

# A Two-Center Randomized Controlled Feasibility Trial of Insulin Pump Therapy in Young Children With Diabetes

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**OBJECTIVE** — Our goals were to determine if continuous subcutaneous insulin infusion (CSII), compared with those continuing multiple daily injections (MDIs), can be safely used in young children, if those on CSII will have superior glycemic control, if subjects using CSII will have less hypoglycemia for their level of control, and if families using CSII will report an improved quality of life.

**RESEARCH DESIGN AND METHODS** — We conducted a randomized 1-year feasibility trial comparing CSII with continuing MDIs in preschool children with a history of type 1 diabetes for at least 6 months' duration. Prospective outcomes included measures of overall glycemic control (HbA<sub>1c</sub> and continuous glucose monitoring system), the incidence of severe hypoglycemia and diabetic ketoacidosis, the percent of glucose values below 3.9 mmol/l, and the parents' report of quality of life.

**RESULTS** — The 19 subjects' ages ranged from 1.7 to 6.1 (mean 3.6) years, duration of diabetes ranged from 0.6 to 2.6 (mean 1.4) years, and baseline HbA<sub>1c</sub> ranged from 6.7 to 9.6% (mean 7.9%). Seven subjects were male. Nine subjects were randomized to start CSII and 10 to continue on MDI. All baseline characteristics were well balanced. Overall metabolic control, diabetes quality of life, and the incidence of hypoglycemia were similar in the two groups. No subject had diabetic ketoacidosis, while one subject in each group had an episode of severe hypoglycemia. No CSII subject discontinued using the pump during or after the study.

**CONCLUSIONS** — CSII can be a safe and effective method to deliver insulin in young children.

*Diabetes Care* 28:15–19, 2005

Since its introduction in the late 1970s, continuous subcutaneous insulin infusion (CSII), or insulin pump therapy, has become an increasingly popular option for type 1 diabetes management (1,2), particularly following

the push for improved metabolic control in the post-Diabetes Control and Complications Trial era (3). The potential advantages of such therapy over multiple daily injections (MDIs) include ease of insulin administration, improved metabolic con-

trol with reduced swings in glucose and decreased risk of hypoglycemia, better matching of insulin to carbohydrate intake, improved coverage of the dawn phenomenon and adjustment of basal insulin delivery at other times of the day, increased flexibility in daily living, and improved coping with diabetes (4,5). Potential disadvantages of CSII relative to MDI include increased cost, inconvenience of wearing a device, risk for subcutaneous infection at the pump infusion site, and diabetic ketoacidosis.

CSII has traditionally been reserved for savvy adolescents and adults, but it is gaining more widespread acceptance in children as well (6–12). One age-group in which the technology has been used sparingly but who may benefit from CSII is infants and toddlers. Although parents or other adult supervisors are available to oversee frequent glucose monitoring and multiple insulin injections, it is usually difficult to achieve near-normal metabolic control in this population. Potential limiting factors include marked sensitivity to insulin that require extremely small insulin doses, unique patterns of eating, with unpredictability of food intake and small frequent meals or grazing rather than distinct meals, and varied activity level. Finally, there are reports that recurrent hypoglycemia in children under age 6 years may predispose to neurocognitive damage, which often leads clinicians and investigators to use looser target ranges in this patient population (13). Thus, CSII would appear to be an attractive treatment option for toddlers, because it may facilitate dosing of insulin for small frequent meals and insulin dosing at fine increments, serving to minimize the risk for hypoglycemia while improving overall metabolic control. CSII use in this population has been controversial, and debate has arisen as to the safety and suitability of such therapy in these young patients. There are a few small reports of CSII use for toddlers suggesting that it may be effective for this population (7,14,15).

Although numerous studies in both adult and pediatric populations report

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Received for publication 7 July 2004 and accepted in revised form 27 September 2004.

B.A.B. has received honorarium for speaking engagements and grant support from MiniMed. M.M.S. is on an advisory panel for and has received honoraria for speaking engagements from Novo Nordisk.

