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Research Article

RISK FACTORS FOR LIPODYSTROPHY IN INSULIN-TREATED DIABETICS: ABOUT 1000 CASES

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ABSTRACT

Introduction: Lipodystrophy is a common complication of insulin therapy. The objective of our study was to evaluate the frequency of lipodystrophy in diabetic patients and its contributing factors. **Materials and methods:** A prospective study including insulin-treated patient for more than 6 months. The variables studied were treatment, injection techniques, hypoglycemia and its criteria. The results for the group of patients with lipodystrophy were compared to the group without lipodystrophy. **Results:** During the study period, 1000 patients were included. The prevalence of lipodystrophies was 48%. The main location was the arms in 84%. The predisposing factors for the development of lipodystrophy were essentially: the lack of rotation of injection sites ($p < 0.000000001$), the practice of the injection fold, the use of insulin syringes more than 6 times ($p = 0.0000004$) and the number of education sessions. Unexplained moderate hypoglycemia was present in 72% of patients with lipodystrophy versus 30% in patients without lipodystrophy. For insulin injection techniques, the vector used was the insulin syringe in 92% of patients. The antiseptic was used in 12% of patients. The injection fold was performed in 43% of patients and released in 15% of patients. Needle retention after injection was observed in 41% of patients. Rotation of injection sites was noted in 55% of patients. All patients reported reusing the needle and 97% used it more than 4 times. **Conclusion:** The predictive factors for lipodystrophy were essentially the lack of site rotation, the impracticality of the injection fold and the abusive reuse of syringes. This requires further education and assessment of insulin-treated patients.

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INTRODUCTION

Diabetes is a chronic disease with a constantly increasing incidence[1]. Insulin therapy is a treatment that has a key role in the management of the type 1 diabetic patient and a large number of type 2 diabetic patients. [2,3,4]. Despite the emergence of different insulin analogues, the implementation of this therapy still leads to several complications, particularly cutaneous[5,6], including lipodystrophies (LD). These are the cause of several complications including glycemic imbalance and glycemic variability with hypoglycemia. The objective of our study was to evaluate the frequency of lipodystrophies in insulin-treated diabetic patients and to determine the different risk factors for lipodystrophy.

PATIENTS AND METHODS

This is a prospective study, carried out over a period of 28 months, from February 2015 to June 2017, within the

Endocrinology and Metabolic Diseases Department of the University Hospital of Casablanca (Morocco).

Inclusion Criteria

Included in the study were any type 2 diabetic patient > 18 years of age or type 1 diabetic patient over 14 years of age hospitalized at the Ibn Rochd University Hospital or followed in consultation, insulin-treated for at least 6 months

Exclusion Criteria

Non-insulin-treated or insulin-treated patients less than 6 months of age. Non-consenting patients. Any patient included, was examined to determine the presence of lipodystrophy, the site, whether it was observed by the patient or not. Several data were searched for each patient.

These Variables Included

Socio-Demographic Characteristics: Age, gender, grade level

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The Characteristics of Diabetes: Type of diabetes, duration of diabetes progression, duration of insulin therapy, glycosylated hemoglobin level (measured by standardized method)

Characteristics related to insulin therapy: Duration, type of insulin, number of injections, injection site, vectors, preferred sites, injection techniques

The characteristics of hypoglycemia: The number, the severity. Hypoglycemia was defined as blood glucose less than or equal to 0.70 g/l.

Injection technique: Use of an antiseptic, practice of the injection fold, degree of injection, fold released 5 to 10 s after injection, wait 10 seconds before removing the needle, rotation of the injection sites by 1cm

Lipodystrophy zone: Site, observed or not by the patient.

RESULTS

General Characteristics of the Population

The study involved 1000 patients with a high female predominance: 677 women and 323 men (sex ratio F/H: 2/1). The average age of our patients was 42±20 years. The average age of diabetes was 9.6 years (from 6 months to 37 years). The duration of insulin therapy was 5.7 years (6 months to 37 years). Type 2 diabetes was the most prevalent in the study (60%) while 38% of patients had type 1 diabetes and 2% had slow type 1 diabetes.[Table1]

In terms of insulin therapy, 224 patients were under basal regimen (22%), 128 patients under basal bolus (12%), 53 under basal plus and 595 under premixed regimen (59%). Concerning glycemic control, the average HbA1c was 10.2%.

Patient Injection Techniques

The vector used was the insulin syringe in 92% of patients and insulin pens in 8% of patients.

