Short Report: Treatment

Insulin pump failures in Italian children with Type 1 diabetes: retrospective 1-year cohort study

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Abstract

Aims   Insulin pump failure and/or malfunction requiring replacement have not been thoroughly investigated. This study evaluated pump replacement in children and adolescents with Type 1 diabetes using insulin pump therapy.

Methods   Data were collected for all participants younger than 19 years, starting insulin pump therapy before 31 December 2013. For each child, age, disease duration, date of insulin pump therapy initiation, insulin pump model, failure/malfunction/replacement yes/no and reason were considered for the year 2013.

Results   Data were returned by 40 of 43 paediatric centres belonging to the Diabetes Study Group of the Italian Society of Paediatric Endocrinology and Diabetology. In total, 1574 of 11 311 (13.9%) children and adolescents with Type 1 diabetes were using an insulin pump: 29.2% Animas VIBE™, 9.4% Medtronic MiniMed 715/515™, 34.3% Medtronic MiniMed VEO™, 24.3% Accu-Check Spirit Combo™ and 2.8% other models. In 2013, 0.165 insulin pump replacements per patient-year (11.8% due to pump failure/malfunction and 4.7% due to accidental damage) were recorded. Animas VIBE™ (22.1%) and Medtronic MiniMed VEO™ (17.7%) were the most replaced.

Conclusions   In a large cohort of Italian children and adolescents with Type 1 diabetes, insulin pump failure/malfunction and consequent replacement are aligned with rates previously reported and higher in more sophisticated pump models.

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Introduction

By harnessing technology, continuous subcutaneous insulin infusion provides an improvement in metabolic control and quality of life for people with diabetes [1–3]. A Position Statement to improve pump technologies using a more rigorous, standardized approach to safety, has recently been published [4]. This statement suggests a benefit from collecting data about all adverse events related to insulin pump use, especially after its worldwide increased use [5–7]. As with other countries, recent reports have shown that Italy saw a fourfold increase in pump users from 2005 to 2013 [8,9].

Metabolic and non-metabolic complications can occur during pump therapy. The risks of diabetic ketoacidosis and severe hypoglycaemia have been described previously [10]. Few data are available about non-metabolic complications: Pickup *et al.* observed a pump malfunction rate of 48%, without considering replacement [11]; Wheeler *et al.* reported a pump replacement rate of 23% in a population of 230 children and adolescents [12]; Guilhem *et al.* found a pump malfunction rate of 25 per 100 pump-years [13]; and

Ross et al. reported total adverse events, not only pump replacements, in over 40% of pump users/year [14].

The aim of this study was to evaluate the rate of insulin pump replacement due to failure/malfunction in a large cohort of Italian children and adolescents aged < 19 years with Type 1 diabetes during 2013.

Methods

A standardized electronic case report form was sent to 43 paediatric diabetes centres belonging to the Diabetes Study Group of the Italian Society of Paediatric Endocrinology and Diabetology. Pump therapy was regularly administered in all these centres, which include 26 tertiary centres according to Sweet criteria [15].

The electronic case report form included data pertaining to the centre and to children receiving therapy up to 31 December 2013: ID, gender, date of birth, date of Type 1 diabetes onset, date of pump initiation, pump manufacturer and model, infusion set and insulin used, continuous glucose monitoring usage, frequency of sensor use and catheter and infusion set change as days/month, and HbA$_{1c}$ as mean values for 2013.

Data regarding 2013 up to 31 December concerning pump replacement (yes/no, reason for pump failure or accidental damage or replacement following warranty expiration) and related clinical adverse events, diabetic ketoacidosis and severe hypoglycaemia, defined according to International Society of Paediatric and Adolescent Diabetes guidelines [16,17], were collected in the first 6 months of 2014.

HbA$_{1c}$ was measured using a DCA-2000 Analyser (Siemens/Bayer, Italy) or high-performance liquid chromatography, standardized according to the National Glycohemoglobin Standardization Program.

In Italy all pumps are funded by the National Health System.

The study was approved by the local research ethics committee and conducted according to the Declaration of Helsinki. Participants and their parents provided written informed consent.

Data are presented as median with first and third quartile. A non-parametric Mann–Whitney U-test was used to compare quantitative variables between two groups when not normally distributed. The Shapiro–Wilk test was used to evaluate the normality of the distributions. Differences in frequencies were analysed by the chi-square test. Data were analysed using STATISTICA™ (version 9, StatSoft Corporation, Tulsa, OK, USA). All the tests were two-tailed and $P < 0.05$ was considered significant.

Results

Electronic case report forms for each participant using continuous subcutaneous insulin infusion were returned by 40 of 43 centres (93%), for a total of 1574 of 11 311 children and adolescents with Type 1 diabetes, aged 0–18 years (13.9%, 95% confidence interval (95% CI): 13.3 to 14.6%, 92.5% followed at tertiary care centres) using insulin pump therapy. Their clinical and metabolic data are shown in Table 1.

