More Patients with Optimal Glycemic Control after Participation in a CSII-specific Education Program (INPUT): Results from a Randomized Controlled Trial

DOI: https://doi.org/10.20378/irb-47105

URN: urn:nbn:de:bvb:473-irb-471059

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ABSTRACT

Despite the technological advances of CSII-therapy, many patients with CSII-therapy do not achieve optimal glycemic control. We developed an education program for CSII-therapy (INPUT) and evaluated its efficacy in a randomized controlled trial with a six-month follow-up. INPUT addresses the specific knowledge and skills to effectively handle CSII-therapy as well as possible psychological barriers. We analyzed whether participation in the INPUT program increased the number of patients with optimal glycemic control (HbA1c < 7.5%).

254 patients with CSII-therapy were randomized to either receive the INPUT education program or treatment-as-usual and assessed at follow-up. All patients were already performing CSII-therapy for 8.7 ± 6.8 years, with a mean diabetes duration of 23.1 ± 12.6 years. HbA1c at baseline was 8.3 ± 0.9%. Optimal glycemic control at baseline was achieved by 13% in the INPUT group and 20% in the control group.

Logistic regression with group as independent factor controlling for optimal glycemic control at baseline was performed. Dependent variable was optimal glycemic control at the six-month follow-up. Group was a significant predictor with INPUT patients having a 2-fold higher chance to achieve optimal glycemic control (OR = 1.98; 95% CI 1.04 – 3.78; p = 0.037) compared to patients in the control group. At follow-up, 27% of the INPUT group had achieved optimal glycemic control while only 18 % in the control group.

In this study, patients performed CSII-therapy for almost 10 years without achieving optimal glycemic control. After participation in INPUT, patient more often achieved optimal glycemic control compared to a treatment-as-usual control group. Thus, the INPUT education program was effective in improving glycemic control in patients with long-standing diabetes. Considering the higher costs of CSII-therapy, this beneficial effect of the education program has health-economic implications.

BACKGROUND

Insulin pump therapy (CSII therapy) is the most advanced form of insulin delivery and offers several technological features such as temporary basal rates, different basal rate profiles and bolus options. However, many patients do not use these features effectively and do not achieve optimal glycemic control. Furthermore, initiating CSII therapy can be associated with false expectations about the level of necessary self-management, and for performing CSII therapy on a daily basis, still, a very high level of knowledge, skills and motivation is necessary.

We developed a structured education program, called INPUT (INsulin PUmp Therapy), specifically for CSII therapy that focuses not only on the effective use of pump features but also on the specific psychosocial aspects of CSII therapy. INPUT consists of 12 lessons (90 minutes each) and is conducted as a group program for 3-8 participants led by a certified diabetes educator.

In a randomized controlled trial with a 6-month follow-up, the efficacy of INPUT was evaluated. Primary outcome was reduction in A1c 6-months after the end of the intervention. In this analysis, we also analyzed how many participants achieved optimal glycemic control (A1c < 7.5%) at follow-up.

METHODS

Study design

- Randomized, controlled, parallel, open-label trial with 6-month follow-up

Eligible participants

- People with diabetes already performing CSII therapy
- Already participated in a structured education on intensified insulin therapy
- Age: 16 – 75 years
- A1c: 7.5 – 13%

Procedure

- At baseline, A1c was assessed at a central laboratory, demographic and medical variables were assessed via Case Report Forms based on patients' files.
- Participants were either randomized to the INPUT intervention or to the waiting-list control group.
- The INPUT intervention was conducted over the course of 6 weeks with 2 lessons each week.
- 6-months after the end of the intervention, follow-up assessment was conducted with both groups at the same time. Again, A1c was assessed at the central laboratory.
- Additionally, incidences of severe hypoglycemia that required third party assistance or medical intervention were assessed.

Outcomes

- Reduction in A1c was analyzed via Analysis of Covariance with A1c at follow-up as the dependent variable, group as between-factor and A1c at baseline as covariate.
- Differences in achieving optimal glycemic control (A1c < 7.5%) was analyzed via logistic regression analysis controlling for optimal glycemic control at baseline.
- Zero-inflated Poisson regression analysis was used to analyze the difference in number of severe hypoglycemia.

