Skin-Related Complications Among Adolescents With Type 1 Diabetes Using Insulin Pump Therapy

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ABSTRACT:

BACKGROUND: To identify the skin-related complications in adolescents with type 1 diabetes (T1D) using the insulin pump therapy (IPT).

METHODS: A total of 64 T1D adolescents (between ages 13 and 19) using the insulin pump were included in this cross-sectional study. They had visited the Diabetes Clinic at Diabetes Treatment Center, Prince Sultan Military Medical City, Saudi Arabia, for treatment from January 2018 to March 2018. Data on the prior and present skin-related complications, for a 6-month interval, were gathered via a closed/structured questionnaire. Besides this, demographic information was also recorded.

RESULTS: From the patients in this study (n = 64), 9.3% experienced 3 or more skin-related complications, whereas 7.8% patients registered 2 and 25% had only 1 such disorder. However, in 37 patients (51.8%), there was no evidence of skin-related complications. Significantly, the female revealed a higher level of issues ($P = .036$), >3 years on IPT ($P = .039$), negligence of infusion set rotation ($P = .001$), needle length of 9 mm ($P = .021$), and beyond 3 days for catheter replacement ($P = .022$). The factors age, body mass index, diabetes duration, and insulin dosage remained quite unaffected. From the regression analysis, the factors female gender, catheter replacement, and infusion set rotation showed up as the independent risk factors for the skin complications.

CONCLUSIONS: The IPT users invariably experience dermatologic conditions. Through this study, female gender, length of IPT usage time, and infusion set rotations were identified as the independent risk factors responsible for the skin issues.

KEYWORDS: Type 1 diabetes, dermatologic complication, skin complications, insulin pump

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Introduction

The *Diabetes Atlas* (eighth edition) reported that in Saudi Arabia, 35 000 children and adolescents had type 1 diabetes (T1D), listing Saudi Arabia at number 8 in the world for the number of patients with T1D and number 4 with respect to the incidence rate of T1D (33.5 per 100 000 population).[1] Although the reasons for and risk factors related to T1D continue to remain obscure, the techniques for the cure and prevention advanced until the present date have failed, with all patients becoming dependent on insulin injection treatment for their lifetime.[2] Recently, however, novel strategies have been proposed such as utilization of insulin pumps, continuous glucose monitoring, and hybrid closed-loop systems.[3-5]

A few practical aspects related to pump therapy include candidate selection, choice of site, and infusion set, in addition to the settings of various parameters for the pump and its handling in the activities of daily living.[6-8] Apart from these, some manual mistakes made by insulin pump users could cause dangerous medical problems such as hypoglycemia and hyperglycemia and culminate in diabetic ketoacidosis, which could be life threatening.[7] According to some studies, however, errors can also result in common dermatologic conditions such as pigmentation changes, scar formation, lipoatrophy, lipohypertrophy, and local skin irritations. Thus, skin issues and the problems linked to pump usage have been reported in some research papers as the principal causes for discontinuing the continuous subcutaneous insulin infusion (CSII).[9] Improved patient education and the correct usage of the insulin pump can reduce such skin problems.

Although insulin pumps are widely used, research related to the correct understanding regarding the insulin pump set and the associated complications such as dermatologic issues is relatively meager. Therefore, the aim of this study was to discover the skin-related problems experienced by adolescents with T1D, using the insulin pump as a means of treatment.

Methods

Study design and setting

This cross-sectional study was performed using 64 adolescents with T1D employing insulin pump therapy (IPT) for more than 1 year (ages 13-19) and visiting the Diabetes Clinic at Diabetes Treatment Center, Prince Sultan Military Medical City, Saudi Arabia, from January 2018 to March 2018. This study followed the protocol prescribed by the Declaration of Helsinki and was approved by the PSMMC Research Ethics Committee.

Table 1. Baseline characteristics of the study population (n = 64).

VARIABLE(S)	FREQUENCY	%
Age, y		
13-15 (n = 24)	24	37.5
16-19 (n = 40)	40	62.5
Gender		
Female	38	59.3
Male	26	40.7
BMI, kg/m^2		
<25	51	79.6
≥25	13	20.4
Duration of diabetes		
≤5	27	42.2
>5	37	57.8
IPT duration		
≥3	35	54.6
<3	29	45.5

Abbreviations: BMI, body mass index; IPT, insulin pump therapy.