**Abbreviations:** CGMS, continuous glucose monitoring system; CSII, continuous subcutaneous insulin infusion; DQOL, Diabetes Quality of Life; MDI, multiple daily injection.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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benefits from CSII, these studies are often limited by several important factors. They may be small and may not follow subjects over a significant time period. They often rely on family recall as a measure of hypoglycemic experience rather than prospective collection of glucose monitoring. Most importantly, they are not randomized prospective studies and are subject to selection bias.

The goal of this study was to prospectively conduct a 1-year, randomized, controlled, open-label feasibility trial comparing CSII with MDI in young children with diabetes. Our hypotheses were that CSII can be safely used in young children and that subjects using CSII would have equivalent or better glycemic control. We also expected that subjects using CSII would have less hypoglycemia for their overall level of control and that families using CSII would report an improved lifestyle.

## RESEARCH DESIGN AND METHODS

We sought toddlers and preschool children less than 6 years old with type 1 diabetes for at least 6 months whose families had not requested an insulin infusion pump. We required that a caregiver, generally a parent, be available at all times, be skilled at carbohydrate counting, and be willing to test glucose concentrations at least four times per day and at least once a week between 12:00 AM and 4:00 AM. Subjects who would be entering first grade during the 1-year duration of the study were excluded. We offered participation in this study to essentially all eligible families (~34) in both centers over a 13-month enrollment period starting in May 2001; those families who accepted form the basis of our sample size for this feasibility trial.

This study was approved by the Stanford University Administrative Panel on Human Subjects and the University of California, San Francisco Committee on Human Research. Signed consent was obtained from the parents.

After consenting to the study, all families met with a registered dietitian to review each subject's dietary prescription and to assure an understanding of carbohydrate counting. The families subsequently met with a certified diabetes educator (CDE) to review approaches to insulin adjustment (16). Subjects were then seen for a baseline visit and were randomized by selecting, in sequence, a single card (concealed in an individual

opaque envelope) that had previously been arranged into blocks of eight, stratified by center, and shuffled. Those randomized to the CSII group then attended two pump initiation sessions and used the Medtronic MiniMed 508 insulin infusion pump. Six subjects (66%) randomized to the CSII group used diluted lispro insulin in their pumps (four subjects used U50, and two used U40). Insulin was diluted by a pharmacist for University of California, San Francisco patients, and parents were carefully instructed in how to dilute insulin at Stanford University.

While the group assignment could not be blinded, both the CSII and MDI had the same glycemic goals. The goals for these young children were a preprandial glucose target of 8.3 mmol/l and a bedtime target of 9.7 mmol/l, with an overall average glucose target between 5.6 and 11.1 mmol/l. Our HbA<sub>1c</sub> target range was 7.5–8.5%.

All subjects were seen at 4, 12, 20, 28, 36, 44, and 52 weeks and met with either a physician or CDE for a review of their interval glycemic control, and adjustments were made to help subjects reach the study's glycemic goals. At each visit, an interval history (including severe hypoglycemia and other adverse events), a physical examination, glucose meter and pump download, and HbA<sub>1c</sub> (as measured by the DCA 2000; Bayer) were conducted. While we attempted to have our subjects use the Precision Xtra meter so that we could also quantify serum ketones, many subjects used an Ultra meter (Lifescan, Milpitas, CA). Diabetes team members were also available between visits to assist families in adjusting their insulin regime.

Near continuous glucose monitoring profiles were obtained using the continuous glucose monitoring system (CGMS) (Medtronic MiniMed, Northridge, CA) at baseline, 4, 28, and 52 weeks. These profiles were directly summarized using MiniMed Solutions CGMS Sensor software (MMT-7310, version 3.0A [3.0.108]).

