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Continuous intraperitoneal insulin infusion in the treatment of type 1 diabetes mellitus

van Dijk, Peter R.

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CHAPTER 6

Quality of life and treatment satisfaction among type 1 diabetes mellitus patients treated with continuous intra-peritoneal insulin infusion or subcutaneous insulin: a prospective, observational study

SUBMITTED AS

Van Dijk PR, Logtenberg SJ, Hendriks SH, Groenier KH, Gans RO, Pouwer F, Bilo HJ, Kleefstra N.
Quality of life and treatment satisfaction among type 1 diabetes mellitus patients treated with continuous intraperitoneal insulin infusion or subcutaneous insulin: a prospective, observational study.

Abstract

INTRODUCTION

Aim of this study was to test whether patients using long-term continuous intraperitoneal insulin infusion (CIPII), a last-resort treatment option for type 1 diabetes mellitus (T1DM), or subcutaneous (SC) insulin therapy differed regarding their quality of life (QoL) and treatment satisfaction.

PATIENTS AND METHODS

In this 26-week prospective, observational matched-control study the effects of CIPII and SC insulin therapy were compared. Self-report questionnaires were used to assess health status (SF-36), general- (WHO-5) and diabetes-related (DQOL and PAID) QoL and treatment satisfaction (DTSQ). Analysis were performed with ANCOVA, taking baseline differences into account.

RESULTS

One patient withdrew consent. Subsequently 183 patients with a mean age of 50 years (standard deviation (SD) 12), diabetes duration of 26 years (SD 13) and a HbA1c of 64 mmol/mol (11) were analysed. At baseline, scores of six out of the eight SF-36 subscales, both SF-36 component scores, the WHO-5 score and the DQOL 'satisfaction' and 'impact' scores were lower, and treatment satisfaction was higher among CIPII treated patients as compared to patients treated with SC insulin therapy. There were no changes within groups during the study. After adjustment for baseline differences, scores of five out of the eight SF-36 subscales and both the mental (6.9, 95% CI 2.4, 11.3) and physical (9.6, 95% CI 4.2, 15.0) SF-36 component scores were lower with CIPII as compared to SC insulin therapy. Besides a lower perceived hypoglycaemia score (0.7, 95% CI 0.1, 1.2) with CIPII, there were no differences in outcomes after adjustment for baseline differences between CIPII and SC insulin therapy concerning general and diabetes-related QoL and treatment satisfaction.

CONCLUSION

In T1DM patients using CIPII, the perceived health status, general- and (parts of the) diabetes-related QoL are rather poor and worse as compared to patients treated with SC insulin therapy, while treatment satisfaction is higher. After adjustment for baseline differences, differences in health status remained present but the perceived hypoglycaemia score was better with CIPII and there were no differences in general- and diabetes-related QoL and treatment satisfaction between treatments.

Introduction

Treatment of type 1 diabetes mellitus (T1DM) consists of exogenous insulin administration or pancreas (islet cells) transplantation. In most patients, insulin is administered in a subcutaneous (SC) manner using multiple daily injections (MDI) or continuous subcutaneous insulin infusion (CSII). Although most patients achieve acceptable glycaemic control using SC insulin, some patients have high HbA1c concentrations or experience frequent hypoglycaemic episodes [1]. For these patients continuous intraperitoneal insulin infusion (CIPII) therapy using an implanted pump is a last-resort treatment option.

Intraperitoneal (IP) insulin administration results in more predictable insulin profiles and improves hepatic glucose production in response to hypoglycaemia [2–4]. Although providing a different route for insulin administration, with positive effects on the number of hypoglycaemic events, CIPII requires a surgical procedure to insert the implantable pump in the SC tissue of the abdomen [5,6]. In addition, every 6 weeks insulin refill procedures are necessary [5]. On the other hand, with CSII and MDI respectively, either infusion sets have to be replaced by the patient every 2 to 3 days or SC injections often have to be administered at least 4 times daily [7]. Using a device, either being for CSII or CIPII, offers the advantage of increased flexibility in diet and activities but requires extensive involvement of both the patient and diabetes professional. All these considerations may well influence quality of life (QoL), diabetes-related distress and treatment satisfaction.