Patient selection criteria

All the participants selected were chosen with deliberation and at their convenience, depending on them being available during their scheduled routine outpatient clinic visits. Verbal and written informed consent was taken from the parents and adolescents regarding the aim and methodology involved in this study. Parents and adolescents signed written consent prior to enrolling in the study. The participants were permitted to drop out of the research at will, with no explanations asked. All the patients were using the MiniMed Quick-set infusion set (Medtronic MiniMed, Northridge, CA, USA).

Inclusion and exclusion criteria

The study included patients with T1D, from 13 to 19 years of age, who had been treated with IPT and followed up for at least 1 year, and not having any other concomitant chronic disease. The patients excluded were those having history of psychopathology, medical instability, or with impairments of the visual, hearing, or cognitive aspects.

Data collection

Using the standardized questionnaire, patient age, weight, height, adjusted body mass index (BMI), duration of diabetes, as well as data regarding the infusion set catheter insertion site region, time between set changes, rotation of insertion sites, needle length of infusion set, and IPT duration were recorded.

Body mass index

By dividing the body weight in kilograms by the square of height in meters (kg/m^2), the BMI of the patient was calculated. The BMI *z* score was also determined (with adjustments for child age and sex). Using the formula (Xi − Mx)/SD, the *z* score (or SD score) was estimated, in which Xi is the actual measured value, Mx is the mean value for that particular age and sex, and SD is the standard deviation corresponding to that specific age and sex.[10]

Skin complications

The skin complications included patients exhibiting pigmentation changes,[11] scar formation,[11] lipoatrophy, lipohypertrophy,[12] and local dermatologic irritations.[13,14] By administering a closed/structured questionnaire, the prior and present skin issues were recorded, for a 6-month period.

Statistical analysis

Data were analyzed using the Microsoft Excel 2010 (Microsoft Corporation, Seattle, WA, USA) and Statistical Package for Social Sciences version 22.0 (SPSS Inc., Chicago, IL, USA). Besides the descriptive analysis, the χ^2 test was done to identify the differences present in the group. Logistic regression analysis was performed to recognize the variables associated with the skin complications. The *P* value of <.05 was accepted as having statistical significance.

Results

Table 1 lists the features of the study group. Most of the study groups are women (59.3%), in the 16- to 19-year category (62.5%), with BMI <25 kg/m2 (79.6%), diabetes for >5 years (57.8%), and patients on the insulin pump treatment for ≥3 years (54.6%).

In Table 2, the demographic and clinical variables associated with the skin complications are listed. Significant differences were evident in the factors female sex (*P* = .036), >3 years on IPT (*P* = .039), nonrotation of the infusion set (*P* = .001), 9 mm of needle length (*P* = .021), and catheter replacement for above 3 days (*P* = .022). However, the factors, age, BMI, diabetes duration, and insulin dosage revealed no significant differences.

Table 3 shows that regression analysis was done for all the variables exhibiting statistical significance in the "χ^2" test, revealing that the independent risk factors for the skin complications included female sex, catheter replacement, and infusion set rotation (Table 3).

Table 4 highlights the general dermatologic issues exhibited among the study population. Pigmentation changes and

Table 2. Demographic and clinical variables associated with skin complications.

VARIABLE(S)	SKIN COMPLICATIONS (N=27, %)	NO SKIN COMPLICATIONS (N=37, %)	*P* VALUE
Age, y			
13-15	12 (50%)	12 (50%)	.236
16-19	15 (38%)	25 (63%)	
Gender			
Female	20 (53%)	18 (47%)	.036
Male	7 (27%)	19 (73%)	
BMI, kg/m^2			
<25	21 (41%)	30 (59%)	.492
≥25	6 (46%)	7 (54%)	
Duration of diabetes, y			
≤5	15 (43%)	20 (57%)	.554
>5	12 (41%)	17 (59%)	
Catheter replacement, d			
<3	7 (26%)	20 (74%)	.022
≥3	20 (54%)	17 (46%)	
Rotation			
Yes	11 (25%)	33 (75%)	.001
No	16 (80%)	4 (20%)	
Needle length, mm			
6	5 (23%)	17 (77%)	.021
9	22 (52%)	20 (48%)	
IPT duration, y			
≤3	13 (33%)	27 (68%)	.039
>3	14 (58%)	10 (42%)	
Dose of insulin, μ/kg/d			
<0.7	7 (33%)	14 (67%)	.233
≥0.7	20 (47%)	23 (53%)	

Abbreviations: BMI, body mass index; IPT, insulin pump therapy.

localized irritations in the skin ranked among the most frequent complications encountered in the group under study, followed by scar formation and lipohypertrophy.

