

Metabolic Control with Insulin Pump Therapy: Preliminary Experience

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Background: The benefits of insulin pump therapy on the metabolic control of both type 1 and type 2 diabetes have been reported. Such reports have prompted our interest to investigate the long-term metabolic effects of insulin pump therapy at our institution.

Methods: We retrospectively analyzed the management of type 1 and type 2 diabetic patients who began extended insulin pump therapy at Changhua Christian Hospital between November 2004 and October 2007. One-way ANOVA and *post hoc* analysis were used to compare baseline glycosylated hemoglobin (HbA1C) values with subsequent values.

Results: We studied 12 patients who were on continuous subcutaneous insulin infusion (CSII) therapy at the time of data collection. Mean duration of CSII therapy was 2.3 years. A reduction in HbA1C was found after administering CSII, which was sustained after 1, 2 and 3 years of therapy (7.0%, 6.7% and 6.6%, respectively), with statistical significance ($p < 0.05$). No incidence of severe hypoglycemia or diabetic ketoacidosis occurred during the treatment period.

Conclusion: Our preliminary experience demonstrated the effectiveness of insulin pump therapy for both type 1 and type 2 diabetic patients. The reduction in their HbA1C values was both statistically and clinically significant. This treatment should be considered for patients poorly controlled by subcutaneous insulin injection therapy. [*J Chin Med Assoc* 2008; 71(7):353–356]

Key Words: continuous subcutaneous insulin infusion (CSII), diabetic ketoacidosis, glycosylated hemoglobin A (HbA1C)

Introduction

The beneficial effects of intensive glycemic control on reducing the risk of chronic complications in type 1 diabetes were firmly established in the Diabetes Control and Complications Trial (DCCT).¹ The UK Prospective Diabetes Study (UKPDS)² and a study³ from Japan showed similar results in type 2 diabetes. Both continuous subcutaneous insulin infusion (CSII) and multiple daily injection (MDI) therapy are effective means of implementing intensive diabetes management. A review⁴ of controlled trials in patients with type 1 diabetes showed that with CSII therapy, the mean blood glucose concentrations and glycosylated hemoglobin (HbA1C) values were either slightly lower than or comparable to those of MDI. In patients with type 2 diabetes, 2 studies^{5,6} found that insulin pump therapy resulted in a marked improvement in blood

glucose concentrations, with a corresponding decrease in HbA1C levels. At our hospital, insulin pump therapy was introduced in November 2004. We evaluate its long-term metabolic effects after 3 years of clinical practice.

Methods

Diabetic patients treated with insulin pump therapy between November 2004 and October 2007 in our diabetes clinic were retrospectively enrolled. Patients treated for less than 1 year or subjects who had used pump therapy during pregnancy were excluded. Body weight, total daily insulin dose, duration of diabetes, and the reasons for pump therapy were recorded at the start of therapy. Patients were observed for possible complications during pump therapy, such as adverse



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Table 1. Clinical characteristics of the 12 patients on insulin pump therapy*

Characteristics	Type 1 DM	Type 2 DM	Total
Gender (male/female)	2/4	3/3	5/7
Age at start of pump use (yr)	31.5 ± 5.3 (25–40)	51.7 ± 14.8 (35–76)	41.6 ± 15.0 (25–76)
Duration of diabetes at start of pump use (yr)	15.7 ± 8.2 (7–29)	11.5 ± 4.3 (5–18)	13.6 ± 6.6 (5–29)
HbA1C before start of pump use	8.8 ± 1.4 (6.8–10.8)	8.6 ± 1.4 (6.8–10.7)	8.7 ± 1.3 (6.8–10.8)
Daily insulin dose before start of pump use (U/kg/d)	0.79 ± 0.24 (0.52–1.12)	0.79 ± 0.25 (0.55–1.20)	0.77 ± 0.22 (0.52–1.20)
Duration of pump therapy (yr)	2.9 ± 0.1 (2.7–3.0)	1.7 ± 0.7 (1.0–2.7)	2.3 ± 0.8 (1.0–3.0)

*Data presented as *n* or mean ± standard deviation (range). DM = diabetes mellitus; HbA1C = glycosylated hemoglobin.

reactions at the infusion site, hypoglycemia, and diabetic ketoacidosis. The total daily dose of infused insulin during the 3 days before the end of the study was recorded for each patient. The last known HbA1C value prior to the initiation of CSII therapy was used as the baseline value. Subsequent HbA1C values were collected at 12-week intervals.