Previous literature demonstrated that prior to initiating CIPII the QoL and treatment satisfaction are poor [7]. Although treatment satisfaction increased significantly during CIPII therapy, QoL remain poor among these CIPII treated patients during 5 to 6 years of therapy [5,8,9]. As short-term comparisons between CIPII and SC insulin therapy demonstrated an improvement of QoL during CIPII therapy, the effects of long-term CIPII versus SC insulin therapy on QoL are unknown.

Aim of the current study was to test whether patients using long-term CIPII or SC insulin therapy differed regarding their QoL and level of treatment satisfaction.

Patients and methods

STUDY DESIGN

This investigator initiated study had a prospective, observational matched-controldesign. Inclusion took place at the Isala (Zwolle, the Netherlands) and Diaconessenhuis hospital (Meppel, the Netherlands). Primary aim was to compare the effects of CIPII to SC insulin therapy, with respect to glycaemic control. As secondary outcome, and presented in this chapter, QoL (including health status, general- and diabetes-related QoL and diabetes-related distress) and treatment satisfaction were assessed.

PATIENT SELECTION

Cases were subjects on CIPII therapy using an implanted insulin pump (MIP 2007D, Medtronic/ Minimed, Northridge, CA, USA) for the past 4 years without interruptions of >30 days, in order to avoid effects related to initiating therapy. Inclusion criteria for cases were identical to those of a prior study in our centre and have been described in detail previously [10]. In brief, patients with T1DM, aged 18 to 70 years with a HbA1c ≥ 58 mmol/mol (7.5%) and/or ≥ 5 incidents of hypoglycaemia (glucose < 4.0 mmol/l) per week, were eligible.

The SC control group was age and gender matched to the cases and consisted of both MDI and CSII users. Eligibility criteria for controls were T1DM, SC insulin as mode of insulin administration for the past 4 years without interruptions of >30 days, HbA1c at time of matching ≥ 53 mmol/mol (7.0%) and sufficient mastery of the Dutch language. Exclusion criteria for both cases and controls included impaired renal function, cardiac problems and current use or oral corticosteroids. Exclusion criteria were similar to the previous cross-over study and have been described in detail previously [10]. The ratio of participants on the different therapies (CIPII:MDI:CSII) was 1:2:2.

STUDY PROCEDURES

There were 4 study visits. During the first visit, baseline characteristics were collected using a standardized case record form, questionnaires were handed out and patients were asked to fill in the questionnaires at home. During the second visit (5-7 days later) the questionnaires were collected and laboratory measurements were performed. During the third visit, 26 weeks after visit 1, clinical parameters were collected and again questionnaires were handed out for the second measurement. During the fourth visit, 5-7 days after the third visit, laboratory measurements were performed and again questionnaires were collected.

MEASUREMENTS

Demographic and clinical parameters included: age, gender, weight, length, blood pressure, year of diagnosis of diabetes, presence of microvascular (nephropathy, neuropathy and/or retinopathy) or macrovascular complications (angina pectoris, myocardial infarction, coronary artery bypass grafting, percutaneous transluminal coronary angioplasty, stroke, transient ischaemic attack, peripheral artery disease) and the number of self-reported hypoglycaemic events grade 1 (glucose <4.0 mmol/l), grade 2 (glucose <3.5 mmol/l) and grade 3 (requiring third party help or losing consciousness) during the last 14 days. Laboratory measurements included, amongst others, HbA1c concentrations measured with a Primus Ultra2 system using high-performance liquid chromatography (reference value 20–42 mmol/mol (4.0-6.0%)).