Figure 1 shows that 9.3% of the study population exhibited 3 or more skin complications, whereas 7.8% patients revealed 2 and 25% showed only 1 complication. In the study population, 37 patients (51.8%) experienced no skin complications.

Table 3. Results of regression analyses with 95% confidence interval for significant confounders of gender catheter replacement, rotation, needle length, and insulin pump duration on skin complications.

VARIABLE	OR (95% CI)	*P* VALUE
Gender		
Male	1	
Female	2.68 (2.27-84.2)	.004
Catheter replacement, d		
≤3	1	
>3	1.48 (0.89-21.8)	.042
Rotation		
Yes	1	
No	3.22 (4.02-87.4)	.001
Needle length, mm		
6	1	
9	0.94 (0.49-13.1)	.26
IPT duration, y		
≥3	1	
<3	0.95 (0.61-11)	.19

Abbreviation: IPT, insulin pump therapy.

Table 4. Skin complications among the study population.

SKIN COMPLICATIONS	NO. (%)
Changes in pigmentation	25 (39.1)
Occurrence of scars	11 (17.2)
Lipoatrophy	1 (1.5)
Lipohypertrophy	11 (17.2)
Local skin irritations	23 (35.9)

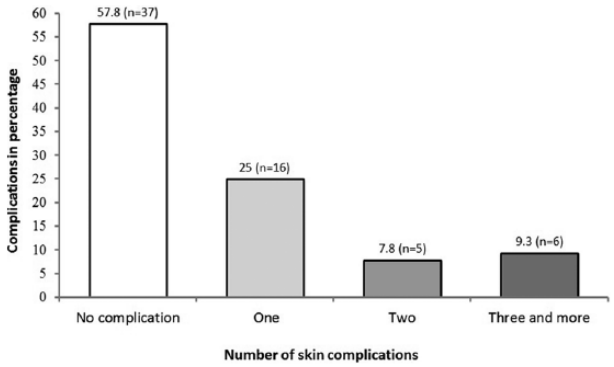

Figure 1. Number of skin complications among the study population.

Discussion

One of the growing forms of intensive insulin therapy is via CSII or IPT, which contains more accurate insulin supply and the ability to correct basal insulin levels to improve the glucose control, reduced risk of hypoglycemia, and better quality of life.[15] However, not all patients are capable to manage their diabetes with a pump. To achieve the complete benefits of IPT, constant adherence to the prescribed diabetes regimen is essential. It is therefore important to identify pump patients who have the probability of succeeding with this form of therapy.[15] Various studies reported that manual errors committed by these insulin pump users may result in dermatologic problems, which can negatively influence the kinetics of insulin absorption and induce glycemic fluctuations higher or lower than the target blood glucose levels, to the point of even inducing life-threatening medical complications.[7,16–18] This study aimed at investigating the skin-related complications among the study group of adolescents with T1D using the insulin pump.

Reports from the univariate analysis of the study group revealed that the most crucial risk factor for the skin problems was the negligence of rotating the infusion set. The regression analysis confirmed that patients who neglected to rotate the infusion set had nearly 3.22-fold greater risk than the ones who rotated the infusion set within the recommended 3-day time limit. Prior research showed that skin issues can arise due to acute reaction to the insulin infusion set (IIS) or its long-term use at the same site and is expressed as redness, pruritus, pain, or scar formation.[18,19] This type of irritation can arise from the insertion itself and/or the plaster used, and in rare instances, inflammation or even infection was noted.[18,20,21] In the nationwide pediatric surveillance of IIS in Germany and Austria, some actual publications showed that 192 (29%) patients exhibited no IIS issues at all. However, in the remaining 475 (71%) patients, 1404 events were reported.[21,22] Also, 33.9% most often revealed IIS obstruction. Then, 14.2% of the patients reported the presence of blood in the IIS, whereas 11.1% showed skin redness and 10.1% demonstrated bent cannula. Interestingly, 36.2% of the problems reported actually took place by the first day of IIS usage and 82.4% by the end of the second day. From a therapeutic perspective, the alterations in insulin absorption reported over time and triggered by the length in time of IIS usage are disquieting.[18] According to Schmidt et al, the incidence of IIS-related occurrences corresponds to the length in time of the IIS usage under clinical conditions. From this study, it is evident that the patients could use the IIS with no harmful effects for a minimum of 2 days; by the third day, several types of skin and infusion set-related and treatment-related tolerance issues began to emerge, necessitating, in part, an IIS change,[23] concurring with our results drawn from the univariate analysis and logistic regression analysis on the interval of catheter replacement. It was Perrin et al[24] who recorded that the possible issues which could arise in the adult and adolescent patients when infusion sets were used beyond the recommended 48 to 72 hours may be technical in nature and include, although not be restricted to, the local reactions of the skin to the adhesive, causing the redness, itching, and other indications of irritated skin. According to the manufacturers of IISs and insulin formulations employed in the insulin pumps, a change in the IISs and infusion site every 2 to 3 days is suggested to prevent skin and infusion issues.[18] It must be noted that such infusion site-linked recommendations are given, depending only on the findings drawn from anecdotal data regarding the daily usage of the IIS.[18] However, meticulous and exhaustive research that can offer a scientific justification for predicting a safe interval for the infusion set changes continues to be a pressing need.