RESULTS

Baseline characteristics

- A total of 268 people with diabetes were recruited and randomized, 254 participants were included in the per-protocol analysis (Figure 1).
- Participants had diabetes for 21 years and were performing CSII therapy for a median time of 8 years. Glycemic control was suboptimal with a mean A1c of 8.3% (Table 1).
- The mean number of previously attended structured education courses was 4.5 indicating a rather high level of diabetes-specific knowledge.

Reduction in A1c

- A1c at follow-up could be significantly more reduced in the INPUT group than in the control group (-0.28% vs. -0.06%; Δ -0.22, 95% CI -0.38 to -0.06; p = 0.003) (Figure 2).
- Additionally, the percentage of participants achieving optimal glycemic control at follow-up was significantly higher in the INPUT group compared to the control group (Figure 3). The chance of achieving optimal glycemic control was 2-times higher after participating in INPUT (OR = 1.98; 95% CI 1.04 – 3.78; p = 0.037).
- Figure 4 shows that reduction in A1c in the INPUT group could be achieved along the whole range of A1c values. Whereas in the control group, the distribution of baseline and follow-up A1c values was nearly identical.

Severe hypoglycemia

- The rate of severe hypoglycemia requiring third party assistance or medical intervention in the 6-months after the end of the intervention was lower in the INPUT group than in the control group (0.7 vs. 0.18 events per patient-year) (Figure 5). This corresponded with an Incidence Rate Ratio (IRR) of 3.55 (95% CI 1.50 to 8.43; p = 0.0041).
- Analyzing third party assistance alone also resulted in a significant IRR (IRR = 4.26; 95% CI 1.77 to 10.23; p = 0.0012) favoring the INPUT group (Figures 5 and 6).
- IRR for the severe hypoglycemia with medical intervention only could not be computed due to 0 events in the INPUT group. However, the overall CHI²-statistic became significant (Figure 6) and the number of affected patients was significantly lower in the INPUT group (0 vs. 6 participants; 0 % vs. 4.8%; p = 0.014).

CONCLUSIONS

Participation in INPUT led to an improvement in A1c that was higher than in the control group. Furthermore, the chances to achieve optimal glycemic control 6-months after the end of the intervention was 2-times higher in the INPUT group.

The improvement in A1c did not lead to a worsening of hypoglycemia problems. In contrast, the risk of having severe hypoglycemia was 3.5 to 4.3-times higher in the control group compared to the INPUT group.

Taken together, INPUT led to a significant improvement of glycemic control in people with diabetes who were performing CSII therapy for a rather long period of time.

This study was funded by Berlin-Chemie AG.

Table 1: Sample Characteristics

	INPUT (N=135)	Control group (N=133)
Age in years, *Md (IQR)*	45.0 (29.5 - 53.0)	45.0 (34.0 - 55.0)
Male gender, *n (%)*	44 (33.6 %)	64 (48.1 %)
Years of education, *M (SD)*	11.3 (2.2)	11.5 (2.3)
Body Mass Index in kg/m², *M (SD)*	28.2 (5.7)	27.9 (5.5)
Type 1 diabetes, *n (%)*	134 (99.3 %)	133 (100 %)
Diabetes duration in years, *Md (IQR)*	21.0 (12.5 - 32.8)	21.0 (13.0 - 30.1)
Duration of CSII-therapy in years, *Md (IQR)*	7.8 (4.0 - 14.3)	7.3 (3.6 - 13.5)
< 1 year n (%)	6 (4.4 %)	8 (6.0 %)
< 5 years n (%)	39 (28.8 %)	48 (36·1 %)
< 10 years n (%)	86 (63.6 %)	83 (62·4 %)
≥ 10 years n (%)	49 (36.3 %)	50 (37·6 %)
A1c (central lab) in %, *M (SD)*	8.3 (0.8)	8.3 (0.9)
in mmol/mol, *M (SD)*	67.2 (9.1)	67.5 (10.3)
Self-monitored blood glucose measurements per day, *M (SD)*	5.4 (1.8)	5.2 (1.9)
Structured diabetes education courses, *M (SD)*	4.6 (3.6)	4.3 (3.2)
Time since last education course in years, *M (SD)*	4.7 (4.2)	4.2 (3.6)
Late complications		
at least 1, *n (%)*	63 (46.7 %)	54 (40.6 %)
Number of complications, *M (SD)*	0.8 (1.1)	0.8 (1.1)
Severe hypoglycemia (3rd party assistance + medical intervention)		
at least 1, *n (%)*	13 (9.6 %)	15 (11.3 %)
Number of events (incidence per patient-year)	27 (0.40)	27 (0.41)

