Original Article

Frequency and Risk Factors of Lipohypertrophy in Insulin Treated Patients with Diabetes: An Experience from a Tertiary Care Center in Multan

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ABSTRACT

Objective: The present study aimed to evaluate the frequency and risk factors of lipohypertrophy in insulin treated patients in a tertiary care center in Multan.

Study Design: cross sectional descriptive study

Place and Duration of Study: This study was conducted at the Diabetic Outdoor of Nishtar Hospital, Multan between 1st January 2022 to 31st June 2022.

Materials and Methods: We included 360 patients, taking insulin for more than one year in our study. The patients were interviewed about insulin injection habits and the injection sites examined according to a preformed questionnaire.

Results: We included 360 patients with diabetes mellitus who used insulin for more than one year. The frequency of lipohypertrophy was 43.6%. Mean duration of diabetes and mean duration of insulin use were 14.68±7.62 years and 8.45±6.1 years, respectively. Longer disease duration, longer insulin use, higher doses, use of ice cold insulin and lack of rotation of injection site were the major risk factors of lipohypertrophy.

Conclusion: Lipohypertrophy is a common complication of insulin use related largely to improper injection technique. Patient education and frequent examination of the injection site can help prevent lipohypertrophy.

Key Words: Diabetes mellitus, insulin, lipohypertrophhy, injection site.

INTRODUCTION

Diabetes mellitus (DM), a major public health problem, affects 536.6 million adults globally. This is estimated to increase to 700 million by 2045.[1] Insulin is an essential medication for all patients with type 1 diabetes. Many patients with type 2 diabetes ultimately need insulin as well.[2]

In order to optimize glucose control and insulin use safety, it is crucial to teach the correct insulin injection technique to all patients and care givers. Insulin must be injected into the subcutaneous tissue in the abdomen, thigh, buttock or upper arm.

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A shorter needle length (4 mm) in pen and a 6 mm needle in syringe is recommended to avoid accidental intramuscular injection. The skin should be raised by the thumb and index finger to make a fold and insulin injected slowly at 90 degree angle. The patient should count to 10 before withdrawing the needle. Use of short needles and injection site rotation should be taught to all patients and care givers.[3]

In addition to hypoglycemia, a major adverse effect of insulin therapy, there are a number of side effects related to insulin administration. These include local pain and discomfort, bruising, infection, needle stick injuries and lipodystrophy.

Lipodystrophy (LD) is the most frequent local complication of insulin administration and may present either as lipoatrophy (LA) or lipohypertrophy (LH). LA manifests as skin indentation and is thought to be due to lipolytic reaction to impurities in insulin preparation. Since the advent of purified insulin, its prevalence has dropped to only 1- 2%.[4] Lipohypertrophy, on the other hand is still, fairly common. A recent meta- analysis has shown the pooled prevalence of LH as 38%.[5] Other studies have reported the prevalence as 37.3- 53.1%.[6-8] In a recent Indian study, the prevalence of LH in patients with Type 1 Diabetes mellitus was as high as 69.8%.[9]

Lipohypertrophy presents as a firm swelling of the sub cutaneous tissue and results from the growth promoting properties of the insulin molecule combined with incorrect insulin administration. Failure to rotate insulin injections, use of ice cold insulin, use of long needles, increased insulin dose and prolonged duration of insulin therapy are the predisposing factors for development of LH.[10] LH is diagnosed by visual observation and palpation of insulin injections sites, using tangential light and different patient angles. A lubricant gel can be used, if needed.[11,12] Injection into LH site leads to erratic insulin absorption and high glycemic variability. Lipohypertrophy can be prevented by targeted education of patients and their care givers. All insulin using patients should have their injection sites checked at regular intervals, both visibly and by palpation, for detection of LH. All patients must be instructed to correctly rotate injection site which means that injections are spaced at least 1cm (an adult finger breath from each other).[3] LH lesions have been shown to regress significantly after 6 months of systematic rotation and single use of needles.[13]

MATERIALS AND METHODS

It was a cross sectional descriptive study, including 360 patients from the diabetic outdoor department of Nishtar Hospital, Multan, using non probability sampling technique. Study was done from 1st January 2022 to 31st June 2022. All diabetic patients more than 12 years old, taking insulin for more than one year were included in the study. Patients with gestational diabetes were excluded. Informed consent was taken from all patients. Clinical history about the type and duration of diabetes, type (basal-bolus or premixed) and duration of insulin use, technique of insulin use including site (abdomen, thigh, buttock or arm), rotation of injection site, type of insulin device (insulin syringe or pen), needle length, reuse of needle and use of cold insulin was enquired. Patients were also asked other injection site reactions like bruising, pain, redness, leakage, and swelling.