A Diabetes Quality of Life (DQOL) questionnaire, designed for parents of toddlers with diabetes, was administered to a parent at baseline, 28 weeks, and 52 weeks. This 51-item instrument used a 5-point Likert scale scored 1 (very satisfied) to 5 (very dissatisfied). Low scores represent greater satisfaction. This questionnaire was based on a questionnaire used in the Diabetes Control and Compli-

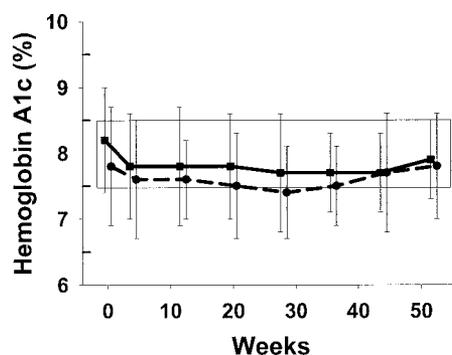
cation Trial (17) and was modified for use in families with young children. Socioeconomic status was estimated by mean of the parents' years of education.

## Statistical analysis

Data were entered into Microsoft Access and subsequently analyzed using an intent-to-treat model with the Statistical Analysis System program (version 8.2; SAS, Cary, NC). Height and BMI Z-scores were calculated using data from the Centers for Disease Control and Prevention (18). Between-group comparisons of continuous measures were made using Student's *t* tests or Wilcoxon's rank-sum test, while frequency comparisons were made using  $\chi^2$  test. Correlations between continuous variables were calculated using Spearman's method. *P* values <0.05 were considered significant. Results are expressed as means  $\pm$  SD unless otherwise indicated.

**RESULTS**—Twenty-four subjects consented to the study, but two discontinued before randomization. Three randomized subjects discontinued their child's involvement in the study shortly after randomization (one in the CSII was lost to follow-up shortly after randomization visit, one in the CSII group because of delay in getting the pump, and one in the MDI group because they moved out of the state just following randomization). Seventeen of the remaining 19 randomized subjects completed the full year of the study. One subject moved out of the area after the 36-week visit, and one subject's last visit was at 44 weeks. Data from all 19 subjects (9 in the CSII and 10 in the MDI group) are included in the analysis.

Seven boys and 12 girls with a mean age of  $3.6 \pm 1.0$  ( $\pm$ SD) years and a mean duration of diabetes of  $1.4 \pm 0.6$  years form the basis of this report. At baseline, subjects were receiving  $0.68 \pm 0.17$  (units  $\cdot$  kg<sup>-1</sup>  $\cdot$  day<sup>-1</sup>) of insulin using  $3.3 \pm 0.7$  injections/day (three subjects, two injections per day; eight subjects, three injections per day; and eight subjects, eight injections per day). At baseline, three (16%) subjects were using glargine, five (26%) were using ultralente, and 15 were using NPH at baseline (some subjects received both NPH and ultralente or glargine). Mean HbA<sub>1c</sub> was  $8.0\% \pm 0.8$ . The height Z score was  $0.2 \pm 1.5$ , and the BMI Z score was  $0.9 \pm 1.4$ . The mean duration of parental education was



**Figure 1**—Mean  $\pm$  SD HbA<sub>1c</sub> over the course of the study. —■—, CSII (9 subjects); -●-, MDI (10 subjects). The boxed area highlights the HbA<sub>1c</sub> goal for these subjects.

15.7  $\pm$  2.8 years (range 8.5–22). These baseline characteristics of subjects in the two groups were similar ( $P > 0.05$ ).

### CSII initiation

The nine CSII subjects were started on 0.54  $\pm$  0.11 units  $\cdot$  kg<sup>-1</sup>  $\cdot$  day<sup>-1</sup>, 83  $\pm$  10% of pre-CSII total daily dose of injected insulin. Six subjects were started on three basal rates per 24 h, and one subject each was started on one, two, and five basal rates per 24 h.

### Changes in glycemic control

Overall, HbA<sub>1c</sub> values (Fig. 1) fell only slightly (NS) over the year of the study ( $-0.08 \pm 0.68\%$ ). There was no significant difference ( $P = 0.44$ , Student's *t* test) in the change in HbA<sub>1c</sub> between the two groups ( $-0.21 \pm 0.67\%$ , CSII;  $0.04 \pm 0.71\%$ , MDI). Likewise, the percentages of glucose reading below target, within target, and above target, whether measured by CGMS (Fig. 2) or home glucose monitoring (data not shown), were similar at all time points and between groups. Likewise, the percent of glucose levels  $<3.9$  mmol/l did not differ between groups at any time point (data not shown).

