Original Article

Cutaneous complications of insulin therapy in patients with Type1 diabetes mellitus

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Summary:

Background: Common complications of subcutaneous insulin injection include lipoatrophy and lipohypertrophy which may lead to erratic absorption of the insulin with the potential for poor glycemic control and unpredictable hypoglycemia. Other cutaneous complications are local and systemic insulin allergy.

Patients and methods: The study included 150 patients with type1 diabetes mellitus attending thediabetic clinic of Children Welfare Teaching Hospital who were assessed for cutaneous omplications of insulin therapy especially at the sites of the injections. Data collected evaluated using chi square and Pvalue.

Results: Out of 150 patients, the male to female ratio was 1:1.3, with mean age of 11.34 years ± 4.461SD.The cutaneous complications of insulin therapy present in (56.7%) of patients, (94.1%) of them had lipohypertrophy and (5.9%) had allergy to insulin while lipoatrophy and other cutaneous complications were not reported.The cutaneous complications were associated with increase in the incidence of other complications of diabetes mellitus (72.9%).Most of cutaneous complications developed in the upper arms (69.4%) especially in those who did not change the sites and those with wrong technique of injections.

Conclusions: The cutaneous complications developed because of poor education about the proper use of insulin or failure to follow the instructions, as the school achievement of the person who injects the insulin for the patient had no role. So I recommend proper education about the sites and the technique of insulin injection and the maintenance of this education.

Key words: Type1diabetes mellitus, cutaneous complications, insulin therapy, lipohypertrohy.

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Introduction:

The most common type of diabetes mellitus occurring in childhood is type I diabetes mellitus (T1DM), which is caused by autoimmune destruction of the pancreas. Patients with T1DM have sever, and usually permanent insulin deficiency and require insulin for survival and prevention of lifethreating episodes of Ketoacidosis(1). Common complications of subcutaneous insulin injection include lipoatrophy and lipohypertrophy. In lipoatrophy, a dimple or well-circumscribed depression at the site of injection is typically seen, although loss of fat may extend beyond the site of injection, leading to an extensive, depressed plaque (2).The development of lipoatrophy may have an immunological basis, predisposed by lipolytic component of certain insulin(3). Lipoatrophy has been extremely rare since the introduction of recombinant human insulin (4). Hypertrophy is the most common complication of insulin therapy (3). Its incidence is affected by the level of patient education, the frequency that they changed needles, the frequency of changing their injection sites and the amount of time they had been using insulin (5). Children and adolescents may refuse to rotate their injection sites because repeated injection in the same site is associated with less pain sensation. Failure to rotate injection sites results in subcutaneous scar formation (Lipohypertrophy). Insulin injection into the lipohypertrophic skin is usually associated with poor insulin absorption and/or insulin leakage with resultant suboptimal glycemic control (2).Allergic reactions to insulin may be immediate or delayed. The immediate local reaction is probably IgE mediated. It starts as erythema, becomes urticarial within 30 minutes and subsides within an hour.

The delayed reaction is the most common reaction; it is due to delayed hypersensitivity. About 2 weeks after the initiation of insulin therapy, a pruritic nodule develops with one to two days at the site of injection, lasts for days and heal with hyperpigmentation and scarring(3). Edema of feet and abdomen is a rare phenomena accompanying initiation of insulin therapy (6), which appear shortly after starting or increasing the dose of insulin, it commonly seen in women, and is unrelated to cardiac or renal disease. The pathogenesis is unclear (7). Other cutaneous complications like localized induration, ulceration and scar formation, cutaneous abscess formation and development of keloid may result from faulty injection techniques. Idiosyncratic reactions are very rare, and skin reaction resembling acanthosis nigricans has been reported (7). Local complications resulting from incorrect injection technique may be common among insulin requiring diabetic patients (8).Regarding diabetic education,

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unfortunately, most children who meet the hospital's admitting criteria may only have four to five days in the hospital for blood glucose regulation and education (9). This leaves very little time for the educators to get to know the families and ensure that everyone involved with the child's diabetes control has been properly educated; in addition, some of the patients do not meet the hospital admission criteria, in these instances the insulin regulation and education must be accomplished on an outpatient basis (10). This study aimed to study the cutaneous complications of insulin therapy in type1diabetes mellitus and some factors that may affect their development.