Statistical data analyses were performed using SPSS version 12.0 (SPSS Inc., Chicago, IL, USA). Descriptive statistics were used to describe the cohort. The differences in body weight and required daily insulin dose per kilogram of body weight between baseline and the end of the study were compared using the paired *t* test. One-way ANOVA and *post hoc* multiple comparisons with the least significant difference method were used to compare baseline HbA1C values with the follow-up data. Statistical significance was defined as $p < 0.05$.

Results

Between November 2004 and October 2007, 26 diabetic patients were treated with insulin pump therapy at our diabetes clinic. Five of the patients were treated only during pregnancy. At the time of data collection, 16 patients had been treated continuously for at least 1 year. Of them, 3 became pregnant and 1 was lost to follow-up. After excluding these 4 cases, the 12 remaining cases had continued with CSII therapy up to the time of data collection, with mean treatment duration of 2.3 years. The clinical characteristics of the patients are shown in Table 1. Twelve patients (7 females, 5 males) were included in the study. Their mean age at the start of pump therapy was 41.6 years (range, 25–76 years), and mean duration of diabetes was 13.6 years. Prior to CSII therapy, mean insulin requirement was 46.4 ± 15.0 U/day, corresponding to 0.77 ± 0.22 U/kg body weight/day. Seven patients had been on twice-daily injections of premix insulin, and 5 had been on MDI therapy. The reasons for starting pump therapy

were to optimize metabolic control in 10 (83%) patients, to enable a more flexible lifestyle in 8 (67%) patients, to reduce fluctuation of blood glucose in 3 (25%), and to prevent severe hypoglycemia in 1 (8.3%). All patients had ≥ 2 indications for starting pump therapy. HbA1C values improved significantly after beginning CSII therapy (Figure 1), decreasing from $8.7 \pm 1.3\%$ at initiation to $7.2 \pm 0.6\%$ at 3 months and $7.4 \pm 1.1\%$ at 6 months of therapy. The reduced level was maintained at 1, 2 and 3 years of therapy (HbA1C values were 7.0%, 6.7% and 6.6%, respectively; $p < 0.05$ vs. baseline).

Mean body weight did not change significantly from the start to the end of the study (60.2 vs. 61.4 kg). The required insulin dose was 0.77 ± 0.22 U/kg/day before CSII and 0.72 ± 0.28 U/kg/day at the end of the study; the difference was also not statistically significant.

Whereas 1 patient experienced several episodes of severe hypoglycemia (defined as an episode with symptoms consistent with hypoglycemia in which the patient requires the assistance of another person and which is associated with prompt recovery after oral carbohydrate or intravenous glucose) with subcutaneous insulin injection therapy twice daily, severe hypoglycemia did not develop in any of the patients during CSII therapy. Diabetic ketoacidosis likewise did not occur in any patient throughout the entire duration of CSII therapy. Only 1 patient reported infusion site infection during pump therapy, which resolved with the application of topical antibiotic. He did not report any adverse injection site reaction (redness or soreness) during the course of intermittent subcutaneous insulin injection therapy.

Discussion

In the 12 patients, HbA1C improved from a mean baseline value of $8.7 \pm 1.3\%$ to 7.0%, 6.7% and 6.6% at 1, 2 and 3 years of CSII therapy, respectively. Some studies^{7,8} have shown the benefit of lowering blood