### Changes in insulin doses

Over the course of the study, the mean number of injections per day among the MDI subjects remained at 3.4  $\pm$  0.7 injections per day, and the insulin dose increased insignificantly (from 0.70  $\pm$  0.18 to 0.73  $\pm$  0.20 units  $\cdot$  kg<sup>-1</sup>  $\cdot$  day<sup>-1</sup>). The percentage of MDI subjects using glargine increased from 10 to 60% ( $P < 0.05$ ,  $\chi^2$ ).

Among the CSII subjects, the mean number of basal rates per day increased

significantly from 2.9  $\pm$  1.1 at the pump initiation to 4.8  $\pm$  2.2 at the end of the study ( $P < 0.02$ , Wilcoxon's rank-sum test). The total daily insulin dose increased insignificantly ( $P = 0.08$ , paired Student's *t* test) from 0.54  $\pm$  0.11 to 0.62  $\pm$  0.12 units  $\cdot$  kg<sup>-1</sup>  $\cdot$  day<sup>-1</sup>.

### DQOL

Both groups had similar mean DQOL scores at baseline (CSII, 2.3  $\pm$  0.3; MDI, 2.3  $\pm$  0.6). DQOL improved slightly in both groups ( $\Delta$  DQOL: CSII,  $-0.24 \pm 0.25$ ; MDI,  $-0.08 \pm 0.19$ ). The improvement in the CSII group, baseline to the end of the study, was significant ( $P = 0.03$ , paired Student's *t* test). The difference between the two groups, CSII versus MDI, however, was not.

### End of study selections

All nine subjects randomized to CSII continued to use their insulin pumps at the end of the study. Three of the 10 subjects in the MDI group elected to switch to CSII at the end of the study, with an additional subject switching to CSII 1 year later. Many of the MDI subjects were to enter first grade at the end of the study, and families were reluctant to transition to CSII during this immediate period.

### Adverse events

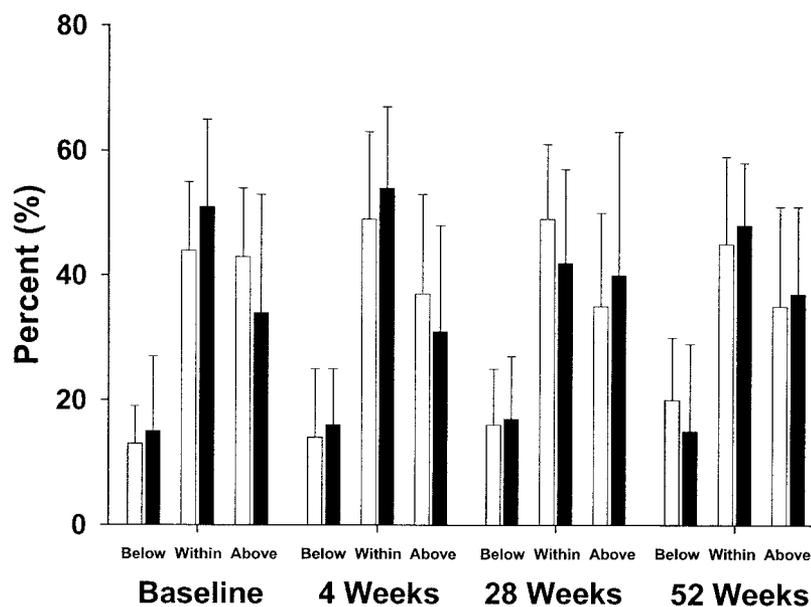
No subject developed diabetic ketoacidosis during the study. One CSII subject and one

MDI subject had an episode of severe hypoglycemia. Of note, this CSII subject had multiple severe hypoglycemic episodes while on MDI before randomization.

**CONCLUSIONS**— We report on the safety and efficacy of CSII in young children with type 1 diabetes. One underlying concern with the use of CSII in this age-group has been the potential risk for diabetic ketoacidosis, but no diabetic ketoacidosis occurred during this study. The incidence of hypoglycemia was very similar in both groups. Concerns that young children might be tempted to remove or meddle with the pump did not materialize. These data indicate that CSII can be used safely in this population, provided that the family is given appropriate instruction and backup.

