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ORIGINAL ARTICLE

Nonmetabolic Complications of Continuous Subcutaneous Insulin Infusion: A Patient Survey

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Abstract

Background: Little is known about the frequencies and types of nonmetabolic complications occurring in type 1 diabetes patients being treated by modern insulin pump therapy (continuous subcutaneous insulin infusion [CSII]), when recorded by standardized questionnaire rather than clinical experience.

Subjects and Methods: A self-report questionnaire was completed by successive subjects with type 1 diabetes attending an insulin pump clinic, and those with a duration of CSII of ≥6 months were selected for analysis ($n=92$). Questions included pump manufacturer, insulin, infusion set type and duration of use, frequency of infusion set and site problems, pump malfunctions, and patient-related problems such as weight change since starting CSII.

Results: Median (range) duration of CSII was 3.3 (0.5–32.0) years, and mean ± SD duration of infusion set use was 3.2 ± 0.7 (range 2–6) days. The commonest infusion set problems were kinking (64.1% of subjects) and blockage (54.3%). Blockage was associated with >3 days of use of infusion sets plus lispro insulin in the pump (relative risk [95% confidence interval], 1.71 [1.03–2.85]; $P=0.07$). The commonest infusion site problem was lipohypertrophy (26.1%), which occurred more often in those with long duration of CSII (4.8 [2.38–9.45] vs. 3.0 [1.50–4.25] years; $P=0.01$). Pump malfunction had occurred in 48% of subjects (43% in the first year of CSII), with "no delivery," keypad, and battery problems commonly occurring. Although some patients reported weight gain (34%) and some weight loss (15%) on CSII, most patients (51%) reported no change in weight.

Conclusions: Pump, infusion set, and infusion site problems remain common with CSII, even with contemporary technology.

Introduction

The potential complications of continuous subcutaneous insulin infusion (CSII) (insulin pump therapy) can be categorized into metabolic problems such as ketoacidosis and hypoglycemia, infusion set issues such as kinking and blockage, infusion site problems such as lipohypertrophy and infection, pump malfunction, and patient-related problems such as weight gain and adverse psychological issues.[1] The comparative frequencies of ketoacidosis[2,3] and hypoglycemia[4] on CSII versus insulin injection therapy have been well researched in recent years. However, although the possible nonmetabolic, technical problems associated with modern CSII are given due note in recent reviews of this therapy[1,2,5–7] and indeed widely recognized from clinical practice, there have been few if any surveys that formally record the types and frequencies of these risks using a standardized questionnaire, since the 1980s.[8]

Complications of CSII may have changed in the last 25 years because of improvements and increasing sophistication in technology and clinical care; this should ideally reduce risks, but it may possibly exacerbate problems or introduce new ones. In the last decade or so, Guilhem et al.[9] reported on insulin pump failures recorded in France from 2001 to 2007, and Cope et al.[10] discussed adverse insulin pump events in adolescents reported to the Food and Drug Administration from 1996 to 2005. Dermatological complications at the infusion site with CSII have also been described.[11] The frequencies of infusion set problems have been less well documented.

An important unanswered question therefore remains as to whether contemporary pump technology is more reliable and associated with fewer complications than was early CSII. Here, we report a survey of patients with type 1 diabetes who had been treated by CSII for more than 6 months and where we sought responses on patient-perceived, nonmetabolic complications of pump therapy.

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Subjects and Methods

We distributed a self-report questionnaire concerning nonmetabolic complications of CSII to successive adult patients with type 1 diabetes attending an insulin pump clinic over a period from October 2012 to May 2013 ($n=104$). We then excluded all responses from those subjects who had used CSII for <6 months ($n=12$). The survey asked for demographic details (age, duration of diabetes, and pump therapy), pump manufacturer and model used by the patient, pump insulin, type of infusion set, and usual duration of use. The frequency of complications was sought for the last year and at any time and referred to set problems (kinking, leakage, apparent blockage, and other), infusion site problems (infection at the site, lipohypertrophy ["fat or lumpiness at the site"]), and other problems. The survey then sought details of pump malfunction (how many times has it broken in any way; what was the nature of the malfunction; did it occur within the first year, after 1 year, or at any time?). Finally, we asked about patient-related problems (perceived weight change since starting CSII and an open question inviting views about any other problems with CSII such as coping, psychological issues, or social problems at work). (The questionnaire is available on request from the authors.)

We arbitrarily defined "frequent infusion set kinking" as responses that recorded "regular," "frequent," or "very often" instead of absolute numbers of episodes or when kinking occurred ≥10 times at anytime or five or more times in the last year. We defined "frequent infusion set blockage" as ≥10 blockages at any time or five or more in the last year.

