AMD-OSDI Consensus on Injection Techniques for People with Diabetes Mellitus

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Received date: September 01, 2016; Accepted date: September 19, 2016; Published date: September 26, 2016

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Citation: Gentile S, Grassi G, Armentano V, et al. AMD-OSDI Consensus on Injection Techniques for People with Diabetes Mellitus. Med Clin Rev. 2016, 2:3.

Abstract

It goes without saying that all people with diabetes should be taught the best injection technique before starting insulin treatment. Nevertheless the extremely high rate of local injection-related skin reactions—i.e., lipodystrophic lesions—described in literature, proves otherwise.

We are hereby presenting a Consensus Document on Injecting Techniques which highlights 18 key points based on a thorough analysis of the available literature and ranked by "Level of evidence" and "Strength of recommendation" according to our National Guideline System.

It is meant at providing all professionals involved in diabetes care with a practical guide on how to help patients on insulin perform well.

Keywords: Insulin injections; Diabetes mellitus; Recommendations; Lipohypertrophy
Conflicts of Interest:

None

Abbreviations:

AMD: Association of Clinical Diabetologists; OSDI: Italian Diabetes Healthcare Professionals; MD: Medical Doctor; Prof: Professor; HN: Head Nurse

Was a Consensus Document on Injecting Techniques really needed?

According to data from ISTAT (National Institute of Statistic) 2011 report [1] about 3 million people with diabetes mellitus (DM) are living in Italy nowadays, mostly in the South of our country, with a 5.1% prevalence of type 1 DM (T1DM). ARNO 2011 report, on the other side, witnessed in favour of a 10-year lasting ever increasing utilization of newer insulin preparations endowed with a more physiological pharmacokinetics profile, such as rapid-acting and basal analogues, as well as, of innovative therapeutic regimes [2]. In spite of technological progresses, and a general improvement in the quality of care, the 2012 AMD Annals [3] reported that only 22.2% T1DM and 43.8% T2DM patients reached HbA1c levels below 7% (53 mmol/mol), and T2DM patients above 9% (75 mmol/mol) accounted for 25.7% monitored people.

Many factors related to insulin administration, storage and handling might contribute to poor metabolic control. Therefore, a major goal of health care teams is to educate patients and caregivers to the best possible injectable drug administration techniques and the most skilful utilization of related available devices.

In order to let them reach that goal, we collected all available scientific evidences on this issue and organised it according to well-defined hierarchically distributed criteria targeted at patient’s self-management/empowerment [4], and based on National Guideline System [5] with structured education on top. Our Consensus Document on Injecting Techniques represents in fact the final result of this strong clinical effort.

Recommendations concerning injectable drug administration

A correct injection technique is essential for insulin and other subcutaneously administered medications to ensure optimal effects in people with diabetes mellitus (DM). It implies the ability to (i) choose the best needles, (ii) rotate injection sites regularly, (iii) handle and store insulin appropriately, (iv) insert needles correctly into the skin, (v) let pen needles inside the skin long enough to get the whole dose be absorbed and (vi) manipulate the skin before and after injection (Table 1) (Level of evidence III, Strength of recommendation B).

Insulin must be injected into intact subcutaneous tissue and intramuscular shots have to be avoided, which would result into fast absorption and consequent risk of hypoglycaemia (Level of evidence II, Strength of recommendation B).

Insulin effects are not affected by injection depth, provided the latter falls within the subcutaneous tissue (Level of evidence V, Strength of recommendation B).

Injection site rotation within large surfaces, needle disposal after each shot and pinch technique utilization at a 45° angle with respect to the skin whenever needles longer than 6 mm are chosen are essential factors to ensure optimal insulin absorption and prevent skin injury (Level of evidence II, Strength of recommendation A).

An effective rotation scheme consists of dividing injection site into quadrants and regularly spacing shots 1-2 cm apart from one another within each quadrant in order to avoid causing repeated traumas to the same site (Level of evidence I, Strength of recommendation A).

Rapid acting insulin analogues can be injected anywhere as their absorption is not site-dependent. On the opposite, regular human insulin is preferentially injected into the abdomen where absorption is faster and rather stable (Level of evidence I, Strength of recommendation A).

Areas of lipodystrophy can occur as a consequence of missed injection site rotation and needle reuse, especially when certain insulin preparations are chosen (Level of evidence III, Strength of recommendation B).

