

Insulin Pump Therapy

A meta-analysis

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OBJECTIVE — To conduct a meta-analysis of the metabolic and psychosocial impact of continuous subcutaneous insulin infusion (CSII) therapy on adults, adolescents, and children.

RESEARCH DESIGN AND METHODS — Studies were identified and data regarding study design, year of publication, sample size, patient's age, diabetes duration, and duration of CSII therapy were collected. Means and SDs for glycohemoglobin, blood glucose, insulin dosages, and body weight for CSII and comparison conditions were subjected to meta-analytic procedures. Data regarding pump complications and psychosocial functioning were reviewed descriptively.

RESULTS — A total of 52 studies, consisting of 1,547 patients, were included in the meta-analysis. Results indicate that CSII therapy is associated with significant improvements in glycemic control (decreased glycohemoglobin and mean blood glucose). A descriptive review of potential complications of CSII use (e.g., hypoglycemia, diabetic ketoacidosis [DKA], pump malfunction, and site infections) suggests a decreased frequency of hypoglycemic episodes but an increased frequency of DKA in studies published before 1993.

CONCLUSIONS — CSII therapy is associated with improved glycemic control compared with traditional insulin therapies (conventional therapy and multiple daily injections) and does not appear to be associated with significant adverse outcomes. Additional studies are needed to further examine the relative risks of CSII therapy, including the potential psychosocial impact of this technologically advanced therapy.

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Interest in the efficacy and utility of continuous subcutaneous insulin infusion (CSII) therapy in patients with type 1 diabetes began in the late 1970s (1–3). Research over the past 20 years has examined the relative impact of CSII versus conventional or intensified injection therapies on metabolic control.

Both the Diabetes Control and Complications Trial (DCCT) (4) and the U.K. Prospective Diabetes Study (UKPDS) (5) have highlighted the importance of intensive therapy in achieving tight metabolic

control and improving long-term health. Since the release of the DCCT and UKPDS, health care providers have been working with their patients to optimize glycemic control either through multiple daily injection (MDI) or CSII therapy. The release of these studies has also renewed interest in the role of CSII therapy in improving metabolic outcomes, because it offers a more precise physiological method of insulin administration.

Advances in technology have allowed individuals with diabetes a choice in

insulin delivery methods: MDI or CSII. This choice has made it more feasible for individuals to meet the intensive regimen goals recommended by the DCCT and UKPDS. Although both methods of insulin administration appear to improve metabolic functioning, the relative risks and benefits of each approach remain unclear. The primary reason for this lack of clarity in outcomes is the methodological flaws in many of these studies. Many have poor research designs, no comparison controls, and small sample sizes. Some combine subjects with type 1 and type 2 diabetes, and others combine subjects from different age-groups. Furthermore, while these intensified regimens (MDI and CSII) are technologically advanced, they also increase the daily diabetes self-care demands on the patient and the patient's family. This increase in demand (and therefore time) often makes the balance between living a well-rounded life and caring for the medically specific needs of the person's diabetes a challenge for all concerned. The World Health Organization (6) defines health as a "state of complete physical, mental, and social well-being, and not merely the absence of disease or infirmity." Successful therapy must demonstrably improve a person's medical symptoms as well as that person's daily functioning. Although interest in the impact of CSII therapy on psychosocial outcomes has increased, the amount of literature on psychosocial outcomes is considerably less than the amount of literature on metabolic outcomes.

We believe that a clear understanding of the metabolic and psychosocial impact of CSII therapy on adults, adolescents, and children has been hampered by the lack of a comprehensive quantified review of the existing literature. Therefore, we have conducted a meta-analytic review of the research related to CSII use.

RESEARCH DESIGN AND METHODS

Selection of studies

Literature searches were conducted on MEDLINE and PubMed using the key-

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Abbreviations: CSII, continuous subcutaneous insulin infusion; CT, conventional therapy; DCCT, Diabetes Control and Complications Trial; DKA, diabetic ketoacidosis; MDI, multiple daily injection; UKPDS, U.K. Prospective Diabetes Study.