Perceived health status was assessed using the 36-item short-form health survey (SF-36). The SF-36 is a widely used, self-administered generic questionnaire with 36 items involving 8 subscales: physical functioning, social functioning, role limitations due to physical problems, role limitations due to emotional problems, mental health, vitality, bodily pain and general health perception. Scale score range from 0 to 100, higher scores indicating better health status. In addition, a mental and physical component summary (MCS and PCS) score can be determined [11]. General QoL was assessed using the WHO-5 questionnaire. The WHO-5 is designed to measure positive well-being and is reported to be better in identifying depression than the MCS of the SF-36 questionnaire [12,13]. It consists of 5 items with a total score ranging from 0 to100. A total score below 50 or an answer of "0 or 1" on a single item suggests poor emotional well-being [14]. Diabetes-related QoL was measured using the diabetes-related QoL (DQOL) questionnaire. The DQOL contains 46 items, which the patients rank on a 5-point scale. Scores are presented on a score range from 0 to 100: a score of 100 represents no impact or worries and always satisfied and a score of 0 represents always affected, worried or never satisfied [15,16]. The measure has four scales: satisfaction with current mode of therapy, impact of diabetes and treatment on living, diabetes worry and social/vocational worry [15]. Diabetes-related distress was measured using the problem areas in diabetes (PAID) questionnaire, a 20-item questionnaire in which each item represents a unique area of diabetes-related psychosocial distress. Scores were calculated using a five-point likert-scale with options ranging from "0-not a problem" to "4-serious problem". Summing all item scores and multiplying by 1.25 resulted in an overall PAID score of 0 to 100, with higher PAID scores indicating greater emotional distress. Treatment satisfaction was measured with the diabetes treatment satisfaction questionnaire (DTSQ). All 8 items are scored on a 7-point scale. Two items assess perceived frequency of hyperglycaemia and hypoglycaemia, and six items comprise the treatment satisfaction scale, with higher scores indicating higher satisfaction (range 0 to 36) [17].

STATISTICAL ANALYSIS

Results were expressed as mean (with standard deviation (SD)) or median (with interquartile range [IQR]) for normally distributed and non-normally distributed data, respectively. A significance level of 5% (two-sided) was used. Normality was examined with Q-Q plots. Analysis were performed in a intention to treat manner. A regression model based on covariate analysis (ANCOVA) was applied in order to take possible baseline imbalance into account. In the model the fixed factors CIPII and SC insulin therapy were used as determinants. The difference in scores was determined based on the b-coefficient of the particular (CIPII or SC) group. Significance of the b-coefficient was investigated with the Wald test based on a $p<0.05$. The quantity of the b-coefficient, with a 95% CI, gives the difference between both treatment modalities over the study period adjusted for baseline differences. Statistical analyses were performed using SPSS (IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.) and STATA version 12 (Stata Corp., College Station, TX: StataCorp LP). The study protocol was registered prior to the start of the study (identifiers: NL41037.075.12 and NCT01621308). The study protocol was approved by the local medical ethics committee, and all patients gave informed consent.

Results

PATIENTS

From December 2012 through August 2013, a total of 335 patients were screened and received information about the study, of which 190 (57%) agreed to participate. After baseline laboratory measurements, 6 patients were excluded because of reasons presented in Figure 1. (see Chapter 5, page 83) Consequently, 184 patients were followed during the 26-week study period. After the first visit one patient withdrew informed consent due to lack of interest. Therefore, 183 patients were analysed.

Baseline characteristics of these patients are presented in Table 1. Age and gender were well matched between groups and no grade 3 hypoglycaemic events were reported. Compared to patients using SC insulin therapy, CIPII patients had microvascular complications more frequently. Baseline SF-36 health status scores for physical and social functioning, role limitations due to physical limitations, vitality, bodily pain, general health, both component scores and the WHO-5 score were significantly lower among CIPII treated patients as compared to patients using SC insulin therapy (Table 2).