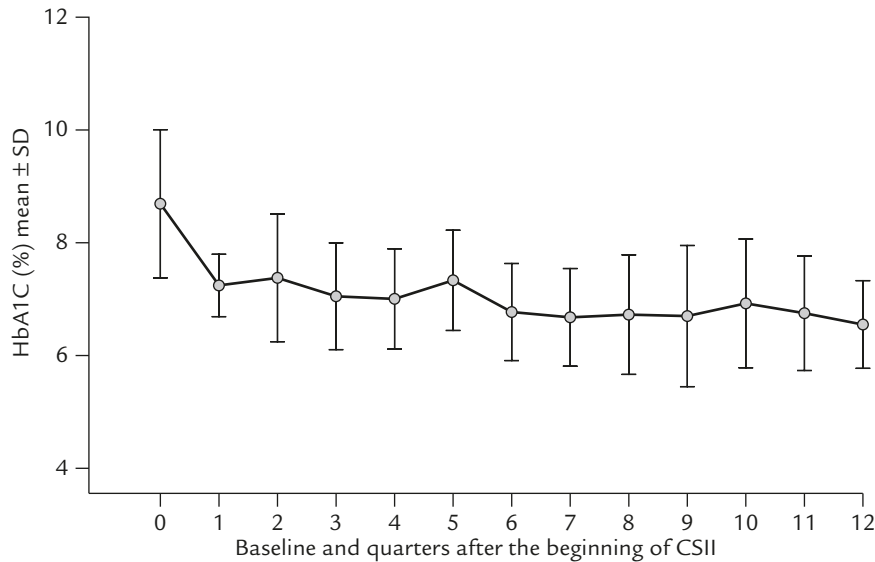


Figure 1. Glycosylated hemoglobin (HbA1C) levels before and after insulin pump therapy (all subsequent HbA1C values were significantly decreased compared to baseline, $p < 0.05$).

glucose level with pump therapy regardless of the type of diabetes mellitus and the age of the subject. At the end of our study, mean body weight had not changed significantly, implying that caloric intake remained consistent during the study period. Since mean body weight and the average daily dose of insulin per kilogram of body weight did not change significantly after CSII therapy, the reduction in HbA1C level may indicate improved insulin sensitivity with the use of continuous insulin infusion. While some investigators reported a deterioration in metabolic control after 6 months of CSII therapy,⁹ some studies demonstrated that the initial lowering of HbA1C with CSII was sustainable for more than 1 year.¹⁰⁻¹² This was corroborated by our subjects, who demonstrated significant improvements in HbA1C levels that were sustained for 3 years after switching from conventional intermittent insulin injection to CSII therapy.

In our study, a 76-year-old patient was poorly controlled with MDI therapy. After insulin pump therapy, her HbA1C improved significantly. Other case studies have also shown the feasibility of insulin pump therapy in elderly patients with type 1 diabetes mellitus.^{13,14} For optimal results, it is important that patients in this age group be selected carefully for pump therapy, educated thoroughly, and followed diligently by a team of trained professionals.

The improved glucose control in our CSII-treated patients might have been the result of several factors. Besides tailoring insulin delivery to an individual's requirement on a 24-hour basis, factors other than the pump technology itself could also have contributed to

the improvement. The availability of a multidisciplinary diabetes care team with the required skills and experience in pump therapy is critically important.^{15,16} Long-term support and guidance should also be available to address questions and promptly resolve problems unique to special circumstances.¹⁷ Proper selection of candidates for pump therapy is also vitally important. They need to be familiar with various aspects of self-care and to maintain close contact with members of the diabetes care team. In addition, they have to be taught carbohydrate counting and other practical issues, including insulin replenishment, timely replacement of tubing, proper care of the needle insertion site, and procedures to follow in case of pump malfunction. They should also be instructed to watch for potential problems during pump therapy, such as inadvertent interruption of insulin delivery and irritation or infection at the needle insertion site.

For 10 of our patients, pump therapy was initiated after a few hours of instruction in the ambulatory setting. Two subjects began pump therapy during a week-long hospitalization. One might argue that the improved control during pump therapy might partly be due to the more extensive instructions that resulted in more educated patients. However, several controlled trials investigating the effect of education in type 1 diabetes patients failed to show improvement in glycemic control through education alone.^{18,19}

No severe hypoglycemia or diabetic ketoacidosis occurred in our patients during the study period. Although earlier studies^{20,21} showed increased rates of severe hypoglycemia and diabetic ketoacidosis with pump

therapy, some newer studies^{22,23} showed decreased risks of these complications. This improvement may be attributed to improved diabetes education, self care, and improved pump technology.²⁴ For our patients, we gave thorough instructions on the prevention of severe hypoglycemia and diabetic ketoacidosis.

Our study was a retrospective analysis, which excluded 14 of the 26 treated patients from the cohort for various reasons. The omission of those data might have introduced confounders and bias into the study. Since pregnancy was the main reason for most of the excluded patients, their inclusion would have shown even better glycemic control with pump therapy.^{25,26} Second, both types of diabetes were represented equally in our study. The results may therefore not apply to the predominantly type 2 diabetes mellitus population as a whole. By adding future data to our preliminary experience, we trust that a more clear-cut picture will eventually emerge.

In conclusion, our experience has shown that insulin pump treatment results in a significant reduction in HbA1C (by more than 1%) that is sustainable for at least 3 years. Pump therapy may therefore be warranted when intermittent insulin injection fails to achieve treatment goals.

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