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

words “insulin,” “pump,” “insulin infusion,” and “continuous subcutaneous insulin infusion (CSII)” to identify relevant studies. Studies were also obtained from review articles and from references contained within individual articles. To be included in this meta-analysis, studies must have met the following criteria: 1) be original research reports published in peer-reviewed journals; 2) have subjects who are children, adolescents, and/or adults using CSII for a minimum of 4 weeks for the treatment of type 1 diabetes; 3) be studies that presented outcomes in a manner that permitted data analysis (i.e., means and SD) for the quality of glycemic control (HbA_{1c} and/or mean blood glucose values); and 4) compare CSII use with other diabetes treatments (e.g., conventional therapy [CT] or MDI) either for the same individual or between treatment groups. Non-English studies (e.g., French, Spanish, German, and Italian) were translated and included if they met the above criteria. Case studies, review articles, letters, opinion pieces, studies including subjects with other major health complications (e.g., kidney transplantation), and studies assessing CSII use during nighttime only were excluded.

Of the 2,483 studies identified through our initial search, 61 studies met the criteria listed above and were then subjected to an in-depth review for the meta-analysis section of this report. Two studies (7,8) reported data separately for pediatric (<20 years of age) and adult samples. Data from these studies were abstracted according to the above-defined specifications and were treated as independent data points. One study (9) reported data separately for two different treatment modalities (wearing the pump full-time and wearing the pump at nighttime only). Only the data from wearing the pump full-time were used. Therefore, 63 studies were reviewed from 61 published studies.

Methodological criteria

Studies were reviewed and data were abstracted for the following variables: year of publication, sample size, age of subjects, diabetes duration, length of time on CSII therapy, assay used to determine glycemic control (e.g., HbA_{1c}, HbA₁), means and SDs for HbA_{1c} or HbA₁, mean blood glucose values, units of insulin per kilogram per day, total daily insulin dose, and body weight for CSII and comparison

conditions/groups. Studies were classified according to one of the following study designs: paired (pre-/postpump: the same individuals were assessed before and after initiation of CSII; *n* = 37) (2,3,8,10–41), randomized crossover (subjects underwent both CSII and CT/MDI for distinct periods of time, the order of which was randomized; *n* = 15) (7,9,42–53), and parallel (subjects using CT/MDI were compared with those using CSII; *n* = 11) (54–64). If the study used a parallel design (e.g., compared CSII with MDI in separate groups of patients) but also reported pre-pump data for the CSII group, the study was classified as a paired design and only the data from those subjects using CSII were used, because a paired design is more powerful for detecting within-person changes.

To incorporate the 15 randomized crossover studies into the meta-analysis, they were reclassified into either paired or parallel design categories, based on the carryover effects. Carryover is the effect of treatment in the first period that continues into the second. Of these 15 studies, carryover effect was reported in only four (45,46,49,53), all of which were found to be not significant at a 0.05 level of significance. Because the order of administering insulin via CSII or MDI was irrelevant, data from both periods were combined and the studies were reclassified as paired designs. The remaining 11 studies that did not report carryover effects could not be included in the present meta-analysis. In cases where carryover effect is not reported or is significant, it is recommended to use data from the first period only (65), as if it were from a parallel design study. However, none of these 11 studies reported results from each treatment (CSII and MDI) for each period separately. Therefore, of the 63 studies originally eligible for intensive review, 52 were eligible for inclusion in the meta-analysis. A total of 41 studies were classified as paired design, and 11 were classified as parallel group design. Of the 41 paired design studies, 5 used random assignment procedures, whereas the rest enrolled self-selected patients. Of the 11 parallel design studies, 1 used random assignment procedures.

Comparison conditions were defined as CT if subjects used two or fewer injections and as MDI therapy if three or more injections were taken per day. When articles reported data for both CT and MDI

comparison groups, MDI values were used as the comparison group because it has already been conclusively demonstrated that intensive insulin therapy is superior to conventional treatment in improving glycemic control and in reducing the risk of serious diabetes-related complications (4,66).