TABLE 1 Baseline characteristics

Characteristic	All patients (n=184)	CIPII (n=39)	SC (n=145)
Male sex (%)	67 (36)	14 (36)	53 (37)
Age (years)	50 (12)	50 (12)	50 (12)
Current smokers (%)	78 (43)	20 (51)	58 (40)
BMI (kg/m^2)	26.4 (4.5)	25.9 (4.4)	26.5 (4.6)
Systolic blood pressure (mmHg)	137 (19)	138 (17)	136 (19)
Diabetes duration (years)	26 (13)	29 (10)	26 (13)
Microvascular complication present (%)	87 (47)	25 (64)	62 (43)*
Retinopathy (%)	64 (35)	17 (44)	47 (32)
Neuropathy (%)	53 (29)	20 (51)	33 (23)*
Nephropathy (%)	5 (3)	2 (5)	3 (2)
Macrovascular complication present (%)	26 (14)	7 (18)	19 (13)
HbA1c (mmol/mol)	64 (11)	67 (14)	63 (9)
HbA1c (%)	8.0 (1.0)	8.3 (1.3)	7.9 (0.8)
Hypoglycaemia grade 1[a]	1 [0, 4]	2 [0, 4]	1 [0, 4]
Hypoglycaemia grade 2[b]	2 [0, 4]	1 [0, 2]	2 [1, 4]

Data are presented as n (%), mean (SD) or median [IQR]. *p<0.05 as compared to CIPII, P-values are based on appropriate parametric and non-parametric tests. [a] Defined as the number of hypoglycaemic events < 4 (grade 1) during the last 14 days. [b] Defined as the number of hypoglycaemic events < 3.5 (grade 2) during the last 14 days. Abbreviations: BMI; body mass index, CIPII; continuous intraperitoneal infusion, SC; subcutaneous.

In addition, CIPII treated patients had worse scores for the DQOL satisfaction and impact subscales and a higher treatment satisfaction score as compared to SC patients.

HEALTH STATUS AND GENERAL QOL

No significant differences within both groups regarding change of health status and general QoL were observed (Table 2). After adjustment for baseline differences, the SF-36 subscales for social functioning (9.6, 95% CI 2.6, 16.6), role limitations due to physical functioning (23.8, 95% CI 10.0, 37.6), vitality (9.7, 95% CI 3.7, 15.6), bodily pain (15.2, 95% CI 7.7, 22.7) and general health (7.3, 95% CI 2.1, 12.6) were significantly lower at the end of the study period among patients treated with CIPII as compared to patients treated with SC insulin. In addition, both the mental (6.9, 95% CI 2.4, 11.3) and physical (9.6, 95% CI 4.2, 15.0) component scores were lower. After additional adjustment for baseline differences in microvascular complications these differences remained present. After adjustment for baseline differences, the scores of the WHO-5 questionnaire did not differ between the treatment groups. However, the percentage of patients with a WHO-5 score indicative of a depression was significantly higher among CIPII treated patients as compared to the SC treatment group: 37% vs. 28% at visit 1 and 47% vs. 24% at visit 2 (p<0.05 for both).

DIABETES-RELATED QOL, DIABETES-RELATED DISTRESS AND TREATMENT SATISFACTION

During the study period, no differences within both groups regarding diabetes-related QoL, diabetes-related distress and treatment satisfaction were observed (Table 2). After adjustment for baseline differences, CIPII treated patients reported the same diabetes-related QoL for all 4 subscales of the DQOL questionnaire as compared to patients using SC insulin therapy. Additionally, after adjustment for baseline differences, there were no differences in diabetes-related distress between both treatment groups and subjects on CIPII perceived significantly less hypoglycaemic events than subjects on SC insulin therapy: 0.7 (95% CI 0.1, 1.2).

MDI AND CSII VERSUS CIPII

Subgroup analysis of patients using MDI (n=70) and CSII (n=74) as SC mode of insulin therapy versus CIPII treated patients are presented in Table 3. Health status scores were lower for CIPII treated patients as compared to both MDI and CSII users. In addition, CIPII treated patients had a lower score on the perceived hypoglycaemia score, as compared to both MDI and CSII users.

