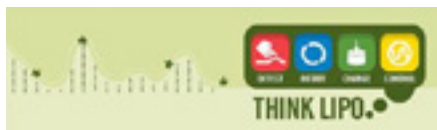


Improving control through better injections



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Summary

Lipohypertrophy (LH) has been a recognized complication of insulin therapy for many years, yet research shows that its prevalence in insulin-injecting patients with diabetes remains high. The problem for the patient is 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 glycaemic control and unpredictable hypoglycaemia. Despite the important implications of this for diabetes control in insulin-injecting patients, there is a dearth of information and completed research into the condition. Correct injection site rotation appears to be the critical factor in preventing LH, which is associated with reduced glucose variability, hypoglycaemia, insulin consumption and costs. Also the choice of the needle is a critical factor, in fact, shorter needles minimize errors of injection technique.

Riassunto

Nonostante che la lipoipertrofia sia una complicazione della terapia insulinica nota da molti anni, la ricerca mostra che la sua prevalenza nei pazienti diabetici insulino-trattati rimane alta. L'iniezione d'insulina fatta in un nodulo lipoipertrofico, anche se indolore, può portare ad assorbimento irregolare dell'insulina e, se ripetuta, può provocare uno scarso controllo glicemico, ipoglicemie imprevedibili ed ampia variabilità glicemica, con un crescente ricorso alle prestazioni mediche e a i ricoveri. La corretta rotazione del sito di iniezione, il non riutilizzo dello stesso ago, l'uso di aghi molto corti ed una corretta tecnica iniettiva sono in grado di prevenire la formazione di lipoipertofie e di ridurre dimensioni ed effetti dannosi, migliorando così il compenso glicemico, riducendo le ipoglicemie e la variabilità glicemica ed i costi.

Frequency of lipohypertrophy

Lypodystrophy means 'disorder of fat tissue'. There are two main types of Lypodystrophy: *Lypoatrophy*, which is a scarring and indentation of fat tissue and *Lipohypertrophy* (LH) which is a swelling and/or induration of fat tissue⁽¹⁾.

LH is common although studies vary on the exact frequency. These are the prevalence rates of LH amongst insulin injecting patients with DM in five recent studies, from lowest to highest: 14.5% (Hajheydari, 2008);

27.1% (Raile, 2001); 34.5% (Partanen, 2000); 48.0% (Kordonuri, 2002); 64% (Blanco, 2013)⁽²⁻⁶⁾.

Vardar⁽⁷⁾ found that the incidence of LH at insulin injections sites was 48.8% in 215 Turkish patients who had been using insulin for at least 2 years; Seyoum⁽⁸⁾ found LH in 31% of 100 insulin injectors in Ethiopia; and Hauner⁽⁹⁾ reported that 28.7% of the 233 German patients studied with type 1 diabetes had the condition.

In the 2010 Injection Technique Questionnaire (ITQ) Survey⁽¹⁰⁾ 48% of the over 4200 patients insulin answered yes to the following question, 'Have you ever noticed swelling of fatty tissue or small bumps at your injection sites?' The percentages in all 16 countries surveyed were all in double digits and ranged from 30 to 88%. In Italy the percentage of LH was 44%. A number of earlier surveys^(4, 11-13) have shown similar findings.

Vardar⁽⁷⁾ also identified, by logistic regression analysis, three independent risk factors for LH: Duration of insulin use, with longer use associated with more LH ($p = 0.001$); Site rotation, with a failure to rotate associated with higher LH risk ($p=0.004$); Changing needles, with needle reuse also associated with LH ($p = 0.004$). Two other studies^(6,14) have identified the same factors.

Almost all studies of patients injecting into LH⁽¹⁵⁻¹⁸⁾ show insulin absorption to be delayed or erratic, potentially worsening diabetes management.