Although many studies report a benefit in CSII relative to MDI, we found that both CSII and MDI were equally efficacious in this patient population. Specifically, both modalities resulted in similar metabolic control, similar frequency of hypoglycemia, and no difference in quality of life. There was an improvement in the reported quality of life among those families randomized to CSII.

Although there are numerous published studies describing experiences with CSII, a number of methodological considerations may confound evaluation of the efficacy of CSII as compared with



**Figure 2**—Mean percent  $\pm$  SD of CGMS-derived glucose concentrations below target ( $<5.6$  mmol/l), within target (5.6–11.1 mmol/l), and above target ( $>11.1$  mmol/l) in the CSII (□, 9 subjects) and MDI (■, 10 subjects) groups.

MDI. Many of these studies have poor research design. They usually are not randomized prospective trials or conducted in a crossover study design and lack a comparison control group, instead using the subject as their own control over time. These studies are subject to a selection bias of both the treated subject and the treating investigator. One inherent bias in such studies is that one has to determine a baseline measure of metabolic control, and yet this may be improving as the subject and family is receiving intensive education before or at the time of CSII initiation. Finally, the studies may use a wide range of ages and often do not include young children.

Two meta-analyses have reviewed the CSII experience, attempting to select the best studies that take the above limitations into account. Pickup et al. (19) analyzed 12 randomized controlled trials that compared CSII with optimized MDI regimens. They noted in general, but not in all studies, that the CSII groups exhibited a relatively small improvement in blood glucose concentration of  $\sim 1$  mmol/l and a 0.5% reduction in HbA<sub>1c</sub>. These studies were performed primarily in adults, with some adolescents represented. Limitations of this analysis include the fact that the studies range from 1982 to 2000, and much has changed in diabetes management over this time, including the use of newer insulin analogs as well as improved pump technology. Nonetheless, the investigators found that the comparisons between MDI and CSII seemed to hold over time. However, the duration of the particular study seemed to be an issue, with longer studies more likely to note a larger impact of CSII on metabolic control. Weissberg-Benchell et al. (20) reported on a broader meta-analysis of 52 studies on CSII, of which 41 were paired design (comparing control before pump and then changes over time on CSII) versus 11 parallel design studies (comparing subjects randomized to CSII versus MDI over time, as with our study), and also found similar trends toward improvement in metabolic control.

In the pediatric population, there are two recent prospective randomized trials of CSII versus MDI in an older cohort of children and adolescents with type 1 diabetes. The first was a 3-month crossover study, with one group starting with MDI and the other with CSII (12). The 23 subjects had a mean age of 11.8 years. The

findings in this study were similar to what was noted in our prospective randomized toddler study over 1 year; the changes in HbA<sub>1c</sub> and fructosamine were similar in the two arms over time, with no difference in severe hypoglycemic or hyperglycemic events and no episodes of diabetic ketoacidosis. No difference was noted in quality of life, although the CSII group exhibited a higher treatment satisfaction than the MDI group. Several important issues from this study bear commentary. First, the duration of pump therapy was short, and one can speculate as to whether more time on the pump would have resulted in continued improvement in metabolic control over time as opposed to a plateau. Second, the MDI group may have benefited further from a more sophisticated insulin regimen. Instead of the lispro used in the CSII group, they used regular insulin at meals, and the MDI group also used evening NPH rather than glargine. Third, the investigators noted that a significant improvement in metabolic control occurred between the time of the initial education session 3 months before the start of the study and the onset of the study, with no significant difference noted between CSII and MDI during the course of the study. Thus, further diabetes education and expectations for intensive management, regardless of the method of insulin administration, appeared to be the most important factor in optimizing metabolic control in this study. In the second randomized study, Doyle et al. (21) recently demonstrated improved HbA<sub>1c</sub> with 16 weeks of CSII as compared with glargine among 32 subjects aged 8–21 years.