TABLE 2 Outcomes during baseline and last visit and differences between the CIPII and SC insulin therapy groups.

	CIPII		Change within CIPII group	SC		Change within SC group	Difference between SC and CIPII (adjusted for baseline)
	Start	End		Start	End		
SF-36 Subscales							
Physical functioning	71 (23)	70 (29)	-1.9 (-8.3, 4.4)	86 (18) †	86 (19) †	-0.2 (-2.5, 2.1)	4.8 (-0.8, 10.4)
Social functioning	70 (25)	69 (23)	-2.3 (-10.5, 4.4)	82 (20) †	84 (20) †	1.2 (-2.2, 4.6)	9.6 (2.6, 16.6) *
Role limitations-physical	42 (42)	41 (47)	-2.3 (-20.1, 15.4)	77 (35) †	80 (32)	1.0 (-5.2, 7.2)	23.8 (10.0, 37.6) *
Role limitations-emotional	76 (40)	77 (39)	-2.1 (-17.9, 13.8)	87 (30)	87 (29)	-0.8 (-5.8, 4.2)	5.7 (-5.1, 16.5)
Mental health	79 (17)	78 (15)	-1.9 (-6.3, 2.4)	77 (15)	77 (14)	-0.4 (-2.7, 1.9)	0.5 (-3.7, 4.7)
Vitality	52 (19)	49 (19)	-3.2 (-11.3, 4.9)	63 (19) †	64 (17) †	0.8 (-2.1, 3.5)	9.7 (3.7, 15.6) *
Bodily pain	65 (23)	61 (27)	-8.6 (-17.0, 0.3)	78 (23) †	81 (21) †	1.5 (-2.3, 5.2)	15.2 (7.7, 22.7) *
General Health	48 (19)	46 (18)	-2.6 (-7.6, 2.4)	62 (19) †	62 (18) †	0.3 (-2.3, 2.9)	7.3 (2.1, 12.6) *
SF-36 component scores							
MCS	65 (18)	64 (17)	-2.6 (-8.6, 3.4)	74 (17) †	75 (14) †	1.0 (-1.1, 3.2)	6.9 (2.4, 11.3) *
PCS	58 (19)	56 (21)	-3.6 (-10.1, 2.9)	75 (17) †	76 (16) †	1.1 (-1.1, 3.4)	9.6 (4.2, 15.0) *
WHO-5							
Total score	54 (22)	56 (20)	1.9 (-3.1, 6.9)	63 (19) †	64 (18) †	1.3 (-1.6, 4.2)	2.9 (-2.6, 8.5)
DQOL							
Satisfaction	53 (14)	57 (10)	4.2 (-0.8, 9.2)	58 (10) †	57 (8)	-0.4 (1.8, 1.1)	-2.6 (-5.8, 0.7)
Impact of diabetes	51 (8)	51 (8)	0.5 (-1.4, 2.5)	54 (8) †	54 (8) †	0.1 (-0.8, 1.0)	0.2 (-1.8, 2.1)
Diabetes worry	69 (21)	69 (19)	0.6 (-6.9, 8.1)	73 (16)	72 (17)	0.1 (-3.9, 2.3)	3.5 (-7.5, 14.6)
Social worry	47 (30)	44 (31)	2.2 (-10.0, 14.0)	52 (28)	51 (31)	2.9 (-2.8, 8.7)	0.8 (-5.4, 7.1)
PAID							
Total score	24 (14)	19 (14)	-3.1 (-6.9, 0.7)	21 (14)	21 (14)	-0.1 (-2.1, 2.0)	2.4 (-1.7, 6.5)
DTSQ							
Perceived hyperglycaemia score	4.0 (1.6)	4 (1)	0.0 (-0.7, 0.7)	3.8 (1.5)	3.7 (1.4)	-0.2 (-0.4, 0.1)	-0.2 (-0.7, 0.4)
Perceived hypoglycaemia score	2.5 (1.4)	2 (1)	-0.3 (-0.9, 0.3)	2.9 (1.5)	3.1 (1.4)	0.2 (-0.1, 0.5)	0.7 (0.1, 1.2) *
Total score	31.1 (3.5)	31.5 (3.3)	0.4 (-1.0, 1.8)	29.3 (4.5) †	29.3 (4.7) †	-0.1 (-0.8, 0.7)	-1.1 (-2.5, 0.4)

