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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 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.

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Fat distribution on the human body

The subcutaneous fat distribution on the human body obviously shows an enormous variation. There are also sex differences influenced by the sex hormones, women having more fat on thighs and buttocks and men having their fat more centrally distributed. One need to remember though that we treat individuals, not statistical means. Our general advise regarding injections need to be right for at least 95% of the population, i e also for our patients right at the end of the normal distribution curve. In papers published from 1986 and onwards[2-4] it has been shown that fat tissue can be very thin in locations commonly used for insulin injections. From published studies and personal experience from many CT scans, MRI´s and ultrasound measurements a few facts regarding fat distribution in adults can be established. I use the available needle lengths as points of reference. Please note that the following should be regarded as observations, not population-based evidence.

1. *Women.* Many have less than 8 mm (1/3 inch) of fat tissue laterally in the thigh. A few have less than 5 mm (1/5 inch) of fat tissue laterally in the abdomen. All have more than 12 mm (1/2 inch) of fat in the upper gluteal area.
2. *Men.* A majority have less than 5 mm (1/5 inch) of fat tissue laterally in the thigh. Many have less than 5 mm (1/5 inch) laterally in the abdomen. All have more than 12 mm (1/2 inch) in the upper gluteal area.

Insulin absorption from different tissues and areas on the body

It is well established that soluble human insulin (Actrapid for example) is absorbed slower from the thigh compared to abdomen and also that the absorption is faster from the muscle tissue compared to fat tissue[2]. The same is true for NPH insulin[5, 6]. This has led to the commonly used recommendations to inject rapid-acting soluble human insulin in the abdomen and NPH insulin in the thigh or the buttock although there is a lack of studies regarding insulin absorption from the gluteal area.

What about the modern insulin analogues? The absorption of insulin aspart (NovoRapid) is as fast from the thigh as it is from the abdomen[7] although the peak is somewhat lower and the duration of effect slightly longer in the thigh. The same is also true for the other rapid-acting insulin analogues. When it comes to differences between fat and muscle tissue it has been shown that there is no statistical difference in absorption of insulin aspart between these tissues[8], in contrast to studies of human soluble insulin where there is a much faster absorption from the muscle tissue. One should remember though that the studies of insulin analogues have only been made in resting conditions. In a working muscle the blood flow is increases at least 10-fold and this can potentially influence the absorption.

Regarding the long-acting insulin analogues Owens et al[9] found that the absorption of insulin glargine (Lantus) was absorbed somewhat slower from the abdomen compared to thigh in 12 healthy volunteers. The difference was not statistically significant but is interesting all the same since this is the first time an insulin is shown to be absorbed slower from the abdomen compared to thigh. There is no available data regarding insulin glargine and absorption from fat vs muscle tissue but there is a published case report of rapid hypoglycemia following accidental intramuscular injection of insulin glargine[10]. This shows that old knowledge regarding insulin absorption needs to be reassessed when using the new insulin analogues. Each new insulin seem to have different characteristics, they all need to be evaluated separately!

Practical guidelines for insulin therapy

The distance from skin surface to muscle may be less than 4 mm (1/5 inch), currently the length of the shortest available injection needle on the market, in both abdomen and thigh in some patients. This means that even if our general rule is to inject without a pinched skinfold in the abdomen and in the thigh when using the shortest needles some patients will still have to pinch a skinfold. In the gluteal area no skinfold is needed since the fat tissue depth is always more than 12 mm, currently the length of the longest available needle for insulin injection.

These facts also need to be considered when designing infusion systems for insulin pumps, devices for fixed-depth injections etc.

Since skin thickness at the injection sites is 3.5 mm at the most[11] injection needles do not need to be much longer than that. 4 6 mm may very well be our standard needles in all patients, leakage of insulin doesn't appear to be a problem[12].

For traditional human insulins the rapid-acting insulins should be injected in the abdominal area to have as fast absorption as possible. NPH insulin should be injected in the thigh (or gluteal area) for a slower absorption.

For insulin glargine the choice is wider. Since, in most patients, the effect has a longer duration than 24 hours, the small differences in absorption between thigh and abdomen probably is clinically insignificant, all areas can be used. It can be noted though that, in the few patients with clinical evidence of effect duration less than 24 hours, injection in the abdomen may be tried for longest possible absorption time.

For insulin Levemir there is circumstantial evidence that the absorption is faster from the abdomen making thigh and buttock the preferred sites if longest possible action is needed.

For both glargine and detemir it seems clear that intramuscular injection will lead to rapid absorption and risk of hypoglycaemia making injection technique and needle length extremely important in order to avoid intramuscular injection.

Rapid-acting insulin analogues can be injected in abdomen, thigh or gluteal area, although the peak may be

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somewhat lower from the thigh. The consequences of accidental intramuscular injection of these insulins also seems much less dramatic than for other insulins, the rate of absorption being almost the same from muscle compared to fat tissue, at least during resting conditions.

It seems like a few simple facts can be established regarding fat tissue depth, insulin injection technique and insulin absorption in humans and these facts need to be considered when designing our insulin therapy.

What insulins and what injection sites?

- All insulins should normally be given subcutaneous (sc)
- Soluble human insulins in the abdominal area
- NPH-insulins in the thigh or gluteal area
- Rapid-acting insulin analogs in the abdomen, may be given elsewere
- Insulin glargine in abdomen, thigh, or gluteal area (no studies), strictly sc
- Insulin Detemir in the thigh (or gluteal area, no studies), strictly sc
- Premix insulins abdominal area in the morning; thigh or gluteal area in the afternoon/evening

Absorption of rapid-acting insulin analogs

- No statistically significant difference between abdomen and thigh in time-to-peak
- Peak is somewhat lower and effect more protracted in thigh
- No statistically significant difference in insulin absorption between fat and muscle tissue; however, only studied in resting muscle
- There is a 100-fold increase in blood flow in the working muscle!
- International consensus is still to recommend subcutaneous (sc), i e, intralipomatous injection

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Il ruolo educativo del team diabetologico

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Keywords: Therapeutic Education, Team, Continuity of care

*La cura del paziente diabetico riconosce nella terapia educativa l'elemento indispensabile per un trattamento realmente efficace**

*Esiste l'evidenza scientifica che si può prevenire e curare meglio la malattia con l'educazione***

Riassunto

Accettare la malattia cronica, abbandonando l'idea della completa guarigione, è la grande sfida che devono raccogliere non solo i pazienti, ma anche gli operatori sanitari che affiancano pazienti e care-givers nei percorsi di assistenza e di cura.

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