Data regarding the risks of CSII therapy (e.g., diabetic ketoacidosis [DKA] or severe hypoglycemia) and psychosocial outcomes of CSII use (e.g., quality of life, depression, satisfaction, etc.) were also abstracted. However, these data could not be analyzed using meta-analytic procedures because few studies included this information, and when data were presented, they were not reported in a common metric. Studies examining CSII therapy, which were excluded from the meta-analysis because of insufficient data (e.g., means and/or SDs of glycohemoglobin/blood glucose were not reported), were included in the descriptive analysis of potential risks of insulin pump therapy when such data were reported.

Statistical methods and analysis

Two different approaches were used to analyze the data, based on the design of the study. Homogeneity among the studies that used a parallel design was determined via the *Q*-statistic, which follows a χ^2 distribution with *df* equaling one less than the total number of parallel design studies. To test the effect of CSII compared with MDI or CT, a summary mean difference over all 11 studies was computed, which was the average of the differences in each of the studies, weighted by the inverse of the respective variances. The 95% CI of this summary mean was used to determine whether the difference in mean outcome was of statistical significance.

Paired design studies were analyzed using a repeated-measures model (67) with pre- and postpump summary means as the response, weighted by the inverse of the respective variances. A compound symmetry variance structure was used for the time (pre- vs. postpump) variable, which is the repeated factor in the model. The variables assessed included glycemic control (glycohemoglobin and blood glucose), total insulin dose, and body weight.

Several other study characteristics were also assessed for their effect on data from the paired design studies. Because the technology in determining glycohe-

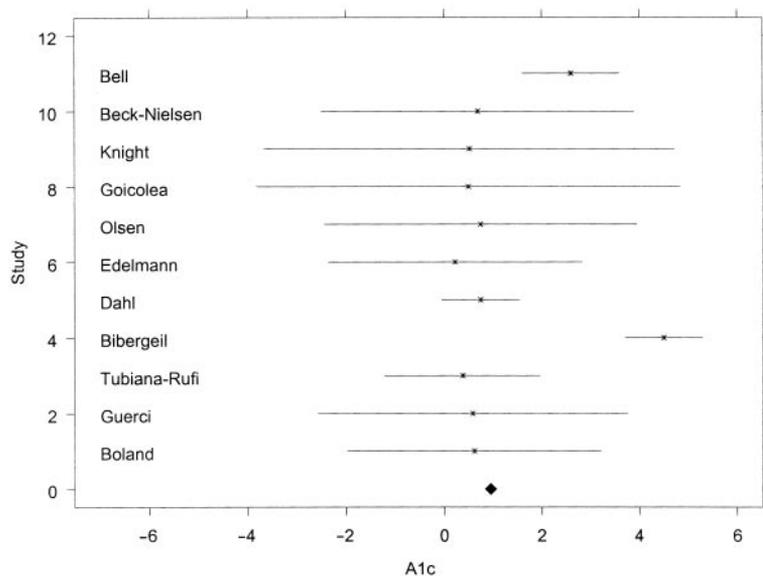


Figure 1—Effect sizes for parallel design studies. Studies are presented in increasing order of chronology from the bottom, with primary authors' names along the left side of the graph. *Mean effect size. Bars denote the 95% CIs of the mean. Mean effect size for the 11 studies was $d = 0.95$.

glycemic control has changed over the years and studies included in this analysis spanned over 20 years, different assays were used to determine glycemic control. A total of 31 studies reporting glycohemoglobin used the HbA_{1c} assay, whereas 19 used the HbA₁ assay. Moreover, in 47 of the 52 studies meeting criteria to be included in the meta-analysis, the comparison group could be classified according to the intensity of insulin therapy (CT vs. MDI). In addition to the type of assay for glycemic control (HbA₁ vs. HbA_{1c}) and intensity of comparison treatment (CT vs. MDI), other covariates studied were duration of pump use (≤ 1 year vs. > 1 year), age of study subjects, and year of study publication (in or before 1992 vs. 1993 and later). We chose to evaluate the year of study by comparing data reported before and after the release of the DCCT results because this seminal study on the importance of tight metabolic control fundamentally changed treatment practices and recommendations.