During 2013, 332 pump replacements (0.21 replacements per patient-year) were recorded. The reasons for replacement were: pump failure/malfunction not due to accidental damage (186/332; 56%), accidental damage (73/332; 22%) and replacements for warranty expiration (73/332; 22%). This means that the real rate of pump replacement due to failure/malfunction, excluding warranty expiration, in our large cohort sample is 0.165 replacements per patient-year (259/1574), 11.8% for pump failure/malfunction and 4.7% for accidental damage. The mean lifetime of each device was 2.92 ± 2.07 years. In 15.7% of the cases, pump failure occurred in the first year of pump therapy; in 62.3% pump failure occurred after at least 2 years of pump therapy.

The age group in which pump replacement for failure appeared more frequent was the 6–10-year-olds, followed by the 1–5-year-old group and the 11–18-year-old group (20.1% vs. 18.4% vs. 15.1%, although this did not reach statistical significance, chi-square test, $P = 0.076$).

No relationship was observed between pump replacement for malfunction or accidental damage and type and duration of catheter used, or with type of centre (tertiary vs. primary/secondary). However, in tertiary centres, the percentage of pump replacements was higher, but did not reach statistical significance (chi-square test, $P = 0.06$).

Table 2 shows the replacement rate by the insulin pump model. Animas VIBE™ and Medtronic Minimed Veo™ showed the highest rate of pump replacement (chi-square test, $P = 0.0003$).

A sensor-augmented pump was used in 28.7% of participants (451/1574 with a mean of 14.9 ± 9.6 days/month). The sensor was used more frequently ($P < 0.0001$) and for longer periods (> 20 days/month, $P < 0.005$) in children < 6 years when compared with other age groups.

Pump replacement was more frequent in sensor-augmented pump users, but without reaching statistical significance when compared with conventional pump users (chi-square

Table 1 Clinical characteristics of children and adolescents with Type 1 diabetes using an insulin pump in Italy during 2013

Number (%)	1574 of 11 311 (13.9)
Gender, %	49.9 M; 50.1 F
Mean age, years	12.9 [9.4–15.3]
Diabetes duration, years	2.6 [1.2–5.1]
Pump therapy duration, years	3.1 [2.2–4.0]
Pump model, n (%)	
Animas Vibe™	460 (29.2)
Medtronic Veo™	540 (34.3)
Medtronic 515/715™	148 (9.4)
AccuCheck Spirit Combo™	382 (24.3)
Others (including Omnipod™)	44 (2.8)
Insulin analogue type, n (%)	
Aspart	819 (53.9)
Lispro	526 (34.6)
Glulisine	174 (11.5)
HbA$_{1c}$ as mean of 2013, mmol/mol	60 [53–65]
HbA$_{1c}$ as mean of 2013, %	7.6 [7.0–8.1]
Frequency of infusion set replacement, days	3.0 [2.8–3.2]
Sensor augmented pump use, n (%)	451 (28.6)
Sensor usage, days per month	12.9 [7.2–18.6]

Data are presented as absolute numbers and percentages (categorical data) or as median values with the first and third quartiles [quantitative data].

Table 2 Pump replacement rate according to the insulin pump model

Total pump models, n (%)	259 of 1574 (16.5)
Animas Vibe™, n (%)	102 of 460 (22.1)*
Medtronic Veo™, n (%)	96 of 540 (17.7)*
Medtronic 515/715™, n (%)	16 of 148 (10.8)
AccuCheck Spirit Combo™, n (%)	41 of 382 (10.7)
Others (including Omnipod™), n (%)	4 of 44 (9.1)

*Highest rate of pump replacement (chi-square test, $P = 0.0003$).

test, $P = 0.05$). When considering the two most frequently replaced pump models (Animas VIBE™ and MedtronicMinimed VEO™), no significant differences in the number of pump failures were found between sensor-augmented and conventional pump users.

No relationship between metabolic control and insulin pump failure was found. In the cohort of children who required pump replacement, one severe hypoglycaemic episode (0.3 episodes/100 participants/year) and seven cases of diabetic ketoacidosis (2.1 episodes/100 participants/year) were declared and no discontinuation occurred.

Discussion

Among 13.9% of children and adolescents with Type 1 diabetes using insulin pump therapy in Italy in 2013, we found a rate of insulin pump failure (0.165 failure per patient-year) similar to that reported in previous papers involving pump replacements [12,13,18] and lower than that in other studies which evaluated malfunction without replacement [11–14]. Furthermore, Animas VIBE™ and

Medtronic Minimed Veo™ were the most frequently replaced models for failure/malfunction.