Lipohypertrophy was determined by clinical examination. All the injection sites were inspected from various angels using tangential light in both upright and supine position. The relevant site was also palpated and an area of skin suspected for LH was pinched to identify difference in thickness or texture from the surrounding skin. Lack of insulin rotation was defined as injecting insulin in the same region or keeping less than a finger breath distance between consecutive insulin injections. Reuse of insulin needles was defined as use of a needle more than once. The frequency of needle reuse was further classified according to the number of times the needle was reused.

Approval from ethical review committee of Nishtar Medical University was taken. Data was entered and analyzed by SPSS-23. Mean and standard deviation of descriptive variables, like age, duration of diabetes, duration of insulin use, and daily dose of insulin was determined. For comparison among different groups Chi square test was applied, and P value <0.05 was considered statistically significant.

RESULTS

We included 360 patients with diabetes mellitus who used insulin for more than one year. Among these, 149 (41.4%) patients were male and 211 (58.6%) were female. Mean age of these patients was 50.75 ± 11 years. Of these, 196 (54.4%) patients were uneducated, 65 (18.1%) had primary education, 47 (13.1%) middle school, 29 (8.1%) high school, and only 23 (6.4%) patients had university level education.

Of 360 patients, 322 (89.4%) had type 2 DM and 38 (10.6%) patients had type 1 DM. Mean duration of diabetes and mean duration of insulin use was 14.68 ± 7.62 and 8.45 ± 6.1 years, respectively. Mean daily insulin dose was 63.6 ± 18 units. Most of the patients were using Human insulin (78.6%). Insulin syringe was the preferable device (92.2%) for injection. Majority of the patients injected insulin in the abdomen (68.3%). The reuse of the insulin needle was fairly common (98.3%). Only 233 (64.7%) patients had received education about the technique of injecting insulin.

Table No.I: Insulin injection habits of study participants

Characteristics		No of patients	Percentage%
Insulin Regimen	Pre-mixed	288	80
	Basal-bolus	72	20
Type of insulin	Human	283	78.6
	Analogue	77	21.4
Location of injection site	Abdomen	246	68.3
	Thigh	25	6.9
	Arm	9	2.5
	Mixed	80	22.2
Rotation of insulin injection	Yes	340	94.4
	No	20	5.6

Reuse of insulin injection	Never	6	1.7
	2-4	40	11.1
	5-7	195	54.2
	8-10	76	21.1
	>10	43	11.9
Needle length(in mm)	4	7	0.19
	5	84	23.4
	6	269	74.7
Injection device	Pen	28	7.8
	Syringe	332	92.2
Use of ice-cold insulin	Yes	280	77.8
	No	80	22.2
Injection giver	Self	307	85.3
	Care giver	53	14.7
Other side effects at injection site apart from lipohypertrophy	Bruising	59	16.4
	Pain	100	27.8
	Lipoatrophy	53	14.7
	Redness	38	10.6

Table No.2: Factors associated with lipohypertrophy

Risk factors		Lipohypertrophy		P value
		Yes	No	
Gender	Male	70	79	0.279
	Female	87	124	
Education	None	85	111	<0.001
	Primary	33	32	
	Middle	23	24	
	High school	2	27	
	University	14	9	
Type of DM	Type 1	22	16	0.060
	Type 2	135	187	
Duration of disease (years)	>10	113	108	<0.001
	≤10	44	95	
Duration of insulin use (years)	>8	93	64	<0.001
	≤8	64	139	
Daily dose of insulin (units)	>40	151	166	<0.001
	≤40	6	37	
Insulin regimen	Premixed	129	159	0.366
	Basal-bolus	28	44	
Insulin type	Human	115	168	0.029
	Analogue	42	35	
Insulin device	Syringe	136	196	<0.001
	Pen	21	7	
Rotation of injection site	Yes	143	197	0.014
	No	14	6	
Reuse of insulin Needle (number of times)	Never	0	6	0.143
	2-4	15	25	
	5-7	93	102	
	8-10	31	45	
	>10	18	25	
Needle length(mm)	4	7	0	<0.001
	5	56	28	
	6	94	175	
Use of Ice cold insulin	Yes	129	151	0.078
	No	28	52	