Data are presented as estimated mean (SD), median [IQR] or mean change (95% CI) within and between groups. SF-36 data incomplete for 18 (CIPII n=4, SC n=14) patients, DQOL data incomplete for 18 (CIPII n=4 and SC n=14) patients, DTSQ data incomplete for 25 (CIPII n=5, SC n=5) patients and PAID data incomplete for data 29 (CIPII n=8, SC n=21) patients. Abbreviations: CIPII, continuous intraperitoneal insulin infusion; DQOL, diabetes quality of life; DTSQ, diabetes treatment satisfaction questionnaire; PAID, problem areas in diabetes; MCS, mental component score; PCS, physical component score; SC, subcutaneous; SF-36, 36-item short-form health survey. †$p<0.05$ as compared to CIPII at baseline. *$p<0.05$.

TABLE 3 Outcomes during baseline visit, changes within the MDI and CSII groups and differences with the CIPII group.

	MDI			Difference between MDI and CIPII (adjusted for baseline)	CSII			Difference between CSII and CIPII (adjusted for baseline)
	Start	End	Change within MDI group		Start	End	Change within CSII group	
SF-36 subscales								
Physical functioning	85 (20)	85 (21)	-0.4 (-4.4, 3.7)	4.3 (-1.7, 10.5)	88 (17)	88 (16)	-0.1 (-2.5, 2.4)	5.3 (-0.9, 11.5)
Social functioning	82 (21)	85 (20)	3.0 (-1.3, 7.3)	11.1 (3.5, 18.8) *	82 (19)	83 (20)	-0.6 (-6.0, 4.8)	-3.1 (-9.3, 3.0)
Role limitations-physical	80 (34)	83 (32)	1.2 (-7.5, 9.9)	25.4 (10.3, 40.6) *	74 (37)	77 (33)	0.8 (-8.3, 9.8)	22.3 (7.4, 37.1)*
Role limitations-emotional	84 (32)	86 (30)	2.2 (-5.6, 9.9)	7.1 (-4.7, 18.9)	89 (29)	88 (27)	-3.7 (-10.1, 2.7)	4.3 (-7.6, 16.1)
Mental health	78 (15)	77 (14)	-0.7 (-3.7, 2.2)	0.6 (-4.1, 5.2)	76 (23)	76 (14)	0.0 (-3.5, 3.5)	0.5 (-4.2, 5.1)
Vitality	65 (19)	67 (18)	2.3 (-1.7, 6.2)	11.8 (5.3, 18.2) *	61 (20)	62 (17)	-0.9 (-4.0, 3.2)	7.7 (1.3, 14.1)*
Bodily pain	81 (23)	81 (21)	-0.2 (-5.4, 5.0)	14.4 (6.1, 22.6) *	77 (23)	80 (21)	3.1 (-2.5, 8.7)	15.6 (7.8, 24.2)*
General Health	63 (19)	65 (18)	1.1 (-2.5, 4.8)	8.9 (3.1, 14.7) *	60 (18)	59 (18)	-0.5 (-4.3, 3.3)	5.9 (0.2, 11.6)*
SF-36 component scores								
MCS	75 (17)	76 (15)	2.0 (-1.1, 5.2)	10.1 (4.1, 16.0) *	73 (16)	74 (14)	0.0 (-3.0, 3.0)	9.1 (3.3, 15.0)*
PCS	76 (17)	78 (16)	1.3 (-2.5, 4.8)	8.0 (3.1, 12.9) *	73 (17)	75 (16)	1.0 (-1.9, 3.9)	5.7 (0.9, 10.6)*
WHO-5								
Total score	64 (18)	65 (18)	1.9 (-1.6, 5.5)	3.9 (-2.1, 10.1)	62 (18)	63 (18)	0.8 (-4.0, 5.4)	1.9 (-4.1, 8.0)