Only 12% used the antiseptic before the insulin injection. The injection fold was performed in 43% of patients and released in 15% of patients. Needle retention after injection was observed in 41%. Rotation of injection sites was noted in 55% of patients.

Characteristics of lipodystrophies

The prevalence of lipodystrophies was 48% or 481 patients. Their locations were the arms in 84% of cases (408 patients)[figure 1,2,3,3,4], the belly in 30% (146 patients) [Figure 5,6] and 12% at the thigh level (61 patients), with a double location in 26% of cases or 125 patients.

The lipodystrophy area was observed by 50% of patients by palpation, but 32% continued to inject into it.

Risk factors for Lipodystrophies

The Duration of Insulin Therapy

The presence of lipodystrophy was correlated with the duration of insulin therapy (p= 0.002)

The type of diabetes

LD was more frequent in patients with type 1 diabetes

The Reuse of needles

Regarding the number of needle use: 3% of patients used the needle less than 4 times, 43% between 4 and 6 times, 42% between 6 and 10 times, and 11% of patients 10 times or more. The LD was correlated with the number of needle uses (p=0.000000004)

Rotation of injection sites

The lack of rotation of injection sites was correlated with the presence of LD (23% of patients with lipodystrophy had site rotation versus 74% rotation in patients without lipodystrophy) p<0.000000001

The practice of the injection fold

Only 30% of patients with lipodystrophy practiced the injection fold versus 56% in patients without lipodystrophy (p<00000001).

Consequences of lipodystrophies

Hypoglycemia

Unexplained moderate hypoglycemia has been reported in 72% of patients with lipodystrophy with an average of 2 hypoglycemia per week versus 30% in patients without lipodystrophy with p<0.000000001.

Hyperglycemia

The LD was correlated with HbA1c > 10% (44% of patients with LD had HbA1c >10% vs 36% of patients without LD : p=0.014)

The Number of Education Sessions

Regarding therapeutic education, 90% of patients received sessions with a number of one to two sessions in 55% of patients, 3 to 4 sessions in 30% of patients, and 5% more than 4 SD sessions.

Among patients who received 1 to 4 educational sessions, 45% had lipodystrophies (p=0.33), while in patients receiving more than 4 sessions, lipodystrophies were objectified in only 35% (p=0.008).





Figure 1,2,3,4 areas of lipodystrophy in the arm.

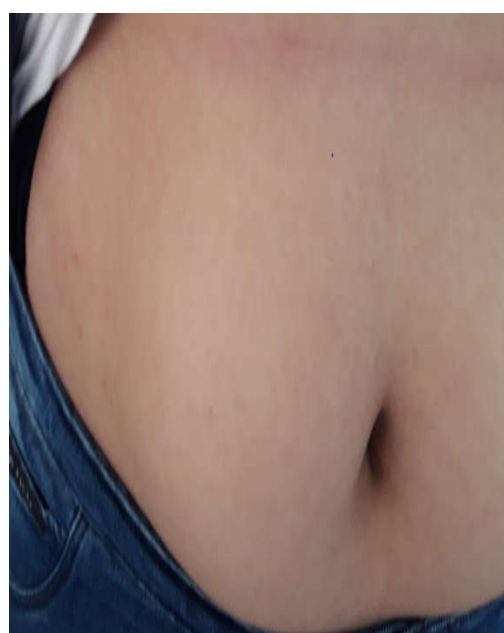


Figure 5, 6 lipodystrophy areas in the abdomen

Table 1 Factors Promoting Lipodystrophies

	Absence LD n = 519	Presence LD n = 481	P
Gender			
Female	329 (63.39%)	348 (72.34%)	0.002
Male	190 (36.60%)	133 (27.65%)	
Type of diabetes			
1	163 (31.40%)	219 (45.53%)	0.000004
2	349 (67.24%)	259 (53.84%)	0.00001
LADA	7 (1.34%)	3 (0.62%)	0.24
Duration of insulin therapy	5.36 ± 5.03	6.34 ± 5.28	0.002
Insulin regimen			
Basal	120 (23.12%)	104 (21.62%)	0.56
Basal bolus	70 (13.48%)	58 (12.05%)	0.49
Basal plus	17 (3.27%)	36 (7.48%)	0.002
Premixed	312 (60.11%)	283 (58.83%)	0.678
Number of syringe use			
<4	16 (3.08%)	15 (3.11%)	0.97
4-6	266 (51.25%)	169 (35.13%)	0.0000003
> 6	237 (45.66%)	297 (61.74%)	0.0000004
Use of antiseptic Practice of injection	72 (13.87%)	56 (11.64%)	0.29
	294 (56.64%)	148 (30.76%)	< 0.00000001