It is reported that it may be more difficult for women to control their blood sugar levels because of several factors, including those like hormone-level fluctuations, especially during puberty. This can influence the sensitivity of the body to insulin-inducing blood sugar level fluctuations, which may precipitate greater injuries and disorders such as skin issues in women than in men.[25] These results imply that young female patients with T1D may require extra monitoring. From this study, it is clear that the skin problems occurred more frequently among the Saudi girls, possibly because these women always wear the abaya (a sleeveless full-length, outer robe), covering the entire body[26] and this attire code could be main reason for the women in Saudi Arabia to ignore the IPT-induced skin complications. Similar to other diabetes-related issues, dermatologic complications occur more frequently among the patients with T1D.

This study includes some limitations, as it was performed in a single medical center, and investigated only a few risk factors, within a restricted number of patients; therefore, further investigative research is necessary. Nevertheless, this study provides significant perception and awareness of skin disorders among adolescent patients with T1D in Saudi Arabia.

Conclusions

Generally, IPT users tend to develop skin-related complications. In this work, the factors female gender, duration of IPT, and infusion set rotations were the crucial risk factors recognized. Therefore, it is the responsibility of the health care providers, the diabetes educators, in particular, to be watchful and examine these indicators when considering and conversing about IPT for children with type 1 diabetes and with those providing them care. Every patient must receive training and be warned against using the insulin pump infusion sets beyond the time period recommended. The diabetes educator requires training to use techniques that will minimize the skin-related complications. Finally, this study could recognize only some conditions, thus reiterating the necessity for prospective studies that would help improve the ways of preventing and treating such skin-related complications in patients with T1D using the insulin pump.

Author Contributions

AAAH and MAAD conceived and designed the study and contributed to the writing of the manuscript. AAAH and AAR wrote the first draft of the manuscript and agreed with manuscript results and conclusions. MAAD made critical revisions and approved the final version of the manuscript. All authors reviewed and approved the final manuscript.

Data Sharing Statement

No data sharing as this manuscript and the data were not published elsewhere.

Ethical Approval

The study protocol was approved by the Research and Ethics committee of Prince Sultan Military Medical City, Riyadh, Saudi Arabia.

Informed Consent

During the informed consent process, study participants are assured that data collected will be used only for stated purposes and will not be disclosed or released to others without the consent of the participants.