Much more limited studies have been conducted on the use of CSII for toddlers and preschool children (7,14,15). Most recently, Litton et al. (7) reported on their experience with nine children (mean age of CSII initiation 34 months) selected to receive CSII. Unlike our study, their group had an average decrease in HbA<sub>1c</sub> from 9.5 to 7.9%, with a decrease in the incidence of severe hypoglycemia. As in our study, they required supervision throughout the day by a parent or caretaker to ensure appropriate use of the insulin pump, but unlike our study, the subjects were not randomized to MDI or CSII. Furthermore, the subjects required poor metabolic control to enter the study, including erratic glucose swings with either a history of diabetic

ketoacidosis or severe hypoglycemia not ascribed to poor adherence to the regimen, or recurrent hypoglycemia, and one of the exclusion criteria was HbA<sub>1c</sub> <9%. Thus, they eliminated subjects who would still in theory benefit from CSII and who would exhibit a lesser degree of change in HbA<sub>1c</sub> as opposed to MDI, i.e., such criteria would self-select for a population that would exhibit a greater benefit in the transition to CSII. Although the authors noted a significant decrease in the number of severe hypoglycemic episodes for subjects during the course of CSII therapy, this was estimated by parental recall, and there was no systematic tracking of daily glucose meter values as performed in our study. The authors report that families had less interaction with the health care providers and no increase in glucose monitoring, although, again, there does not appear to be systematic comparison with downloading of the glucose meters throughout the course of the study. As with any longitudinal study during childhood, one cannot exclude that CSII altered the parents' interaction with the child during the course of the study or that the child's inherent development during the study altered the diabetes control or their clinical course over time.

One additional factor in the comparison between MDI and CSII is the recent introduction of glargine, the first true basal insulin for use in MDI regimens. It was approved in the U.S. several months before this study was initiated and was used in only a subset of the MDI subjects in this study during a portion of the 12-month observation period. However, several initial adult studies note comparable metabolic control in MDI regimens incorporating glargine versus CSII (22–24). Further studies with younger children will be necessary to evaluate the efficacy of glargine in this age-group.

In summary, CSII can be a safe and effective method to deliver insulin in young children but does not appear to have significant advantages over MDI. Moreover, while we did not collect cost data, CSII was likely more costly than MDI. Further randomized prospective studies or crossover trials comparing CSII with MDI will enable us to gauge the relative benefit of these treatment modalities in different patient populations.

**Acknowledgments**— This research was supported by a generous gift from the Lucile Packard Foundation for Children's Health and Medtronic MiniMed. We received in kind support from Abbott Laboratories the Precision Xtra by MediSense.

Preliminary data were presented as a poster at the American Diabetes Association 63rd Scientific Sessions, 13–17 June 2003, New Orleans, Louisiana.

This study would not have been possible without the support of all our patients and their families.