Because the interaction effect of these covariates with time (pre- vs. post-CSII) is of primary interest, analyses were conducted using time, each of the above predictors, and their interaction as independent factors in the model. Only those predictors whose interaction effect with time was significant were included in the final model. If interaction effects remained significant, we then compared

the levels of outcome variables before and after CSII treatment at each level of the predictor.

All statistical conclusions were made at the 0.05 level of significance, and the Bonferroni correction was used to adjust for multiple comparisons. However, all *P* values reported are unadjusted. Analyses were carried out using the SAS System, version 8.2.

RESULTS

Meta-analysis

Study characteristics. As previously stated, a total of 52 studies were included in this analysis with a total of 1,547 subjects (mean \pm SD sample size 29.75 ± 36.31 , range 3–177 subjects). Studies were published between 1979 and 2001, with 22 published before 1987 and 13 published since the release of the original DCCT results in 1993 (4). A total of 41 studies were categorized as a paired design, and 11 were classified as a parallel design. The average time on CSII was 52.99 ± 54.68 weeks (range 4–234). Of the studies, 12 consisted solely of pediatric patients, 33 included only adults, and 7 included a mixed sample of both pediatric and adult patients. Study subjects ranged in age from 2.3 to 49.8 years (mean 26.05 ± 10.80). The average length of time since diagnosis of type 1

diabetes was 11.91 ± 5.24 years (range 1.2–22.2).

Glycemic control

Glycohemoglobin. A total of 11 studies with a parallel design reported data on glycohemoglobin. A *Q*-statistic of 65.71 indicated that there was not sufficient evidence to reject the hypothesis of homogeneity ($P > 0.99$). The weighted summary mean difference comparing the effect of CSII with MDI/CT was 0.95, with a 95% CI of 0.8–1.1, indicating that there was a significant difference between the two treatment approaches, with the glycohemoglobin among patients treated with CSII lower than that of patients using MDI/CT. As depicted in Fig. 1, all 11 studies evidenced an effect size in the direction of improved control for CSII relative to CT/MDI.

For the paired design studies, separate models were first used to assess the effect of each of the covariates and their interaction with time (pre- vs. post-CSII) on glycohemoglobin. Interaction effects of time with publication year, type of assay, age-group, and intensity of comparison group treatment were not significant; hence, none of these main or interaction terms was included in the final model. However, there was a significant interaction between duration of pump therapy and time ($P = 0.003$). Results from the final model show that there was a significant change in glycemic control after CSII treatment (mean \pm SD pre-CSII: $9.36 \pm 0.22\%$, post-CSII: $8.96 \pm 0.11\%$; $P = 0.039$), such that glycohemoglobin was significantly lower after patients were treated with CSII. In addition, studies with patients who were on pump therapy for at least 1 year showed significant improvement in glycohemoglobin after CSII treatment (mean \pm SD: 8.68 ± 0.06 vs. $7.48 \pm 0.22\%$; $P < 0.001$), whereas no significant improvement was observed in those studies where the average duration of pump therapy was < 1 year (9.4 ± 0.23 vs. $9.2 \pm 0.01\%$; $P = 0.3$).

Blood glucose. Seven studies with a parallel design reported data on blood glucose levels. A *Q*-statistic of 85.49 indicated that there was not sufficient evidence to reject the null hypothesis of homogeneity ($P > 0.99$). The weighted summary mean difference comparing the effect of CSII with MDI/CT was 17.31, with a 95% CI of 13.45–21.16, indicating that there was a significant difference be-

tween the two treatment approaches, with the blood glucose among patients treated with CSII lower than that of patients using MDI/CT. All studies evidenced a difference in the direction of improved mean glucose for CSII relative to MDI/CT.