DQOL								
Satisfaction	61 (11)	60 (11)	-0.5 (-2.6, 1.5)	-1.4 (-5.4, 2.5)	56 (10)	55 (9)	-0.2 (-2.3, 1.8)	-3.1 (-6.7, 0.5)
Impact	54 (9)	55 (9)	0.1 (-1.1, 1.4)	0.2 (-1.9, 2.4)	54 (7)	54 (8)	0.2 (-1.1, 1.5)	0.1 (-2.1, 2.4)
Worry: diabetes related	74 (17)	74 (19)	-0.1 (-4.6, 4.2)	1.9 (-5.2, 9.1)	73 (14)	71 (17)	-1.4 (-5.8, 2.8)	-0.1 (-4.0, 6.8)
Worry: social/vocational	49 (26)	51 (9)	5.9 (-2.7, 14.6)	5.0 (-7.7, 17.8)	55 (29)	52 (29)	0.2 (-7.6, 8.1)	2.2 (-9.8, 14.2)
PAID								
Total score	19 (14)	19 (15)	-1.1 (-3.7, 1.6)	1.0 (-3.6, 5.6)	22 (14)	23 (13)	0.9 (-2.4, 4.1)	3.6 (-0.9, 8.1)
DTSQ								
Perceived hyperglycaemia score	3.6 (1.6)	3.6 (1.5)	-0.1 (-0.5, 0.4)	-0.2 (-0.8, 0.4)	4.0 (1.3)	3.7 (1.3)	-0.2 (-0.6, 0.1)	-0.1 (-0.7, 0.4)
Perceived hypoglycaemia score	3.6 (1.6)	3.2 (1.4)	-0.1 (-0.4, 0.3)	0.6 (0.03, 1.2) *	2.7 (1.4)	3.0 (1.4)	0.4 (-0.01, 0.9)	0.7 (0.2, 1.3)*
Total score	29.1 (5.6)	29.7 (4.6)	0.1 (-1.0, 1.2)	-0.7 (-2.3, 0.8)	28.8 (5.1)	28.4 (4.9)	-0.2 (-1.2, 0.7)	-1.3 (-2.9, 0.2)

Data are presented as estimated mean (SD) and mean change (95% CI) within and between groups. SF-36 data incomplete for 14 (MDI n=6, CSII n=8) patients, WHO-5 data incomplete for 14 (MDI n=6, CSII n=8) patients, DQOL data incomplete for 14 (MDI n=7, CSII n=7) patients, DTSQ data incomplete for 20 (MDI n=10, CSII n=10) patients and PAID data incomplete for 31 (MDI n=21, CSII n=8) patients. Abbreviations: CIPII, continuous intraperitoneal insulin infusion; DQOL, diabetes quality of life; DTSQ, diabetes treatment satisfaction questionnaire; MCS, mental component score; PAID, problem areas in diabetes ; PCS, physical component score; SC, subcutaneous; SF-36, 36-item short-form health survey; WHO-5, world health organization-five well-being index. *p <0.05.

Discussion

The present study demonstrates that the perceived health status, general- and (parts of the) diabetes-related QoL are lower, while treatment satisfaction is higher among T1DM patients currently treated with CIPII as compared to patients treated with SC insulin therapy. After adjustment for baseline differences, health status remained lower and, besides a lower perceived hypoglycaemia score with CIPII, there were no differences in outcomes between CIPII and SC insulin therapy concerning general and diabetes-related QoL and treatment satisfaction.