Statistical analysis

Mean or median values were compared using an unpaired *t* test or the Mann–Whitney test for skewed data. Proportions were compared using Fisher's exact test, and a relative risk (RR) with 95% confidence interval (CI) was reported. Results are otherwise reported as mean ± SD or median (interquartile range [IQR]) values, unless otherwise stated.

Results

We analyzed responses on perceived complications of insulin pump therapy from 92 patients who had been treated by CSII for ≥6 months (Table 1). The mean age of the patients was 45.3 years, their mean diabetes duration was 28.8 years, and the median duration of CSII was 3.3 years, with the longest duration on CSII 32 years. Seventy-eight percent of the subjects had used CSII for 5 years or less. Table 1 shows the percentage of pumps used by different manufacturers, the type of pump insulin, and the type of infusion set: most pumps were made by Medtronic (Northridge, CA), aspart and lispro were the commonest pump insulins, with glulisine used only rarely, and the Medtronic Quick-Set® was the most common infusion set in use. Subjects obtained pumps and infusion sets from the same vendor, usually the manufacturer.

Table 1. Clinical Features, Technology, and Insulins Used by Subjects Completing the Survey of Complications of Continuous Subcutaneous Insulin Infusion

Parameter	*Value*
Number of subjects	92
Age (years)	45.3 ± 12.8
Mean (range) diabetes duration (years)	28.8 ± 12.8 (2.0–67.0)
Median (range) duration of CSII (years)	3.3 (0.5–32.0)
Mean (range) duration of infusion set use (days)	3.2 ± 0.7 (2.0–6)
Pump manufacturer (% of subjects)	
Medtronic	84.8
Roche	9.8
Animas	5.4
Pump insulin (% of subjects)	
Aspart	55.8
Lispro	40.7
Glulisine	3.5
Infusion set (% of subjects)	
Medtronic Quick-Set[a]	72.0
Medtronic Mio[a]	6.5
Animas Inset[b]	5.4
ACCU-CHEK FlexLink[b]	4.3
Medtronic Silhouette[a]	4.3
Medtronic Sure-T[b]	3.2
ACCU-CHEK Tender[a]	3.2
ACCU-CHEK Rapid-D[b]	1.1

[a]Teflon.
[b]Metal.
CSII, continuous subcutaneous insulin infusion.

Infusion set problems

The mean duration of infusion set use was 3.2 ± 0.7 (range 2.0–6.0) days. The commonest problem reported was kinking (64.1% of subjects at some time, with 12% of the total number of patients observing frequent kinking); blocking of the infusion set was noted by 54.3% at some time, with 9.8% of the total patient number recording frequent cannula blocking. Leakage at the infusion set-pump connection was observed by 16.3% of subjects at some time (Table 2). The duration of infusion set use did not differ between kinked and non-kinked infusion sets (3.23 ± 0.68 vs. 3.13 ± 0.67 days; $P=0.49$). Kinking was reportedly not associated with the use of Teflon® (Dupont, Wilmington, DE), as opposed to metal, cannulae (RR = 1.02 [95% CI 0.58–1.82]; $P=1.0$).

Table 2. Infusion Set and Infusion Site Problems

Problem	*%*
Infusion set	
Kinking	64.1
Frequent kinking	12
Blockage	54.3
Frequent blockage	9.8
Leakage	16.3
Infusion site	
Lipohypertrophy	26.1
Site infection	17.4
Bleeding or bruising	14.1
Pain or soreness	9.8
Adhesion problems	5.4
Irritation or itchiness	5.4

Data are percentages of all subjects reporting problem at some time during pump treatment.

Table 3. Relative Risk for Infusion Set Blockage Associated with Various Factors

Risk factor	*RR*	P *value*
>3 days set use with lispro	1.71 (1.03–2.85)	0.07
Insulin analog use, any duration		
Lispro	1.39 (0.95–2.10)	0.12
Aspart	0.76 (0.51–1.13)	0.27
Glulisine	0.62 (0.12–3.12)	0.60
Kinking	1.36 (0.89–2.10)	0.17
Teflon cannula use	0.76 (0.51–1.12)	0.28

RR, relative risk.

Table 3 shows the RR for perceived infusion set blockage (number of patients experiencing any blockage vs. no blockage), associated with possible risk factors. The strongest risk factor was use of the infusion set for more than 3 days in combination with lispro insulin in the insulin pump (RR = 1.71 [1.03–2.85]; $P = 0.07$). Use of a Teflon rather than metal cannula was not significantly associated with blocking, but numbers of subjects using metal cannulae were small (17.6% of infusion sets).