Impact of LH

The impact of LH on insulin PK-PD is rather poorly documented in the literature. While there are case reports indicating reductions in insulin consumption with improvements in HbA1c when patients with LH were taught to inject into normal areas, and a small N of studies that evaluated insulin PK-PD when patients have been injected into areas of LH vs normal areas, the overall quality of such studies is poor. It is assumed that LH reduces and/or slows insulin uptake, and perhaps increases PK-PD variation, but it is by no means proven rigorously.

Franzen⁽¹⁹⁾ evaluated children with diabetes injecting into clinically detectable LH. The children received simple but direct instructions: Rotate injection sites; and Don't reuse your needles. In 3 months 90% of LH had resolved. HbA1c was improved significantly and insulin requirements had decreased.

A recent Spanish study on Prevalence and Risk Factors of Lipohypertrophy in Insulin - Injecting Patients with Diabetes⁽⁶⁾ showed that LH is extremely common, present in 2/3 of diabetic (>50% DM2 and >70% DM1) and is strongly associated with both incorrect rotation of sites of injection and with reuse of needles, especially > 5 times. Unexplained hypoglycemia and glycemic variability were also greatly increased in those with, Vs those without LH. A critical finding of this study is the correlation of total daily dose (TDD) of insulin to the presence of LH and its cost to the health care system. Subjects with LH had significantly higher TDD, overall and in both DM1 and DM2 groups. DM2 patients had the highest TDD differences. Such patients tend to have increased weight and insulin resistance compared to DM1 patients, and these factors

probably contributed to their greater TDD – however, the T2DM patients with LH had similar weight and BMI as the T2DMs without LH. Another major contributor is the practice of injecting into LH where the absorption properties of insulin are distorted. The cost of the additional insulin consumed by injecting into LH was calculated to be over 122 million euros in Spain. This is an obvious opportunity for savings to both patients and health care payers.

Injection technique and blood glucose control

We know that injecting properly is just as important as choosing the right dose of insulin. But until recently we knew nothing about the impact of injection training on glucose control and the consumption of insulin. But in a study 346 patients with diabetes from 18 ambulatory centers throughout northern Italy⁽²⁰⁾ who had been injecting insulin \geq four years we now have answers. Patients were given a questionnaire about their IT and then nurse then examined the patient's injection sites for the presence of LH, followed by an individualized training session in which sub-optimal IT practices highlighted in the questionnaire were addressed. All patients were taught to rotate sites correctly to avoid LH and were begun on 4 mm pen needles to avoid intramuscular (IM) injections. They were instructed not to reuse needles. Results showed that 49% of patients were found to have LH at study entry. After three months, patients had mean reductions in HbA1c of 0.58%, in fasting blood glucose of 14 mg/dL and in total daily insulin dose of 2.0 IU, all statistically significant with $p < 0.05$ (Table 1). Follow-up questionnaires showed significant numbers of patients recognized the importance of IT and were performing their injections more correctly. The majority found the 4 mm pen needle convenient and comfortable. This is the first published study to show improved glucose control (both by HbA1c and blood glucose values) from improving injection technique (IT), including switching all patients to 4 mm pen needles.

Table 1. Parameters under study and 3-month follow-up⁽²⁰⁾.

Clinical parameter	n.	Mean	Δ
HbA1c at entry	346	8.49	
HbA1c at 3 months	259	7.91	-0.58*
FBG (mg/dL) at entry	249	186.7	
FBG (mg/dL) at 3 months	182	172.5	-14.2*
TDD (IU) insulin at entry	326	50.5	
TDD (IU) insulin at 3 months	256	48.5	-2.0*
BMI at entry	304	28.2	
BMI at 3 months	235	27.7	-0.5*

* $p < 0.05$

The implications of this study are striking. Patients and professionals do not have to wait for months and years to see improvements in the most important clinical parameters when appropriate IT training and devices are provided. These improvements can be expected

early enough in the course of insulin therapy to provide motivation for continuous improvement.

TEST FOR LECTURE

Please choose the ONE BEST answer.