Patients and methods:

Across sectional study of 150 patients with T1DM who were interviewed with their parents and examined in the diabetic clinic of Children Welfare Teaching Hospital over a period of 9 months from the 1st of January to the 1stof October 2005 to study the cutaneous complications of insulin therapy in T1DM and some factors that may affect their development. Data were collected including the age, sex, date of onset of diabetes, sites of insulin injections and if these were changed occasionally, always, or not changed, the person who injected the insulin to the patient and his school achievement, whether education about the usual sites and technique of insulin injection done or not, as the usual sites for insulin injection include the upper and the outer arms , either side and below the umbilicus, anterior and lateral thigh and upper and outer buttock(11). Checking (by history and examination of the patient) for presence of any cutaneous complications (lipohypertrophy, lipoatrophy, allergy and others).Checking the technique of insulin injection as the patient should give the injection at 45^0 angle to the surface of the skin with or without pinching the skin (11), any new instructions about the technique and site of the insulin injection given to patient with complications, and did the patient follow the instruction given to him/her or not?.Statistical analysis was done by the use of chi square test and a P value of < o.o5 considered significant.

Results:

The total number of patient in this study was 150 patients of whom 64 (42.7%) were males and 86 (57.3%) were females with male to female ratio of 1:1.3, with mean age of 11.34 years ± 4.461 SD. One hundred and two (68 %) patients had diabetes for less than five years. The cutaneous complications of insulin therapy were present in 85 (56.7%) patients and 65 (43.3%) patients had no cutaneous complications, (P value = 0.0079) (Table 1).

Table1: Frequency distribution of patients according to the duration of diabetes mellitus.

Duration of disease in years	Patients with cutaneous complications No. %	Patients without cutaneous complications No. %	Total No. %
< 5 years	50 (49.1%)	52 (50.9%)	102 (68.0%)
>5-10 years	21 (65.6%)	11 (34.4%)	32 (21.3 %)
> 10 years	14 (87.5%)	2 (12.5%)	16 (10.7%)
Total	85 (56.7%)	65 (43.3%)	150 (100%)

(P value = 0.0079).

Eighty (94.1%) patients with cutaneous complications of insulin therapy, had lipohypertrophy and 5 (5.9%) patients had allergy while lipoatrophy and other complications were not reported. The commonest sites for cutaneous complications were the right and left arms (69.4%) (Table 2)

Table2: Frequency distribution of patients with cutaneous complications according to the different sites of insulin injection.

Sites of insulin injections and cutaneous complications	Number of patients	%
Right and left arm hypertrophy and allergy	59	69.4%
Right and left thigh hypertrophy	8	9.4%
Right and left arm and thigh hypertrophy	5	5.9%
Right arm hypertrophy	7	8.2%
Left arm hypertrophy	4	4.7%
Unusual sites : leg hypertrophy forearm hypertrophy	 1 1	 1.2% 1.2%
Total	85	100%

Sixty two (72.9%) patients of those with cutaneous complications had other complications of T1DM, compared with 20 (30.8%) patients without cutaneous complications who had other complications of T1DM (P value < 0.0001) (table 3).

Table3: Frequency distribution of the patients according to the common complications of the diabetes mellitus.

Common complications of Diabetes Mellitus.	Patient with cutaneous complications No. %	Patient without cutaneous complications No. %	Total No. %
Diabetic ketoacidosis*	35 (41.2%)	10 (18.5%)	45(31.3%)
Hypoglycemia*	14 (16.5%)	4 (6.2%)	17 (12.0%)
Retinopathy	13 (15.3%)	3 (4.6%)	16 (10.7%)
Nephropathy	10 (11.8%)	2 (3.1%)	12 (8.0%)
Neuropathy	4 (4.7%)	1 (1.5%)	5 (3.3%)
Growth failure	6 (7.1%)	1 (1.5%)	7 (4.7%)
No complications	23 (27.1%)	45 (69.2%)	68 (45.3%)

***Some patients had more than one complication of diabetes mellitus**

Twelve (8%) patients injected insulin in one site, all of them (100%) had cutaneous complications, 74 (49.3%) patients changed the sites occasionally,67 (90.5%) of them had cutaneous complications while 64 (42.7 %) patients changed the sites always, only 6 (9.4 %) of them had cutaneous complications (P value <0.0001).One hundred and forty two (94.7 %) patients used right technique for insulin injection, 78(52%) had cutaneous complications while 8 (5.3%) patients use wrong technique, all of them (100%) had cutaneous complications (P value = 0.01).There was no difference between the two groups regarding the school achievement of the person who inject the insulin (P value = 0.967) (table 4).

