

## Continuous Subcutaneous Insulin Infusion in the Very Young

a report by

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Throughout the world, the incidence of type-one diabetes mellitus is increasing. Over the past thirty years, the disease has increased by three per cent per year in all populations.<sup>1</sup> This trend is even more marked in very young children, in whom an annual increase of four per cent in children less than four years of age has been noted.<sup>2</sup> As advancements in technology and medical care of type-one diabetes continues, new insulin delivery devices are increasingly marketed and used in the treatment of children with diabetes.

One device in particular is the insulin pump, which is also known as continuous subcutaneous insulin infusion (CSII). Although insulin pump therapy has been available since the 1970s, this treatment was initially used exclusively in adults with type-one diabetes.<sup>3</sup> Insulin pumps are programmed to deliver a small amount of continuous short-acting basal insulin throughout the day. Insulin can be delivered through the pump to give food doses, which are used to cover the amount of food that is ingested at a particular meal or snack, and corrective doses, which are used to bring the blood sugar down to a target or goal blood sugar. Modern pumps can be programmed to easily calculate the food and corrective insulin doses, and insulin can then be delivered by pressing just a few buttons. The insulin pump is worn on the body, and insulin is delivered through specialized tubing and a cannula that inserts into the subcutaneous tissue at a site where insulin would typically be given by injection. The insertion site, insulin reservoir, and tubing are changed every two to three days.

Over the past several years, with the use of rapid-acting insulin analogs such as lispro (Humalog®), aspart (NovoLog®), or glulisine (Apidra®), and improvements in pump technology, the popularity of CSII in the pediatric population has risen exponentially. Many studies have been published acknowledging that insulin pump therapy in children and adolescents is safe and effective.<sup>4</sup> Few prospective clinical studies have focused on insulin pump therapy in young children, especially in those less than six years of age. Despite this, media hype and 'testimonials' from parents of young diabetic children have resulted in increased pressure on pediatric

endocrinologists to prescribe CSII for their young patients. In order to promote realistic expectations, practitioners need to have a good understanding of the current state of knowledge in this area and of the questions that remain to be answered.

### Are Insulin Pumps in Toddlers Safe and Effective?

The first study to prospectively investigate insulin pump therapy in diabetic pre-school aged children was published in 2004.<sup>5</sup> This controlled clinical trial enrolled 42 patients, of whom 37 completed six months of therapy. Compared with multiple daily injections (MDI), pump therapy was not associated with differences in blood sugar control, severe hypoglycemia, or episodes of diabetic ketoacidosis. Pump therapy appeared to be safe and was well tolerated. Parental satisfaction with CSII was high, and nearly all families chose to continue to use an insulin pump after completion of the study.

Two additional prospective controlled trials of insulin pump therapy in children less than six years of age were subsequently performed.<sup>6,7</sup> In the first, CSII was compared to a conventional insulin regimen consisting of MDI over a period of twelve months.<sup>6</sup> Overall metabolic control, diabetes quality-of-life, and incidence of hypoglycemia were similar in the two groups. None of the subjects experienced diabetic ketoacidosis. Similar to the previous study, all of the patients elected to continue to use CSII after the study ended. In the other study, similar results were reported, and again, all of the patients elected to continue on CSII after completion of the study.<sup>7</sup>

Although the above studies involved small numbers of patients treated for short periods of time, the results from these prospective clinical trials are remarkably consistent. Contrary to what is often believed by the lay public, use of an insulin pump does not necessarily improve glycemic control in very young children.<sup>8</sup> The lack of improvement in diabetes control from CSII in the very young child suggests that justification for this approach may come from lifestyle concerns rather than



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**Table 1: The Pros and Cons of Insulin Pump Therapy (CSII) in Young Children**

<b>Pros</b>	<b>Cons</b>
No shots	Increased cost (dependent on health insurance coverage)
Improved flexibility	Need for a knowledgeable caregiver who can operate pump properly and know when to troubleshoot
Strong parental preference	Potential for mechanical failure
Excellent safety	Attached to a device at all times
Ability to suspend insulin delivery during times of hypoglycemia	

a medical imperative. The nearly universal preference for insulin pumps on the part of parents of young diabetic children is striking. Although untested, it is possible that other parameters, in addition to parental stress, such as behavioral and cognitive indices, are improved in young children treated with CSII as compared with conventional insulin therapy. In combination with numerous retrospective reports,<sup>9,10</sup> the safety of CSII in young children has clearly been established. There is no lower limit of age for which insulin pumps may be employed.

In cases of neonatal diabetes mellitus, which manifests in the first six months of life, CSII has also been reported to be beneficial.<sup>11</sup> As infants with neonatal diabetes often require very small amounts of basal and bolus insulin, CSII can allow for more physiologic and accurate administration of insulin than MDI. Some insulin pumps can deliver a basal rate as low as point-zero-two-five units per hour, and pumps can even be programmed for intermittent insulin administration if needed. CSII appears to be both safe and efficacious in the very young patient with insulin-dependent diabetes mellitus.

#### **Which Young Children Should be on an Insulin Pump?**

Carefully selecting which child should start on insulin pump therapy is often the most critical factor in determining who will thrive and who will fail on this regimen. A recent position statement from the Lawson

Wilkins Pediatric Endocrine Society about CSII in very young children with type-one diabetes outlined recommendations and clinical management guidelines for this patient population.<sup>12</sup>

As young children with diabetes are not responsible for their everyday medical care, a motivated and involved parent is critical for a young child's success with CSII. Pre-pump HgbA<sub>1c</sub> was one of the few factors identified, which predicts success in school-aged children on insulin pumps.<sup>13</sup> Although insulin pump therapy does allow for increased lifestyle flexibility, the added cost and technical aspects of CSII may be overwhelming for some families. Newer long-acting basal insulins, such as the 24-hour peakless glargine (Lantus®), combined with rapid-acting insulin analogs at meals, can afford the same level of flexibility as on an insulin pump. The ability to spare young children from requiring frequent injections is a huge benefit for many families.

The extra expense of insulin pump therapy largely depends on the child's health insurance reimbursement, deductible, and prescription co-payment. In a recent cost analysis from the United Kingdom, researchers concluded that the additional resources required to pay for insulin pump therapy for a proportion of children with diabetes would be minimal given the potential benefits in these patients of improved diabetes control and anticipated reduction in long-term morbidity.<sup>14</sup> Further research is needed to see if such potential medical benefits of insulin pump therapy in young children are substantiated. Given the clinical experience and data that we have to date, it appears that the positive aspects of insulin pump therapy in a young child outweigh the extra expense, provided that the parents or other supervising adults maintain appropriate vigilance. Pros and cons of CSII in young children with diabetes are listed in *Table 1*. Further in depth analyses of the cost-to-benefit ratio of CSII in this population are badly needed.

#### **Summary and Conclusions**

The use of CSII in very young diabetic children is on the rise. As insulin pumps appear to be effective and safe in this age group, CSII should be considered an option for pre-school-aged patients with insulin-dependent diabetes. Attempts to identify optimal candidates for this approach must continue. Long-term, large-scale studies are needed to further elucidate the impact of insulin pumps on diabetes control and quality of life in young children. ■

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