Although retrospective data collection was performed, in Italy the need for pump replacement must be evaluated by the diabetologist, and a formal request by the latter must be made to the regional health agency. The need for such a procedure makes our data collection less subject to data loss. Only pump replacement was evaluated because it was easier to recall and verify.

Interestingly, most pump replacements occurred after 2 years from initiation of continuous subcutaneous insulin infusion (62.3%), suggesting that pump failure or malfunction are not related to user error due to inexperience in pump use.

Only one-third of participants in the study used continuous glucose monitoring consistently, especially pre-schoolers, and they used a sensor for > 20 days/month. This is probably due to the parent's desire to improve the quality of life of their child and a greater fear of hypoglycaemia, which has been reported in this age group [19,20]. In our data, the use of sensors does not seen to affect the risk of pump failure.

Ross *et al.* [18] recently found no association between adverse events and pump type. However, in our study, the risk of pump failure seems to increase in the newer and more sophisticated pump models.

The increased frequency of insulin pump failure in 6–10 year-old group is comparable with previously reported data [12].

Finally, no relationship was found between metabolic control and insulin pump failure, as previously suggested [18]. We can hypothesize that the few metabolic severe adverse events in our study might be related to causes other than pump failure requiring replacement.

In conclusion, insulin pumps are an established part of Type 1 diabetes treatment. Pump use is growing and is likely to continue to expand. Insulin pump replacement in a large cohort of Italian children and adolescents with Type 1 diabetes is similar to that reported previously and more frequent in sophisticated pump models. With the ever-growing circulation of new technologically advanced pumps, the assessment of pump failure rates under real-life conditions is fundamental because it provides crucial information on pump safety in real-life use.

RS, ST, ST, and SZ provided database and performed data quality control, contributed in interpretation of results and to discussion; AP conducted statistical analysis and contributed to interpretation of results; AES collected database, contributed to the discussion of the results and to write the manuscript.

References

1 Misso ML, Egberts KJ, Page M, O'Connor D, Shaw J. Continuous subcutaneous insulin infusion (CSII) versus multiple insulin injections for type 1 diabetes mellitus. *Cochrane Database Syst Rev* 2010; CD005103.

2 Pańkowska E, Błazik M, Dziechciarz P, Szypowska A, Szajewska H. Continuous subcutaneous insulin infusion vs. multiple daily injections in children with type 1 diabetes: a systematic review and meta-analysis of randomized control trials. *Pediatr Diabetes* 2009; **10**: 52–58.

3 Cherubini V, Gesuita R, Bonfanti R, Franzese A, Frongia AP, Iafusco D *et al*. Health-related quality of life and treatment preferences in adolescents with type 1 diabetes. *The VIPKIDS study*. *Acta Diabetol* 2014; **51**: 43–51.

4 Heinemann L, Fleming GA, Petrie JR, Holl RW, Bergenstal RM, Peters AL. Insulin pump risks and benefits: a clinical appraisal of pump safety standards, adverse event reporting and research needs. A joint statement of the European Association for the Study of Diabetes and the American Diabetes Association Diabetes Technology Working Group. *Diabetologia* 2015; **58**: 862–870.

5 Karges B, Rosenbauer J, Kapellen T, Wagner VM, Schober E, Karges W *et al*. Hemoglobin A$_{1c}$ levels and risk of severe hypoglycemia in children and young adults with type 1 diabetes from Germany and Austria: a trend analysis in a cohort of 37,539 patients between 1995 and 2012. *PLoS Med* 2014; **11**: e1001742.

6 Beck RW, Tamborlane WV, Bergenstal RM, Miller KM, DuBose SN, Hall CA *et al*. The T1D exchange clinic registry. *J Clin Endocrinol Metab* 2012; **97**: 4383–4389.

7 Sulmont V, Lassmann-Vague V, Guerci B, Hanaire H, Leblanc H, Leutenegger E *et al*. Access of children and adolescents with type 1 diabetes to insulin pump therapy has greatly increased in France since 2001. *Diabetes Metab* 2011; **37**: 59–63.

8 Bruttomesso D, Laviola L, Lepore G, Bonfanti R, Bozzetto L, Corsi A *et al*. Continuous subcutaneous insulin infusion in Italy: third national survey. *Diabetes Technol Ther* 2015; **17**: 96–104.

9 Bonfanti R, Lepore G, Bozzetto L, Corsi A, Di Blasi V, Girelli A *et al*. Survey on the use of insulin pumps in Italy: comparison between paediatric and adult age groups (IMITA study). *Acta Diabetol* 2016; **53**: 403–412.

10 Cope JU, Samuels-Reid JH, Morrison AE. Paediatric use of insulin pump technology: a retrospective study of adverse events in children ages 1–12 years. *J Diabetes Sci Technol* 2012; **6**: 1053–1059.