REFERENCES

1. International Diabetes Federation. *IDF Diabetes Atlas*, 8th ed. Brussels, Belgium: International Diabetes Federation; 2017. http://www.diabetesatlas.org.
2. von Herrath MG, Korsgren O, Atkinson MA. Factors impeding the discovery of an intervention-based treatment for type 1 diabetes. *Clin Exp Immunol*. 2016;183:1-7.
3. Huo L, Harding JL, Peeters A, Shaw JE, Magliano DJ. Life expectancy of type 1 diabetic patients during 1997-2010: a national Australian registry-based cohort study. *Diabetologia*. 2016;59:1177-1185.
4. Katsarou A, Gudbjornsdottir S, Rawshani A, et al. Type 1 diabetes mellitus. *Nat Rev Dis Primers*. 2017;3:17016.
5. Al Hayek AA, Robert AA, Al Dawish MA. Evaluation of FreeStyle Libre Flash Glucose Monitoring System on glycemic control, health-related quality of life, and fear of hypoglycemia in patients with type 1 diabetes [published online ahead of print December 10, 2017]. *Clin Med Insights Endocrinol Diabetes*. doi:10.1177/1179551417746957.
6. Deiss D, Adolfsson P, Alkemade-van Zomeren M, et al. Insulin infusion set use: European perspectives and recommendations. *Diabetes Technol Ther*. 2016;18:517-524.
7. Saboo BD, Talaviya PA. Continuous subcutaneous insulin infusion: practical issues. *Indian J Endocrinol Metab*. 2012;16:S259-S262.
8. Evert AB, Bode BW, Buckingham BA, et al. Improving patient experience with insulin infusion sets: practical guidelines and future directions. *Diabetes Educ*. 2016;42:470-484.
9. Schifferdecker E, Schmidt K, Boehm BO, Schatz H. Long-term compliance of intensified insulin therapy. *Diabetes Res Clin Pract*. 1994;23:17-23.
10. Al-Hayek AA, Robert AA, Abbas HM, et al. Assessment of health-related quality of life among adolescents with type 1 diabetes mellitus in Saudi Arabia. *Saudi Med J*. 2014;35:712-717.
11. Binder E, Lange O, Edlinger M, et al. Frequency of dermatological side effects of continuous subcutaneous insulin infusion in children and adolescents with type 1 diabetes. *Exp Clin Endocrinol Diabetes*. 2015;123:260-264.
12. Al Hayek AA, Robert AA, Braham RB, Al Dawish MA. Frequency of lipohypertrophy and associated risk factors in young patients with type 1 diabetes: a cross-sectional study. *Diabetes Ther*. 2016;7:259-267.
13. Chen YM, Huang H. Allergy to soft cannula of insulin pump in diabetic patient. *Pak J Med Sci*. 2017;33:245-247.
14. Berg AK, Olsen BS, Thyssen JP, et al. High frequencies of dermatological complications in children using insulin pumps or sensors. *Pediatr Diabetes*. 2018;19:733-740.
15. Riemsma R, Corro Ramos I, Birnie R, et al. Integrated sensor-augmented pump therapy systems [the MiniMed® Paradigm™ Veo system and the Vibe™ and G4® PLATINUM CGM (continuous glucose monitoring) system] for managing blood glucose levels in type 1 diabetes: a systematic review and economic evaluation. *Health Technol Assess*. 2016;20:v-xxxi, 1-251.
16. Cogen FR, Streisand R, Sarin S. Selecting children and adolescents for insulin pump therapy: medical and behavioral considerations. *Diabetes Spectrum*. 2002;15:72-75.
17. 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. *Diabetes Care*. 2015;38:716-722.
18. Heinemann L, Krinelke L. Insulin infusion set: the Achilles heel of continuous subcutaneous insulin infusion. *J Diabetes Sci Technol*. 2012;6:954-964.
19. Schober E, Rami B. Dermatological side effects and complications of continuous subcutaneous insulin infusion in preschool-age and school-age children. *Pediatr Diabetes*. 2009;10:198-201.
20. Mecklenburg RS, Benson EA, Benson JW Jr, et al. Acute complications associated with insulin infusion pump therapy. Report of experience with 161 patients. *JAMA*. 1984;252:3265-3269.
21. Bruttomesso D, Pianta A, Crazzolara D, et al. Continuous subcutaneous insulin infusion (CSII) in the Veneto region: efficacy, acceptability and quality of life. *Diabet Med*. 2002;19:628-634.
22. Du F, Wang X, Shang B, et al. Gastrodin ameliorates spinal cord injury via antioxidant and anti-inflammatory effects. *Acta Biochim Pol*. 2016;63:589-593.
23. Pfutzner A, Sachsenheimer D, Grenningloh M, et al. Using insulin infusion sets in CSII for longer than the recommended usage time leads to a high risk for adverse events: results from a prospective randomized crossover study. *J Diabetes Sci Technol*. 2015;9:1292-1298.
24. Perrin AJS, Guzzetta RC, Miller KM, et al. A web-based study of the relationship of duration of insulin pump infusion set use and fasting blood glucose level in adults with type 1 diabetes. *Diabetes Technol Ther*. 2015;17:307-310.
25. Maiorino MI, Bellastella G, Casciano O, et al. Gender-differences in glycemic control and diabetes related factors in young adults with type 1 diabetes: results from the METRO study. *Endocrine*. 2018;61:240-247.
26. Al Hayek AA, Robert AA, Dawish MA, Braham RB, Goudeh HS, Al Sabaan FS. Efficacy of insulin pump therapy on diabetes treatment satisfaction and glycemic control among patients with type 1 diabetes mellitus in Saudi Arabia: a prospective study. *Diabetes Ther*. 2015;6:227-236.