We recently demonstrated that perceived health status is significantly lower among patients that initiate CIPII therapy as compared to a reference group of subjects that continued SC insulin therapy [19]. In a previous cross-over study in our centre, in which a part of the present study population participated, health status and general QoL improved significantly during 6 months of CIPII as compared to SC insulin therapy [9]. During subsequent 6-years of follow-up, the health status among these CIPII treated patients was stable [5]. The present study adds to these observations by demonstrating that the health status and general QoL among patients treated with long-term CIPII is worse as compared to matched subjects treated with SC insulin therapy. This latter finding was emphasized previously DeVries *et al*. demonstrating low general QoL and a high number of patients with psychiatric symptoms, in particular somatization, depression and insufficiency of thought or behaviour, among CIPII treated patients as compared to a SC treated reference population [8].

In contrast to the poor health status and general QoL we found no differences in diabetes-related worries, diabetes-related distress and even higher treatment satisfaction among patients treated with CIPII as compared to patients using SC insulin therapy. This discrepancy suggests that the poor health status and general QoL among these patients is not due to their diabetes per se but that quite probably other factors also have an important influence. Possible factors may include the poor social functioning, limited support or more (perceived) physical limitations and pain. Additionally, the presence of the psychiatric symptoms, identified previously by DeVries *et al*. and emphasized in the present study by the high number of CIPII patients with a WHO-5 score indicative for depression, may explain this discrepancy. Although it is unlikely that a mode of insulin administration could alleviate these factors, it seems that long-term CIPII therapy stabilizes QoL but is unable to compensate for the full burden of poor QoL.

One might hypothesize that, since the presence of frequent hypoglycaemic episodes (often combined with hypoglycaemia unawareness) is an indication for initiation of CIPII and IP insulin administration results in more predictable glucose profiles and a restoration of the hepatic response to hypoglycaemia, a reduction in perceived hypoglycaemia threat may be an important determinant of (diabetes-related) QoL and treatment satisfaction among CIPII treated patients [2–4]. This is also reflected by the hyperglycaemic profiles and lower perceived hypoglycaemia score even though there was no actual decrease in the number of self-reported hypoglycaemic events, among CIPII treated subjects in the present study as compared to patients treated with SC insulin [18]. In addition to a lower frequency of hypoglycaemic episodes, a reduction of the number of days spent in hospital during CIPII therapy, has been suggested to have a positive influence of CIPII on diabetes-related QoL and treatment satisfaction [5,8,10].

This is the first large-scale study comparing different aspects of QoL among CIPII and SC treated T1DM patients. Strengths include, amongst others, the use of both general and diabetes-related questionnaires (including the PAID questionnaire). Nevertheless, interpretations of the findings from our study are limited by various factors, including missing data and lack of data capturing comorbidity, psychological (dys)function and patients' perceptions toward hypoglycaemia. Furthermore, since CIPII is a last-resort treatment option for T1DM at present, the group of CIPII treated patients is considered selected and more complex as compared to SC treated patients and bias may well have occurred. As there is no data available of QoL during SC therapy prior to CIPII therapy in the current study, no conclusion can be drawn regarding the long-term changes in QoL from initiation of CIPII to the present. Therefore, the results of our study should be interpreted with caution and generalizability is limited. Nevertheless, the current design is the best available for the present study objective given the real-life restrictions.

Conclusions

Among this complex, selected group of T1DM patients treated with long-term CIPII the perceived health status, general- and (parts of the) diabetes-related QoL were lower, while treatment satisfaction was higher as compared to patients treated with SC insulin therapy. After adjustment for baseline differences, there were no differences in general and diabetes-related QoL and treatment satisfaction, while the perceived health status remained lower with CIPII as compared to SC insulin therapy. Taken together, these finding may imply that CIPII positively influence (parts of the) diabetes related aspects of QoL and treatment satisfaction.

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