For the paired design studies, only 21 reported data on blood glucose levels. For these 21 studies, separate models were used to assess the effects of the covariates on blood glucose level. Overall, there was a significant change (pre-CSII: 176.23 ± 9.13 mg/dl, post-CSII: 117.82 ± 4.71 mg/dl; $P < 0.001$) in blood glucose level, with lower blood glucose levels after CSII treatment. Interaction effects of year of publication and duration of pump use with time (pre- vs. postpump) were not significant. Interaction effects of time with intensity of comparison treatment ($P = 0.007$) and age-group ($P = 0.023$) were significant. Improvement in blood glucose level was significant in the CT group (178.83 ± 11.02 vs. 101.01 ± 3.95 mg/dl; $P < 0.001$) but not in the MDI group (158.76 ± 10.99 vs. 139.12 ± 7.09 mg/dl; $P = 0.186$). In addition, both pediatric (212.84 ± 28.83 vs. 96.28 ± 10.3 mg/dl; $P = 0.002$) and adult (160.54 ± 8.94 vs. 127.26 ± 5.15 mg/dl; $P = 0.017$) studies indicated a significant improvement in blood glucose levels while on pump therapy.

Insulin requirements. To examine whether CSII resulted in changes in insulin requirements, total daily insulin dose and units of insulin per kilogram of body weight used per day (units per kilogram) were examined. Six studies with parallel design reported data on insulin requirements. However, three reported on units per day and three reported on units per kilogram per day. The number of studies was too few to conduct a meaningful meta-analysis. Nevertheless, of these six studies, four reported a decrease in insulin requirements, one reported an increase, and one reported no change in insulin requirements while using CSII therapy.

A total of 17 paired design studies reported on insulin requirements, with 10 studies reporting total units per day and 12 studies reporting units per kilogram per day. Separate analyses were conducted for both of these groups. Five studies reported data in both units and were included in both analyses. Pump therapy had a significant effect on both

units per day (pre-CSII: 53.69 ± 0.11 , post-CSII: 44.19 ± 0.07 ; $P < 0.001$) and units per kilogram per day (pre-CSII: 0.74 ± 0.04 , post-CSII: 0.62 ± 0.02 ; $P < 0.001$) with insulin requirement being lower after CSII therapy.

Body weight. Only three studies with parallel design reported data on body weight during CSII and comparison conditions. Therefore, a meta-analysis of this outcome was not conducted. However, two of these three studies reported a decrease in weight, whereas one reported an increase in weight while using CSII therapy.

Seven studies with paired design reported data on body weight. CSII treatment had a significant effect on body weight (pre-CSII: 68.24 ± 0.27 kg, post-CSII: 71.21 ± 0.31 kg; $P < 0.001$), with weight after treatment being higher than before treatment.

Publication bias. To address the issue of publication bias, we reviewed abstracts presented at the American Diabetes Association and the Society of Pediatric Research annual meetings from 1986 to 2000. Eight studies that were never published in peer-reviewed journals were identified. We performed a weighted (by sample size) paired *t* test for these pre-/poststudies. The decrease in HbA_{1c} post-CSII therapy was statistically significant ($P = 0.021$), yielding similar results to the published studies. We also performed a fail-safe *N* analysis to determine how many additional studies, averaging non-significant results, would be necessary to reverse our findings. Ten additional studies would be needed to bring the average effect size down from $d = 0.95$ (for the parallel design studies) to $d = 0.5$. This result would constitute a 100% increase in the existing number of studies meeting inclusion criteria for the meta-analysis.

Descriptive data

Study characteristics. A total of 39 studies (1,7,11,12,14,15,19,21,24,28,31–33,35,37,38,41,44–47,49,50,53,54,57,62,64,68–78) reported on some aspect of potential risks of pump therapy. Potential risks included rates of hypoglycemia, DKA, pump malfunction, and site problems.