folding			
Rotation of injection sites	389 (74.94%)	113 (23.49%)	< 0.00000001
Number of hypoglycemia	157	349	< 0.00000001
Number of education sessions			0.005
0	42	59	0.02
[1-2]	299	252	0.09
[3-4]	158	133	0.33
> 4	37	20	0.008
HbA1c (%)			0.11
<8	24(4%)	15(3%)	0.21
[8-10]	163(31%)	146(30%)	0.71
>10	192(36%)	215(44%)	0.014

DISCUSSION

Lipodystrophy is a disorder of adipose tissue, is one of the most common complications of subcutaneous insulin injections and can occur as lipohypertrophy (LH) or lipoatrophy (LA). The latter is defined as a scar that is often deep and retracted on the skin as a result of a lesion of subcutaneous adipose tissue[7]. Several characteristics of LA suggest an immunological etiology[8]. It appears to be the result of a lipolytic reaction to impurities or other components of certain insulin preparations, since its prevalence is now only 1 to 2% with the increasing use of purified insulin[9,10]

LD was first described as a complication of insulin therapy by Lamar *et al*[11] in 1950. He first suggested that changes in insulin absorption could be influenced by atrophic and hypertrophic LDs at the injection sites.

LH may be the result of the local anabolic action of insulin on adipocytes, promoting fat and protein synthesis. However, other mechanisms such as needle reuse and trauma caused by frequent injections in the same area have also been described[12]. Histologically, it is characterized by an increase in adipocyte size and morphological changes, an acceleration of the metabolic activity of subcutaneous adipose tissue, or even an invasion of the dermis by adipocytes[13]. It is due to the repeated stimulation of adipocytes by insulin.

The reported prevalence of LH in patients receiving insulin injections varies considerably according to published studies[14]. In our study the prevalence was 48%, it was more frequent among women. The main contributing factors were the non-rotation of the injection sites, the impracticality of the injection fold and the use of the injection device more than 4 times. Patients with LD also had frequent unexplained hypoglycemia. A French study conducted in 2013[15] involving 140 patients found a prevalence of 33%. In Spain, the prevalence found was 64.4% in a study also conducted in 2013 involving 430 patients. There was a strong relationship between the presence of LH and non-rotation of sites, as well as with needle reuse. The risk increases considerably when needles were used more than five times. In addition, 39.1% of patients with LH had unexplained hypoglycemia and 49.1% had glycemic variability compared to only 5.9% and 6.5%, respectively. [7]. In Jordan, a study including 1090 patients with type 2 diabetes conducted between October 2011 and January 2012 found a prevalence of 37.3%[16]. LH was significantly associated with the duration of diabetes, needle length, duration of insulin therapy, lack of systematic rotation of insulin injection sites and poor glycemic control. A lower prevalence was described by Hauner *et al*[17] at 3.6% and

Kasha *et al*[18] at 14.5%. The lack of site rotation was the factor associated with LH in other studies[17,18,19].

In the Maghreb too, and more precisely in Tunisia, the prevalence of LD was 62%. The factors found are also the non-rotation of sites, the duration of insulin therapy, and the use of needles more than 4 times[20].

Risk Factors for Lipodystrophies

The Duration of Insulin therapy

In Jordan, the study including 1090 patients with type 2 diabetes found that LH was significantly associated with the duration of diabetes and the duration of insulin therapy.

The duration of diabetes was found as well as a factor of risk of LD in the Maghreb too, and more precisely in Tunisia. [20].

In our study, the presence of lipodystrophy was correlated with the duration of insulin therapy ($p=0.002$).

The Reuse of needles

In the Spanish study [7], including 430 patients. There was a strong relationship between the presence of LD and needle reuse. The risk increases considerably when needles were used more than five times.

The same factor was found in the Tunisian study [20].

In our study the LD was correlated with the number of needle uses ($p=0.000000004$).