Infusion site problems

Lipohypertrophy was recorded by 26.1%, and site infection by 17.4%, of subjects at some time (Table 2). The median duration of CSII was significantly longer in those with lipohypertrophy: 4.80 (IQR 2.38–9.45) versus 3.00 (1.50–4.25) years ($P = 0.01$). In the free text comments about problems with the infusion site, patients most often noted bleeding or bruising, pain or soreness, adhesion issues, and irritation or itchiness (Table 2).

Pump malfunction

Any type of pump malfunction was noted by 48% of subjects at some time, with the commonest problems reported as pump stop/"no delivery," keypad/button problems, rewind malfunction, and battery compartment problems (Table 4). Other problems occurring several times included a broken belt clip, accidental damage by the user, display problems, software malfunction, no cartridge detected, and continuous alarm. The percentage of all subjects reporting any type of pump malfunction within the first year of CSII was 43%.

Table 4. Pump Problems

Malfunction	%
Any pump malfunction (% of patients)	48
Types (% of all malfunctions)	
Pump stop/no delivery	26
Keypad/button problem	12
Rewind malfunction	12
Battery compartment problem	11
Belt clip broken	6
Accidental damage by user	6
Display problem	5
Software problem	5
Other (e.g., no cartridge detected, continuous alarm, O-ring leak, unknown)	17

Data are percentages of subjects reporting.

Patient problems

Most patients reported no change in weight on CSII (51%), whereas 34% reported a gain in weight and 15% a weight loss. In the free text section on patient-related problems, relatively few comments were recorded: only three patients mentioned psychological issues, specifically those related to the pump reinforcing the notion of having diabetes or a long-term illness; two mentioned the pump being bulky; two mentioned problems wearing the pump and concealing it under clothing; two noted problems with swimming/showering; and two again reported weight gain as a particular worry.

Discussion

We report here a clinic-based survey of the technical and patient-related risks of contemporary CSII using a standardized questionnaire. Our main finding is that infusion set, infusion site, and pump problems are common: more than half of the subjects reported issues at some time with either kinking or blockage of infusion sets, and nearly half reported some type of pump malfunction.

Our finding of 48% of subjects having any pump malfunction compares with 36% breakdown of the pumps issued to patients in the study of Guilhem et al.[9] This somewhat higher figure might reflect a different mix of pump manufacturers and models. Also, some of the reported problems might be misinterpretations by patients and thus reflect inexperience in the first year of therapy, although presumably this does not apply to the most frequent problems of "no delivery" or keypad malfunction. Some "no delivery" problems might be due to infusion set blockage and not pump malfunction, but patients are instructed to change the set in the event of such a problem, which would argue that such instances are true pump complications. Our patients usually reported that most of the problems occurred in the first year of CSII. It is interesting that Mecklenburg et al.[8] found in a survey of CSII in the 1980s that 25% of patients had a pump breakdown in the first year of CSII. This indicates that pump malfunction has not improved with the increasing sophistication of the technology over the last 25 years or so, and maybe somewhat worse (perhaps, because of that). The types of pump problems that our patients listed (pump stop/no delivery, keypad, battery, display, alarms, etc.) are similar to those described by others.[8,9]

We also found that infusion set kinking and blockage were very common—about 10% of patients had a frequent problem with either or both. It is possible that some patients misinterpreted blocking as kinking, and vice versa, because early blockage is often caused by kinking and late blockage by insulin aggregation/precipitation. In this respect, we found some evidence, trending to significance, that use of the infusion set for longer than 3 days in combination with lispro insulin in the pump increased the risk of blockage (RR 1.71 [95% CI 1.03–2.85]; $P = 0.07$). This is consistent with in vitro studies showing that beyond 3 days of infusion the probability of occlusion occurring in a catheter is greater with lispro than aspart.[12] Glulisine had the greatest risk of occluding in these in vitro studies (followed by lispro), but the number of subjects using this analog in our survey was too small to make

firm conclusions about whether this insulin was associated with blockage. The short-acting analog insulins precipitate in the order of their isoelectric points,[13] so (probably) as carbon dioxide diffuses into the cannula and lowers the pH of the insulin, glulisine aggregates or precipitates first (pI approximately 6.6), followed by lispro (pI approximately 5.6) and lastly aspart (pI approximately 5.1). These findings on infusion set problems are likely due in large part to patients not following advice on pump practice rather than poor materials and add further support to the general advice that patients using CSII should change the infusion set after no longer than 3 days.[1,5] Delaying infusion set use beyond 2–3 days is known to increase skin complications such as itching, bruising, and pain and to be associated with deteriorating glycemic control.[14,15]