Hypoglycemia. A total of 29 studies (1,7,11,14,24,28,33,37,44–47,49,50,53,54,57,62,64,69–72,75–78) reported comparison data between CSII and injection therapies with respect to the fre-

quency of hypoglycemic events. We categorized hypoglycemic events as either mild or severe according to the specifications of the authors, although not all authors used the same criteria when defining mild versus severe hypoglycemia. Studies reported data as either frequency of events for the duration of the study or as frequency of events per patient-week, per patient-year, or per 100 patient-years. Overall, the risk of hypoglycemic events does not appear to be higher on CSII therapy than on MDI therapy, regardless of the year of the study's publication. One study (1) found an increase in mild hypoglycemic episodes, and one (76) found an increase in severe hypoglycemic episodes. Four (44,47,50,77) studies found a decrease in mild episodes, and seven (11,14,24,28,54,57,64) found a decrease in severe episodes. Finally, four (7,45,46,53) found no change in frequency of mild episodes, and ten (33,37,49,62,69–72,75,78) found no change in frequency of severe episodes.

DKA. A total of 11 studies (11,31,37,46,53,54,57,70,72,75,76) reported comparison data between CSII and injection therapies with respect to frequency of DKA episodes. Definitions of DKA were not always provided by the authors. The risk of DKA appeared to be higher on CSII before 1993 because six studies (31,46,53,54,72,75) found an increase in frequency of DKA and one (70) found no change. However, the data after the release of the DCCT are inconclusive, with two studies (11,57) showing no change, one study (76) showing an increase, and one study (37) showing a decrease in frequency.

Technological difficulties with the pump. A total of 11 studies (12,14,19,32,38,41,44,46,53,68,73) reported on episodes of pump malfunction. These studies reported multiple reasons for the malfunctions. Among these reasons were total pump failure (eight studies), battery complications (four studies), alarm malfunctions (three studies), overdosage by pump (three studies), underdosage by pump (two studies), malposition of battery by patient (one study), and damage to pump by patient error (one study). All studies reporting pump malfunctions were published before 1988. Seven studies reported on the frequency of catheter occlusions or needle obstructions. One reported the frequency as 0.8 episodes per patient per month, whereas the other

six reported a total number of 77 occlusions during the duration of the study. Of these seven studies, five were published before 1988.

Infections. A total of 16 studies (12,14,15,19,21,24,32,35,41,44,46,53,54,67,71,73) reported on episodes of infections at the catheter site. Two studies reported these episodes as infections per patient-month, with one reporting one infection per patient per month and one reporting one infection per 27 patient-months. Four reported these episodes as events per patient-year, with a range of 0.06–0.27 events per patient per year. Eleven studies reported on the number of infections during the study period, for a total of 41. Five studies reported on episodes of skin irritations at the infusion site. One study reported these episodes as one skin irritation per patient per month, and one reported 0.26 episodes per patient per year. Three studies reported on the number of skin irritations during the study period, for a total of 13.

Psychosocial functioning and patient perspectives. A total of 16 studies (16,19,35,44,46,51,53,54,56,57,71,78–83) reported on some aspect of their subjects' psychosocial functioning. Five studies (57,71,79,82,83) assessed a pediatric population and seven assessed adults. Comparison data cannot be made because few studies assessed similar concepts and few studies used the same measures. Moreover, the time frame for these studies ranged from 6 weeks to 24 months. Five studies measured depression. Four (53,57,79,81) reported no difference between therapies, and one (80) reported a decrease in depressive symptoms while on CSII therapy. Five studies measured quality of life. Two (16,54) found improvements on CSII and three (57,78,81) found no difference. Four studies measured anxiety. Three (53,80,81) reported no change in anxiety, and one (83) reported a decreased level of anxiety while on CSII therapy. Four studies (19,53,82,83) assessed responsibility for the regimen demands, and all found that subjects were more adherent to their regimen while on CSII. Three studies (53,71,80) assessed locus of control, and none found differences between CSII and injection therapy. Two studies assessed self-esteem. One (79) found improved self-esteem while on CSII, whereas the other (80) found no change. Two studies assessed family functioning. One (80)

found improved family functioning on CSII, whereas the other (82) found no change. One study (57) examined self-efficacy and found no difference between CSII and injection therapies.