Rotation of injection sites

In Spain [7], there was a strong relationship between the presence of LD and non-rotation of sites. In Jordan and Tunisia [16, 20], LD was significantly associated with the lack of systematic rotation of insulin injection sites. In our study the lack of rotation of injection sites was correlated with the presence of LD (23% of patients with lipodystrophy had site rotation versus 74% rotation in patients without lipodystrophy) $p<0.000000001$

Consequences of lipodystrophies

Hypoglycemia

Glycemic variability and episodes of hypoglycemia have been reported in different studies in patients with LD[28,29,30]. The study by Blanco *et al*[7] found that the rate of unexplained repeated hypoglycemia was more than 6 times higher (39% versus 6%, respectively) and glycemic variability was 7 times higher (49% versus 7%, respectively) in the presence of LD compared to the absence of LD.

In our study, unexplained moderate hypoglycemia has been reported in 72% of patients with lipodystrophy with an average of 2 hypoglycemia per week versus 30% in patients without lipodystrophy with $p<0.000000001$.

Hyperglycemia

In Jordan [16], LD was significantly associated poor glycemic control. In our study, the LD was correlated with HbA1c > 10% (44% of patients with LD had HbA1c >10% vs 36% of patients without LD: $p=0.014$)

Patient Injection Techniques

Concerning injection techniques. In our patients, the injection fold was performed in 43% of patients and released in 15% of patients. Needle retention after injection was observed in 41% of patients. Rotation of injection sites as recommended by the guidelines[21, 22, 23, 24] was noted in 55% of patients. In France, and according to the international survey on self-injection technique[25], the most frequently used injection site was the abdomen (88.9%), thighs (74.6%), arms (48.8%) and buttocks (22.2%). Regular rotation of the injection site was reported by 84%, 16% of patients always reported injecting at the same site. The practice of a skin fold was reported by 44% of patients. Patients reported holding the pen needle in place after injecting insulin, less than 5 seconds for 21% of them, 5 to 10 seconds (47%), and more than 10 seconds for 32% of them[26].

Reuse of needles

Regarding the number of needle use: 3% of patients used the needle less than 4 times, 43% between 4 and 6 times, 42% between 6 and 10 times, and 11% of patients 10 times or more. The main reason given for this reuse was an economic reason. The rate of needle use was correlated with the presence of LD; 61% of patients with LD used needles more than 6 times ($p=0.0000004$), this LD was correlated with the rate of hypoglycemia ($p=0.00000001$).

In France, according to the survey, 32% of people with diabetes reuse needles 3 to 5 times, and more than one in ten (12%) reuse them more than 10 times[27].

CONCLUSION

One out of two patients has a lipodystrophy zone despite systematic education on how to respect zoning as soon as they are put on insulin.

The impact of lipodystrophy on quality of life is demonstrated in our study by the frequency of hypoglycemia. Particular attention should be paid to patients with basal bolus regimens who are not zoning, with systematic examination of the injection areas. The evaluation of education here reveals its importance.

References

1. Rapport mondial sur le diabète. World Health Organization 2016
2. B. Bauduceau, L. Bordier. Diabète de type 2: initiation de l'insulinothérapie. Diabétologie: 55 Démarches Cliniques en Pratique Médicale Courante ; 2017 : 227-235
3. F. Bosquet, A. Hartemann-Heurtier. Insulinothérapie dans le diabète de type 2. EMC - Endocrinologie 2004; 1 :155-65
4. Louis Monnier, Claude Colette. Les indications transitoires de l'insulinothérapie dans les états pathologiques intercurrents. L'insulinothérapie dans le Diabète de Type 2 De la Théorie à la Pratique. Elsevier Masson; 2014: 101-111
5. N. Kluger, S. Halimi. La tolérance de l'injection d'insuline et les réactions cutanées. Médecine des Maladies Métaboliques ; 2016 ; 10(5) : 452-455