Other injection habits of the participants are summarized in table I.

Lipohypertrophy was present in 157 (43.6%) patients. Of these, 80 (50.9%) patients had single lump on examination while 77(49.04%) patients had multiple lumps. Most of the studied patients had never examined the injection site (56.4%). Only 17 (4.7%) patients had their injection site examined by their health care provider regularly.

The association of various risk factors with LH is presented in Table 2. Longer disease duration, longer insulin use, higher doses, use of ice cold insulin and lack of rotation of injection site were the major risk factors of lipohypertrophy.

DISCUSSION

The frequency and risk factors affecting LH in insulin using diabetic patients was investigated. In our study, lipohypertrophy was present in 43.6% patients. A recent meta-analysis had shown the pooled prevalence of LH as 38%[5]. In Turkey, Ireland and Italy the prevalence was 48.8%, 51% and 48.7% respectively, similar to our study[14-16]. The prevalence of LH in Blanco's study[17] was much higher (64.4%) while in a Canadian study, it was 24.6%, much lower than our study.[18]

In this study, LH was more common among Type 1 diabetics (57.9%) than in type 2 diabetic patients (41.9%). Omar and his colleagues found the prevalence of LH as 54.9% in type 1 diabetes[19]. In another study, it was 52.3%.[20] These are comparable to our study results. In a recent Indian study, the prevalence of LH in patients with Type 1 DM was as high as 69.8%[9]. In Youssef's study of type 1 diabetics, only 23.7% had LH. [21] In Ajlouni's study, the prevalence of LH in Type 2 DM was 35.3%.[6] This inconstancy may be related to patient factors as well as variation in examination methods and skills of the health care provider examining the patient in different studies. LH was more common in male (47%) than in female (41.2%), but this difference was statistically insignificant. In other studies, the effect of gender was not significant as well.[8, 9, 22] In our study, lipohypertrophy was more common in older and less educated patients. In another study, no statistically significant effect of education was noted.[22]

In our study, longer duration of diabetes (>10years), longer duration of use of insulin (>8 years) and higher daily dose of insulin (>40 units per day) were significantly associated with lipohypertrophy. Other studies also confirm increased risk of lipohypertrophy with longer duration of diabetes.[9,15,17] The results of a study by Wjitcharoen et al were similar to ours in this regard.[22] Vardar and Kizici also found significant association of longer duration of insulin use and LH, which is comparable to our study.[14] Cunningham, however, did not find the total daily dose of insulin as a

notable risk factor for LH.[15] In this study, insulin regimen (premixed/basal bolus) had no significant relation with LH formation. Use of insulin analogues, and use of insulin pen instead of syringe was associated with higher incidence of LH. In a study by Sunil Gupta, effect of both insulin regimen and type of insulin did not have a significant impact on LH formation.[9] Blanco and Omar also found that insulin type and device used for insulin injection was not significantly related to LH.[17,19]

In our study, LH was more prevalent among those who did not rotate injection site and in those who used longer needles. Cunningham and Blanco also found significant relationship between needle length and LH[15,17]. Although most of our patients (98.3%) reused insulin needles, we did not find a significant association between reuse of needles and LH. Gupta & Vardar studies found significant association of lack of rotation of injection site and reuse of injection needle on LH formation.[9,14]

CONCLUSION

We conclude that lipohypertrophy is a common local complication of insulin injection use. This is largely preventable with targeted education about injecting insulin and regular examination of insulin injection sites.

Author's Contribution:

Concept & Design of Study:	Mehwish Saeed, Wasif Aslam
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