Seven studies (19,35,44,46,51,56,82) asked subjects to describe their perceptions about the advantages of CSII therapy. The most common response was improved flexibility. Other reported advantages included ease of scheduling and timing of meals, greater freedom, decreased sense of physical restrictions, decreased physical complaints, and improved glycemic control.

A total of 19 studies (7,9,24,32,35,41,44–47,49,52,53,55,71,73,74,84,85) asked subjects if they would like to continue on CSII therapy at the conclusion of the study period. Of the 520 subjects approached, 325 (62.5%) chose to remain on the insulin pump.

Five retrospective studies (23,41,55,86,87) published between 1988 and 1993 examined discontinuation rates of pump therapy. Three asked their patients directly during clinic visits, and two obtained information about discontinuation rates from questionnaires sent to the patients' homes. Of the 400 subjects included in these studies, 127 (32%) chose to discontinue CSII therapy. The reasons reported for discontinuing CSII included not feeling comfortable wearing the device, lack of improvement in control, and increased rates of infection. Subjects were more likely to discontinue pump therapy if they were female, younger, had shorter duration of diabetes, were single or divorced, or had psychiatric problems. Additionally, two studies published in 1988 found that subjects who experienced frequent DKA and infrequent hypoglycemia before beginning CSII therapy were more likely to discontinue pump therapy than their peers.

CONCLUSIONS— Research on CSII therapy began in the late 1970s, with a strong resurgence in the 1990s after technological advances in blood glucose monitoring devices and insulin delivery systems. In the current investigation, we analyzed through meta-analytic procedures all of the available data spanning this time period to provide a comprehensive quantified review of the existing literature on CSII therapy. Results of this meta-analysis provide strong evidence that CSII therapy is associated with signif-

icant improvements in glycemic control (decreased glycohemoglobin and mean blood glucose). Glycohemoglobin was lower in patients using pump therapy, with a greater benefit seen for patients using pump therapy for at least 1 year. Blood glucose levels were also lower for patients using pump therapy. Patients who began with CT showed the greatest blood glucose improvements when on pump therapy. It is likely that patients on MDI, who had already begun a more intensive therapy regimen, had fewer opportunities for improvement than patients on CT, which can be considered a floor effect. There were no differences noted between studies for which samples were composed of pediatric patients, adult patients, or mixed (both pediatric and adult), with the exception that studies of pediatric patients showed a greater improvement in blood glucose control during CSII therapy. Although these data suggest that the effects of CSII therapy are equivalent across age-groups, further examination of this issue is warranted because of the unique challenges faced in pediatric diabetes management.

Results of this meta-analysis also indicate that CSII therapy is associated with significant decreases in insulin requirements, although it does appear to result in weight gain, which has previously been reported with intensified insulin regimens (4). However, these data should be regarded cautiously because only 35% of the studies included in the meta-analysis reported on insulin requirements and only 21% of these studies reported on body weight.

With respect to potential complications of CSII use (e.g., hypoglycemia, DKA, pump malfunction, and site infections), 39 studies reported on at least one of these risks; however, they did not use a common metric when reporting the data. Thus, meta-analytic procedures could not be used. Based on this limited descriptive data, it appears that CSII use is associated with a decreased frequency of both mild and severe hypoglycemic episodes. CSII use was associated with an overall increased frequency of DKA. However, this increased risk of DKA was not evident in studies published after 1993, suggesting that CSII may no longer be associated with a greater risk of DKA compared with other forms of insulin administration. It may be that the earlier data on the increased risk of DKA led clinicians to em-

phasize DKA prevention with their patients. However, because only 11 studies reported on DKA risk, and only 4 of those were published since 1993, final conclusions about DKA risk in CSII therapy would be premature. Similarly, the majority of studies reporting on episodes of pump failure and catheter occlusions were published before 1988, suggesting that advancements in CSII technology and/or heightened patient vigilance (e.g., change of infusion set after two consecutive high blood glucose values) have lowered this risk.