- A. Which of the following is an INCORRECT definition:**
1. *Lypoatrophy* means scarring and indention of fat tissue
 2. *Lypohypertrophy* means swelling and induration (hard or rubbery texture) of fat tissue
 3. *Lipodystrophy* means the absence of abnormality in fat tissue
 4. *Lypodystrophy* is a generic term and means 'disorder of fat tissue'
- B. What percentage of patients who inject say they've had swelling or nodules at injection sites?**
1. 100%
 2. Approximately 50%
 3. Approximately 5%
 4. <1%
- C. When Lipohypertrophy has been evaluated under a microscope what features are seen:**
1. Fat in Lipohypertrophy invades the dermis
 2. Fat cells in Lipohypertrophy are twice as large as normal fat cells
 3. Fat cells in Lipohypertrophy contain lipid droplets
 4. All of the above
- D. What factors have been associated with the presence of Lipohypertrophy?**
1. Long duration of insulin use
 2. Failure to appropriately rotate injection sites
 3. Extensive reuse of needles
 4. All of the above
- E. Needle reuse is a:**
1. Proven cause of Lypohypertrophy
 2. Potential facilitator of Lypohypertrophy
 3. Associated with Lypohypertrophy but may or may not be related to the disorder
 4. Both 2 and 3 above

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particular attention to these vital signs and that improving the practice of injecting is a cost-effective method for optimizing the benefits from injected insulin.

We hope that the conclusions of this symposium are able to stimulate a renewed interest of all professionals involved in diabetes care to the insulin injection techniques, because this issue now seems forgotten or uninteresting.

Riassunto

L'efficacia della terapia insulinica nel diabete dipende molto da una corretta tecnica iniettiva, per cui è necessario insegnare come attuare una corretta tecnica iniettiva ed una costante rotazione dei siti di iniezione per prevenire lesioni lipodistrofiche della pelle, che a loro volta impediscono un ottimale assorbimento dell'insulina. L'ispezione dei siti di iniezione non solo permette di scoprire e trattare lesioni lipodistrofiche, ma rappresenta un importante messaggio educativo. Ci auguriamo che le conclusioni di questo convegno siano in grado di stimolare un rinnovato interesse di tutti i professionisti coinvolti nella cura del diabete per le tecniche di iniezione dell'insulina, perché questo tema sembra quasi dimenticato o ritenuto poco interessante da medici e infermieri.

Introduction

The subcutaneous injection was introduced 1853 by Dr Alexander Woods in Edinburgh⁽¹⁾. The idea of injecting a substance into the subcutaneous space to be absorbed and having a general effect on the body is thus a rather new idea in medicine. It is fair to conclude that the subcutaneous injection using a syringe and needle will continue to be the most widely used method for administering insulin for many years to come. Since this is the interface between the drug and the effects on the body a few facts need to be considered regarding where and how to inject insulin.

Questions to be answered

1. In what tissue should insulin be injected?
2. What technique should be used to ensure injection in that tissue?
3. Are there differences in absorption of insulin from different tissues and areas on the body?
4. Do modern insulin analogues differ from older human insulins?
5. How thick is the skin, i.e. how short can a needle be?

The answer to the first question is non-controversial. There is a general consensus that insulin in general treatment should be deposited in the subcutaneous fat tissue. Some additional reasons for that will be given below but one important issue is that the muscle is much more sensitive than the fat tissue, especially to pressure. There are many published cases of muscle damage following intramuscular injections. Once we have chosen the fat as the preferred tissue for insulin injection we need to establish a few facts about fat tissue depth.

Insulin injections, what do we know so far?



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Summary

The effectiveness of insulin therapy in diabetes depends on a proper injection technique whereby must be provided to patients adequate guidance in this field. It is necessary to teach patients to implement always a correct rotation of the injection sites to prevent the formation of lipohypertrophy, which prevent optimal absorption of insulin. Inspecting the site not only allows to discover and treat these conditions, but sends an important message to the people injecting that they should pay