Table4: frequency distribution of patients according to the school achievement of the person who inject the insulin.

School chievement of person who injected he insulin	Patients with cutaneous complications No. %	Patients without cutaneous complications No.%	Total No. %
Illiterate	11(61.1%)	7 (38.9%)	18 (12.0%)
Primary school	24 (57.1%)	18 (42.9%)	42 (28.0%)
Secondary school	35 (54.7%)	29 (45.3%)	64 (42.7%)
The institute or college	15 (57.7%)	11 (42.3%)	26 (17.3%)
Total	85 (56.7%)	65 (43.8%)	150 (100%)

(P value = 0.967).

One hundred and four (69.3%) patients were following the instructions given during education about the sites and technique of insulin injection, 45(43.3%) had cutaneous complications and 59 (56.7%) had no cutaneous complications while 46 (30.7%) patients were not following the instructions, 38 (82.6%) of them had cutaneous complications and 8 (17.4%) had no cutaneous complications (P value <0.0001).

Discussion:

In this study, the number of patients with cutaneous complications is more than those without cutaneous complications; this finding may be related to either poor education of the families and patients or failure of them to follow the instructions given during education and follow up properly. Hypertrophy was the most common complications seen in this study and this finding is similar to Richardson T. and Kerr D.(3) ,and Varder B, Kizilci S. (5) findings, this may be due to poor education or insistence of the patient to keep injecting insulin into the lumpy area as it is associated with less pain(2). Lipoatrophy was not reported, as it is rare since the introduction of recombinant human insulin (4), which is used by my patients. The incidence of these complications is high during the early years of treatment and increase with time as its development does not require much time and most patients fade up from continuous following of the instructions given during educations. This is similar to VarderB,Kizilci S. (5) and Seyoum B. (8) findings. majority of my patients were using the upper arm for insulin injection and hence increased cutaneous complications at these sites, and missing rotation of injection site was a significant cause and this is similar to Varder B, Kizilci S. [(5)], Richardson T, Kerr D(3)and Hauner H, Stockamp B , Haastert B findings(12). More than (70%) of patients with cutaneous complications had other complications of diabetes while (69.2%) of those without cutaneous complications had no other complications of diabetes which could be explained on basis of poor education and management in the first group, beside the fact that the injection of insulin into a site of lipohypertrophy ,although painless, may lead to erratic absorption of the insulin ,with the potential for poor glycemic control and unpredictable hypoglycemia(13).

Lipohypertrophy developed in (100%) of those who inject the insulin in one area (no changes), in (90.5%) of those who change the site occasionally, and this may be related to poor education or because the site of hypertrophy become painless and other sites relatively painful, this is similar to Varder B, Kizilci S. finding(5).

All patients with wrong technique of insulin injection develop cutaneous complication, due to poor education about this point, although many other patients with right technique had complications, which may be related to other factors. The school achievement of person who injects the insulin had no role in decreasing the development of complications and it depends mainly on education given in the diabetic ward and clinics by the doctors and medical staff, this is different from Varder B, Kizilci S. finding (5). It depends also on following of the instructions about the site of injection that were given during the education, so those (82.6%) who did not follow the instructions had the complications.

Conclusions:

Lipohypertrophy is the most common cutaneous complication of insulin therapy in T1DM. It occurs during the first few years after initiation of insulin therapy and their incidence increase with time.The cutaneous complications associated with increase in the incidence of other complications of diabetes and important causes for these complications were poor education about technique and the sites of insulin injection or failure of the patients to follow the instructions given during education as the school achievement of the person who injects the insulin had no role. Examination of the sites of insulin injection should be done in each visit and the technique of insulin injection should be checked periodically. Any diabetic patient with cutaneous complications should be examined for other more serious complications.

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