11 Pickup JC, Yemane N, Brackenridge A, Pender S. Nonmetabolic complications of continuous subcutaneous insulin infusion: a patient survey. *Diabetes Technol Ther* 2014; **16**: 145–149.

12 Wheeler BJ, Donaghue KC, Heels K, Ambler GR. Family perceptions of insulin pump adverse events in children and adolescents. *Diabetes Technol Ther* 2014; **16**: 204–207.

13 Guilhem I, Balkau B, Lecordier F, Malécot JM, Elbadii S, Leguerrier AM *et al*. Insulin pump failures are still frequent: a prospective study over 6 years from 2001 to 2007. *Diabetologia* 2009; **52**: 2662–2664.

14 Ross PL, Milburn J, Reith DM, Wiltshire E, Wheeler BJ. Clinical review: insulin pump-associated adverse events in adults and children. *Acta Diabetol* 2015; **52**: 1017–1024.

15 Danne T, Lion S, Madaczy L, Veeze H, Raposo F, Rurik I *et al*. Criteria for Centers of Reference for Paediatric diabetes – a European perspective. *Pediatr Diabetes* 2012; **13**: 62–75.

16 Wolfsdorf JI, Allgrove J, Craig ME, Edge J, Glaser N, Jain V *et al*. Diabetic ketoacidosis and hyperglycemic hypersmolar state. *Paediatr Diabetes* 2014; **15**: 154–179.

17 Ly TT, Maahs DM, Rewers A, Dunger D, Oduwole A, Jones TW. Assessment and management of hypoglycaemia. *Paediatr Diabetes* 2014; **15**: 180–192.

18 Ross P, Gray AR, Milburn J, Kumarasamy IM, Wu F, Ferrand S *et al*. Insulin pump-associated adverse events are common, but not associated with glycemic control, socio-economic status, or pump/infusion set type. *Acta Diabetol* 2016; **53**: 991–998.

19 Sundberg F, Forsander G. Detection and treatment efficacy of hypoglycemic events in the everyday life of children younger than 7 yr. *Pediatr Diabetes* 2014; **15**: 34–40.

20 Hommel E, Olsen B, Battelino T, Conget I, Schütz-Fuhrmann I, Hoogma R *et al*. Impact of continuous glucose monitoring on quality of life, treatment satisfaction, and use of medical care resources: analyses from the SWITCH study. *Acta Diabetol* 2014; **51**: 845–851.

Appendix

Italian Paediatric Pump Failure Study Group (the following principal investigators listed by city, participated in this study). Alessandria: R. Lera, A. Secco; Ancona: V. Cherubini; Aosta: A. Bobbio, M. Bechaz; Bari: E. Piccinno, M.P. Natale, F. Ortolani, C. Zecchino, A. Lonero; Bologna: S. Zucchini, G. Maltoni; Bolzano: B. Pasquino; Brindisi: F. Gallo; Cagliari: P. Frongia, C. Ripoli; Catania: D. Lo Presti, T. Timpanaro; Catanzaro: F. Citriniti; Cesena: T. Suprani; Chieti: S. Tumini, S. Carinci, P. Cipriano; Crotone: N. Lazzaro; Cuneo: V. De Donno, F. Gallarotti; Firenze: S. Toni, L. Lenzi, B. Piccini; Genova: G. d'Annunzio, N. Minuto, L. Vittorio, C. Russo, R. Borea; Locri: F. Mammì, M. Bruzzese; Messina: F. Lombardo, C. Ventrici, G. Salzano; Milano: R. Bonfanti, G. Frontino, C. Bonura, V. Favalli, A. Scaramuzza, G.V. Zuccotti, M. Ferrari; Modena: L. Iughetti, B. Predieri; Napoli: A. Franzese, E. Mozzillo, P. Buono, D. Iafusco, S. Confetto, A. Zanfardino; Novara: F. Cadario, S. Savastio, C. Fiorito; Novi Ligure: P. Barbieri; Olbia: G. Piredda; Palermo: F. Cardella, R. Ropolo; Pisa: G. Federico, B. Marchi; Roma: R. Schiaffini, D. Benevento, C. Carducci, M.L. Mancabitti; San Giovanni Rotondo: M. Del Vecchio, R. Lapolla; Savona: A. Gaiero, G. Fichera; Torino: I. Rabbone, M.G. Ignaccolo, D. Tinti, F. Cerutti; Trento: V. Cauvin, R. Franceschi; Urbino: M. Biagioni; Varese: A. Salvatoni, A. Scolari; Verona: C. Maffeis, M. Marigliano, A. Sabbion; Viterbo: C. Arnaldi, D. Tosini.