6. C. PIÉRARD-FRANCHIMONT, T. HERMANNNS-LÊ, A.J. SCHEEN *et al.* Complications cutanées de l'insulinothérapie un problème iatrogène sur le déclin. Rev Med Liege 2005; 60 : 5-6 : 564-565
7. Blanco M, Hernandez MT, Strauss KW, *et al.* Prevalence and risk factors of lipohypertrophy in insulin-injecting patients with diabetes. Diabetes Metab. 2013;39:445-53.
8. Holstein A, Stege H, Kovacs P. Lipoatrophy associated with the use of insulin analogues: a new case associated with the use of insulin glargine and review of the literature. Expert Opin Drug Saf. 2010;9:225-31.
9. Lopez X, Castells M, Ricker A, *et al.* Human insulin analog-induced lipoatrophy. Diabetes Care. 2008;31:442-4.
10. Phua EJ, Lopez X, Ramus J *et al.* Cromolyn sodium for insulin-induced lipoatrophy: old drug, new use. Diabetes Care. 2013;36:e204-5.
11. Lamar CP; Insulogenic lipodystrophies: Their relationship to "brittle" diabetes and to insulin resistance; J Am M Assoc. 1950 Apr 29;142(17):1350-53
12. Chowdhury TA, Escudier V. Poor glycaemic control caused by insulin induced lipohypertrophy. BMJ 2003;327:383-384
13. Strauss K, Halimi S. Le tissu sous-cutané et l'insuline : une cohabitation délicate. Revue de la littérature. Médecine des maladies Métaboliques 2015;9:504-13.
14. Gentile S, Guarino G, Guida P, Stollo F, On behalf of the AMD-OSDI Italian Injection Technique Study Group. A suitable palpation technique allows to identify skin lipohypertrophic lesions in insulin-treated people with diabetes. Springer Plus. 2016;5:563.
15. S. Jacqueminet, C. Ciangura, C. Michaux *et al*; Prévalence et facteurs de risque des lipodystrophies : évaluation sur 140 patients insulinotraités suivis en consultation ; Diabetes & Metabolism 2013 ; 39(1): 58
16. Al Ajlouni M, Abujbara M, Batieha A, *et al*; Prevalence of lipohypertrophy and associated risk factors in insulin-treated patients with type 2 diabetes mellitus. Int J Endocrinol Metab. 2015 Apr 30;13(2):e20776.
17. Hauner H, Stockamp B, Haastert B. Prevalence of lipohypertrophy in insulin-treated diabetic patients and predisposing factors. Exp Clin Endocrinol Diabetes. 1996;104(2):106-10.
18. Kasha Z, Haiheydan Z, Akha O, *et al.* Prevalence of lipodystrophy associated with recombinant insulin. Mazandaran Uni Med Sci J. 2008;18:9.
19. Vardar B, Kizilci S. Incidence of lipohypertrophy in diabetic patients and a study of influencing factors. Diabetes Res Clin Pract. 2007;77(2):231-6.
20. S. Sellami, C. Jemaï, S. Chelbi, *et al*; Lipodystrophies et techniques d'injection d'insuline ; Annales d'Endocrinologie ; 2016 ; 77(4): 523
21. Société francophone du diabète (SFD) Paramédical (Coordonateur : D. Durain). Référentiels de bonnes pratiques. Surveillance glycémique et technique

- d'injection d'insuline et des analogues du GLP1. Mars 2012. Paris: SFD Paramédical.
22. Société francophone du diabète (SFD) Paramédical (Coordonateur : D. Durain). Référentiels de bonnes pratiques actualisés. Surveillance glycémique et technique d'injection d'insuline et des analogues du GLP1. Mars 2017. Paris: SFD Paramédical.
 23. Frid A, Hirsch L, Gaspar R, et al. New injection recommendations for patients with diabetes. *Diabetes Metab* 2010;36(Special issue 2):S3-18.
 24. Frid AH, Kreugel G, Grassi G, et al. New insulin delivery recommendations. *Mayo Clin Proc* 2016;91:1231-55.
 25. Frid AH, Hirsch LJ, Menchior AR, et al. Worldwide Injection Technique Questionnaire Study: injecting complications and the role of the professional. *Mayo Clin Proc* 2016;91:1224-30.
 26. J.-P. Sauvanet, S. Halimi ; Technique d'injection de l'insuline : que font les patients diabétiques en France ?; *Médecine des maladies Métaboliques* ; 2017 ; 11(5) : 406-15
 27. S. Halimi, F. Frumy ; Un problème persistant : la réutilisation des aiguilles et son lien avec les lipohypertrophies ; *Médecine des maladies Métaboliques* ; 2018 ;12 (6) : 516-19
 28. Gentile S, Agrusta M, Guarino G, , et al. Metabolic consequences of incorrect insulin administration techniques in aging subjects with diabetes. *Acta Diabetol.* 2011;48:121–5.
 29. Gentile S, Guarino G, Giancaterini A, et al. Italian injection technique study group. A suitable palpation technique allows to identify skin lipohypertrophic lesions in insulin-treated people with diabetes. 2016;5(May 5)563
 30. Heinemann L. Variability of insulin absorption and insulin action. *Diabetes Technol. Ther.* 2002;4:673–82.

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