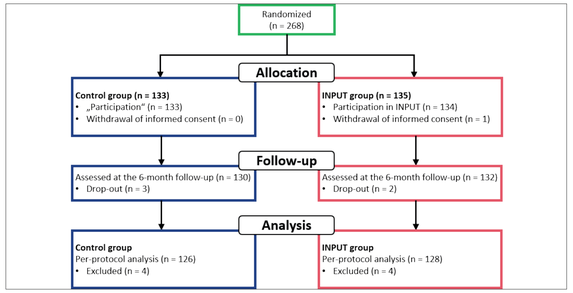

Figure 1: Consort Statement

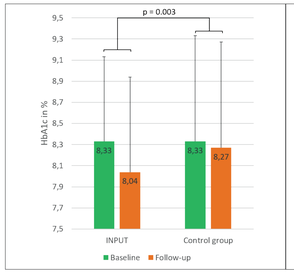

Figure 2: Reduction in A1c for the INPUT and control group

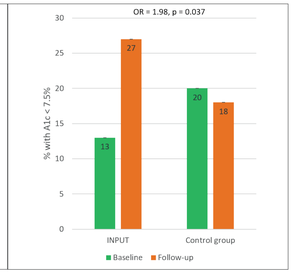

Figure 3: Percentage of participants achieving optimal glycemic control (A1c < 7.5%) at baseline and follow-up

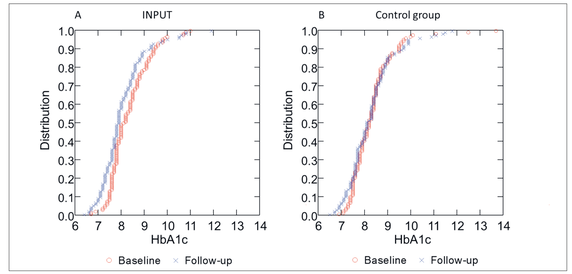

Figure 4: Distribution of A1c-values in the INPUT and control group at baseline and follow-up

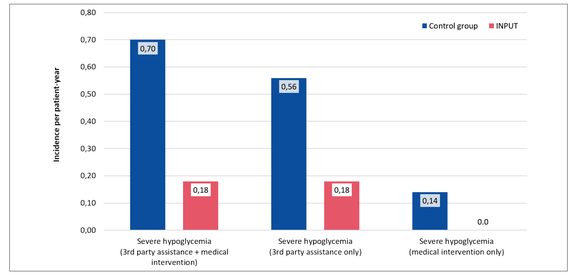

Figure 5: Rate of severe hypoglycemia per patient-year in the 6 months after the end of the intervention

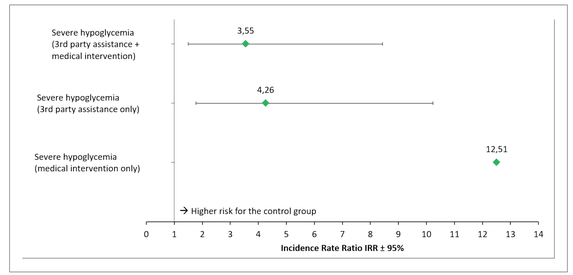

Figure 6: Zero-inflated Poisson regression analysis for the number of severe hypoglycemia (Likelihood-ratio-CHI²-statistic only for the severe hypoglycemia with medical intervention due to 0 events in the INPUT group)

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