Few studies ($n = 16$) assessed any aspect of psychosocial functioning, including the patient's perspectives on treatment options. Whereas these limited data suggest that there is no increased risk for poor psychosocial outcomes for CSII therapy relative to injection therapy, this finding needs to be regarded cautiously. There was little consistency in either the choice of psychosocial construct assessed or the assessment methodology (questionnaire, clinical interview) used. Clearly, additional research on the psychosocial impact of CSII therapy is needed before conclusions can be rendered.

In summary, the results of the current meta-analysis highlight the benefits of improved glycemic control associated with CSII therapy compared with traditional insulin therapies (CT or MDI). Furthermore, today's CSII therapy does not appear to be associated with significant adverse outcomes (e.g., DKA or severe hypoglycemia).

While the data appear promising, firm conclusions about the efficacy of CSII therapy would be premature because of several limitations of the data. First, the present meta-analysis does not include all published articles on CSII therapy in peer-reviewed journals because not all studies reported the data (i.e., means, SDs) necessary for the analyses. Second, not all studies included in the meta-analysis contributed data points for all outcomes variables. Furthermore, the majority of the studies in this meta-analysis were published before 1987, with relatively few studies published in the post-DCCT era that specifically examined the relative risks and benefits of CSII therapy. Additional research is needed that specifically focuses on the relative risks and benefits of CSII therapy in our technologically sophisticated times.

Therefore, the results of the current study should not be viewed as a definitive statement about the efficacy of CSII therapy.

Recommendations for future research

We offer the following recommendations to guide future research in this endeavor. To further our understanding of the potential risks and benefits of CSII therapy, outcome data need to be reported in a standardized and systematic manner. We recommend that means and SDs of all outcome data be reported for both CSII and comparison control conditions. Potential risks and complications of CSII therapy (e.g., catheter occlusions, DKA, and hypoglycemia) should be routinely assessed and reported. Reporting insulin requirements as units per kilogram per day would allow for more reliable comparisons across studies because reporting only daily total insulin doses cannot capture the relationship between an individual's weight and his or her insulin needs. Because the impact of pump therapy on body weight remains inconclusive (studies with parallel designs yielded mixed results, whereas studies with paired designs suggested weight increases on CSII therapy), we also recommend that future studies document subject's body weight, both before initiation of CSII therapy and at the end of the study period.

While CSII therapy may be the most sophisticated and precise insulin delivery method currently available, the opportunity for improved glycemic control is only one of many potential factors that need to be considered when initiating pump therapy. CSII therapy may potentially affect the patient's quality of life and psychosocial functioning. For example, patients who choose CSII therapy often must re-evaluate their previous strategies for diabetes management, including learning new skills, monitoring blood glucose values and urine ketones more frequently, and increasing awareness of insulin-to-carbohydrate ratios, all of which may potentially increase self-care demands. CSII therapy may also affect an individual's body image and sexual intimacy. Future studies that carefully examine the psychosocial impact of CSII therapy on patients and their families are needed. There is an extensive body of research that indicates that diabetes increases one's risk for depression (88); therefore, targeting depression would seem to be a vital psychosocial

variable to include in such assessments. Other areas of psychosocial functioning that are important to assess include measurements of self-management (89–91), quality of life (92), family functioning (93), and patient-provider relationships (94). Longitudinal prospective studies that assess individuals' reasons for initiating, continuing, and discontinuing CSII therapy are also needed. Collectively, this research will help guide clinical decision making regarding CSII therapy with the dual goals of optimizing glycemic control and improving quality of life.

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