## References

1. Tamborlane WV, Sherwin RS, Genel M, Felig P: Reduction to normal of plasma glucose in juvenile diabetes by subcutaneous administration of insulin with a portable infusion pump. *N Engl J Med* 300: 573–578, 1979
2. Pickup JC, Keen H, Parsons JA, Alberti KG: Continuous subcutaneous insulin infusion: an approach to achieving normoglycaemia. *BMJ* 1:204–207, 1978
3. The Diabetes Control and Complications Trial Research Group: The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. *N Engl J Med* 329:977–986, 1993
4. Pickup J, Keen H: Continuous subcutaneous insulin infusion at 25 years: evidence base for the expanding use of insulin pump therapy in type 1 diabetes. *Diabetes Care* 25:593–598, 2002
5. Schade DS, Valentine V: To pump or not to pump. *Diabetes Care* 25:2100–2102, 2002
6. Maniatis AK, Klingensmith GJ, Slover RH, Mowry CJ, Chase HP: Continuous subcutaneous insulin infusion therapy for children and adolescents: an option for routine diabetes care. *Pediatrics* 107:351–356, 2001
7. Litton J, Rice A, Friedman N, Oden J, Lee MM, Freemark M: Insulin pump therapy in toddlers and preschool children with type 1 diabetes mellitus. *J Pediatr* 141: 490–495, 2002
8. Kaufman FR, Halvorson M, Fisher L, Pitukcheewanont P: Insulin pump therapy in type 1 pediatric patients. *J Pediatr Endocrinol Metab* 12 (Suppl. 3):759–764, 1999
9. Conrad SC, McGrath MT, Gitelman SE: Transition from multiple daily injections to continuous subcutaneous insulin infusion in type 1 diabetes mellitus. *J Pediatr* 140:235–240, 2002
10. Boland EA, Grey M, Oesterle A, Fredrickson L, Tamborlane WV: Continuous subcutaneous insulin infusion: a new way to lower risk of severe hypoglycemia, improve metabolic control, and enhance coping in adolescents with type 1 diabetes. *Diabetes Care* 22:1779–1784, 1999
11. Willi SM, Planton J, Egede L, Schwarz S: Benefits of continuous subcutaneous insulin infusion in children with type 1 diabetes. *J Pediatr* 143:796–801, 2003
12. Weintrob N, Benzaquen H, Galatzer A, Shalitin S, Lazar L, Fayman G, Lilos P, Dickerman Z, Phillip M: Comparison of continuous subcutaneous insulin infusion and multiple daily injection regimens in children with type 1 diabetes: a randomized open crossover trial. *Pediatrics* 112:559–564, 2003
13. Ryan CM, Becker DJ: Hypoglycemia in children with type 1 diabetes mellitus: risk factors, cognitive function, and management. *Endocrinol Metab Clin North Am* 28:883–900, 1999
14. Bougneres PF, Landier F, Lemmel C, Mensire A, Chaussain JL: Insulin pump therapy in young children with type 1 diabetes. *J Pediatr* 105:212–217, 1984
15. Tubiana-Rufi N, de Lonlay P, Bloch J, Czernichow P: Remission of severe hypoglycemic incidents in young diabetic children treated with subcutaneous infusion [in French]. *Arch Pediatr* 3:969–976, 1996
16. Buckingham B, Bluck B, Wilson DM: Intensive diabetes management in pediatric patients. *Curr Diab Rep* 1:11–18, 2001
17. The DCCT Research Group: Reliability and validity of a diabetes quality-of-life measure for the diabetes control and complications trial (DCCT). *Diabetes Care* 11: 725–732, 1988
18. Kuczmarski RJ, Ogden CL, Guo SS, Grummer-Strawn LM, Flegal KM, Mei Z, Wei R, Curtin LR, Roche AF, Johnson CL: CDC Growth Charts for the United States: methods and development. *Vital Health Stat* 11:1–190, 2002
19. Pickup J, Mattock M, Kerry S: Glycaemic control with continuous subcutaneous insulin infusion compared with intensive insulin injections in patients with type 1 diabetes: meta-analysis of randomised controlled trials. *BMJ* 324:705, 2002
20. Weissberg-Benchell J, Antisdel-Lomaglio J, Seshadri R: Insulin pump therapy: a meta-analysis. *Diabetes Care* 26:1079–1087, 2003
21. Doyle EA, Weinzimer SA, Steffen AT, Ahern JA, Vincent M, Tamborlane WV: A randomized, prospective trial comparing the efficacy of continuous subcutaneous insulin infusion with multiple daily injections using insulin glargine. *Diabetes Care* 27:1554–1558, 2004
22. Lepore G, Dodesini AR, Nosari I, Trevisan R: Both continuous subcutaneous insulin infusion and a multiple daily insulin injection regimen with glargine as basal insulin are equally better than traditional multiple daily insulin injection treatment. *Diabetes Care* 26:1321–1322, 2003
23. Harmel AP, Mathur R: Similar A1C outcomes in type 1 diabetic patients undergoing intensive diabetes management with preprandial rapid-acting insulin and either CSII or glargine. *Diabetes Care* 27: 272–273, 2004
24. Garg SK, Walker AJ, Hoff HK, D'Souza AO, Gottlieb PA, Chase HP: Glycemic parameters with multiple daily injections using insulin glargine versus insulin pump. *Diabetes Technol Ther* 6:9–15, 2004