The most frequent infusion site problem was lipohypertrophy, which was noted by about one-quarter of the subjects, similar to the 22% of CSII users found to have lipohypertrophy by Conwell et al.[11] We found that this complication was significantly more likely to be present in those with a longer duration of pump therapy. Because lipohypertrophy impairs insulin absorption,[16] this might be a contributor to the deterioration in glycemic control that occurs in some patients during long-term insulin pump therapy.[17] Our results indicate that lipohypertrophy during CSII is more frequent than perhaps commonly assumed and that practitioners should be more alert to its existence from history and physical examination and consider the part it may play in suboptimal control on CSII.

We found that although more patients reported a perceived weight gain than loss, most experienced no change in weight. Weight gain is a known complication of instituting intensified insulin therapy and improved control, as seen in the Diabetes Control and Complications Trial.[18] However, our survey confirms the finding of other reports that there is a mixed response with weight change when CSII is started,[19,20] with often no overall change in weight. Hypoglycemia-prone subjects may lose weight on CSII because of needing less insulin, having to eat less to avoid hypoglycemia, and being able to exercise with less hypoglycemia on pump therapy. Hyperglycemic patients may gain weight on CSII because calories previously lost as glycosuria are retained or because diet is relaxed. Clearly, dietary habits, including contact with the dietitian and adherence, will have influenced weight changes in our subjects, but this was not included in the questionnaire, and we could not access information from the medical records because the survey was anonymized.

It is interesting that psychosocial issues were only rarely mentioned in our survey. This may be an accurate assessment or may have been because patients were reluctant or embarrassed to identify difficulties in, say, coping, changes in mood or problems with work or personal relationships using this kind of questionnaire (albeit that remaining anonymous was a stated option). There is a growing interest in psychological problems associated with CSII, indicating that it would be more appropriate to use specific, validated psychological instruments pertaining to, among other factors, coping, self-efficacy, depressive symptoms, quality of life, and treatment satisfaction for surveying these issues in pump patients.[21]

Our study has some limitations. First, survey responses were based on perceived and not objectively confirmed problems and on recall of events. Recall is likely to be robust for major pump malfunctions but may be less so for, say, number of leaking infusion sets, particularly for those with very long duration of CSII. However, most subjects (78%) had a pump duration of 5 years or less, during which recall would be expected to be fairy good. Lipohypertrophy is another example of a complication that may be over- or underestimated by patients, without confirmation by inspection by healthcare professionals—most likely the frequency is underestimated.

Although the number of subjects was representative of the average established insulin pump practice, larger numbers may have uncovered other significant risk factors for complications. For example, we had expected that use of infusion sets with a flexible Teflon cannula would be a significant risk factor for set blockage or kinking in comparison with metal cannulae, because of the likelihood of crimping in the tissues with the soft cannula. However, the percentage of patients using a metal cannula was small (17.6%), making estimates of any risk reduction for blockage or kinking unreliable and a possible type 2 (false negative) error likely. Studies with larger groups of patients would be valuable. In addition, those currently using metal cannulae might have previously switched from Teflon cannulae because of a problem with kinking and might have referred in the survey to past and not current experiences with kinking. Lastly, one should note that the relatively high percentage of subjects using metal cannulae in this study (and possible complications related to metal vs. Teflon cannulae) may be particular to local or country practice and not necessarily typical of general use. Those who were currently using metal cannulae might change to Teflon cannulae in order to reduce local skin problems and/or defects in insulin infusion related to metal cannulae.

It could be argued that a higher rate of complications might occur in patients who are poorly motivated or nonadherent and that our survey included a higher proportion of such subjects than would usually be seen in clinical practice. However, we surveyed all patients seen in our insulin pump clinic over a given period, who are only treated according to nationally agreed guidelines for pump therapy[19] and therefore represent the clinical problems and patient phenotypes expected in routine clinical practice. We could not record glycosylated hemoglobin levels as an indicator of quality of control achieved in these patients because the survey was anonymous.

Our study also was confined to adults with type 1 diabetes. Different responses might have been elicited in children, although others have described similar insulin pump, infusion set, and skin complications in children and adolescents,[10,11,22] although not using a standardized questionnaire as in the present report.

We conclude that insulin pump, infusion set, and infusion site problems remain common with CSII, even with the use of contemporary technology. There is a need for improvements in the reliability of all these parts of the therapy.

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Author Disclosure Statement

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