford, Rensselear Polytechnic Institute, and the Sansum Diabetes Center. In addition multiple device manufacturers have proposed upcoming trials on next generation systems including Animas, Bigfoot Biomedical, and Tandem. These projects range from predictive low glucose suspend, to hypoglycemia-hyperglycemia minimization, to hybrid-closed loop systems with single and dual hormone designs. Projections for commercial availability of these systems are as soon as late 2016 to 2018.[12]

Future perspectives

While the first generation of AP technology will be a quantum leap forward for diabetes care, it is not the end of the road. Initial devices will still require patients to calibrate their CGM devices two to three times per day, perform self-monitoring of blood glucose (SMBG) at meals, count their carbohydrates, and bolus prior to eating. Current rapid acting insulin analogues are not nearly fast enough to replicate intra-portal delivery from pancreatic islets and sensor lag in detecting post-prandial glucose rise further exacerbates this problem. Development is ongoing for fully closed loop systems which seek to engineer around these system faults and predict meals based on complex modeling. In addition, pivotal trials are upcoming for the next generation of ultra-rapid insulin analogues which use additives and bio-chaperones to speed up capillary absorption of subcutaneous insulin. Such analogues hold immense potential to bridge the gaps in fully closed loop designs. Improvements in CGM are also on the horizon with multi-sensor arrays which cross-check different measurement devices against each other to improve accuracy and precision, calibration-free sensors which do not require finger-stick glucose validation, and dual port designs which combine the CGM and pump site in a single device. Current guidelines are to view CGM values as adjunctive data and to base correction insulin dosing on finger-stick values. Calibration-free sensors with approval for direct dosing from CGM values may alleviate the need for finger-stick glucose testing entirely. These projects all promise to reduce patient burden and improve quality of life for our patients.

As this technology moves forward, substantial additional training will be required for all providers who care for patients with T1D. Providers will need to become well versed in the menu of available devices in order to aid patients in selecting the system which is right for them. In addition, tuning these systems and adjusting their patient-specific parameters will likely be very different from adjusting multiple daily injection doses and modifying CSII pump settings. Providers must also counsel prospective users that these devices represent an improvement towards well controlled diabetes, but are not a panacea. Developments in diabetes technology are fast-moving and hold near-term potential to dramatically improve diabetes care for our patients in terms of both improved glycemic control, decreased burden, and improved quality of life. ■

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