The choice of needle length (for either pens or syringes) is crucial to ensure optimal insulin absorption (Level of evidence III, Strength of recommendation B).

Injections performed with shorter and thinner needles cause less pain and discomfort and ensure better therapy acceptance and adherence (Level of evidence II, Strength of recommendation A).

Injection with a pen and the use of shorter and thinner needles ensure optimal insulin absorption in thin patients and children. This approach does not require the pinch (or skinfold) technique to be used and is therefore easier to follow and to teach. It also causes less fear and pain, thus ensuring better therapy acceptance and adherence (Level of evidence II, Strength of recommendation A).

When injected into lipodystrophic areas, insulin gets altered in terms of pharmacokinetics and pharmacodynamics, which causes variable and unpredictable absorption and affects glycaemic control (Level of evidence II, Strength of recommendation B).

When moving from a lipodystrophic area to a healthy zone, insulin dosage should be reduced because of expected improved absorption. Per cent reduction varies from person to person and should be guided by intensified self-monitoring blood glucose (Level of evidence II, Strength of recommendation A).

All patients should be provided with appropriate education and training sessions by the diabetes care team before starting
any treatment regimens based on drug injections (Level of evidence II, Strength of recommendation A).

Inspection and palpation of injection sites should be carried out systematically in all patients on subcutaneous therapy and education concerning proper injection techniques and injection site self-palpation should be systematically reinforced (Level of evidence II, Strength of recommendation A).

In the hospital pen needles and syringes have to comply with safety criteria to minimize any risks of accidental injuries and to keep health care providers, patients and relatives far from any hazards during all utilization phases including disposal (Level of evidence II, Strength of recommendation B).

Home utilization of safety needles and syringes should be made available also to special populations like AIDS, HBV or HCV infected patients (Level of evidence II, Strength of recommendation B).

According to safety rules aimed at minimizing the risk for any infection transfer among patients, each insulin pen should be utilized in the hospital for a single individual only (Level of evidence II, Strength of recommendation B).

Insulin storage should comply anywhere with approved producer’s leaflet. This should also be the object of careful patient education (Level of evidence II, Strength of recommendation B).

Table 1: Levels of scientific evidence and the strength of recommendations as classified according to our National Guideline System (5).

| Levels of Evidence | Strength of Recommendations |
|--------------------|-----------------------------|
| I                  | A The procedure or diagnostic test is strongly recommended. The recommendation is supported by high quality scientific evidence (not necessarily type I or II) |
| II                 | B There are still doubts concerning whether or not the procedure or intervention should always be recommended, but it is believed that it should be carefully considered |
| III                | C Whether or not to recommend the procedure or intervention is still a matter of debate |
| IV                 | D The procedure is not recommended |
| V                  | E The procedure is strongly discouraged |
| VI                 | - |

Comments

In order to ensure that injected insulin profile keeps in line with expected pharmacokinetics and pharmacodynamics, thus yielding predictable biological effects, it is necessary to perform a correct injection technique [6-9] as avoidable errors might modify insulin action [10,11]. Since they have to deal with a daily treatment, patients with DM are at risk for progressively increasing careless and incorrect habits which in turn are expected to increase glycaemic variability over time [10].

To get optimal absorption, insulin must be injected into the subcutaneous tissue, not into the dermis or into the muscle. That’s why the choice of needle length is crucial. The latter is greater with syringes than with pens and therefore, when allowed to, people with DM choose pens. Nevertheless, it has been proven that, when a proper injection protocol is followed, both effectiveness and safety of the two devices are identical, allowing comparable metabolic control and complication risk [12,13].

Thin adult and children skin displays an average thickness of 2.23 mm in the arms, 1.87 mm in the thighs, 2.15 mm in the abdomen and 2.41 mm in the buttocks, both in [14-16]. As accidental intramuscular shots might cause hypoglycaemia [16-20], it is necessary to inject insulin beyond 2.5 mm without getting into the muscle. This is possible with short (4 mm) needles, which reduce the risk of intramuscular injection and do not increase insulin backflow even when inserted at 90° without pinching the skin [17-23]. The use of a 4 mm needle is suitable for adults, irrespective of BMI [10], as well as for children and adolescents [18,19,24] but the pinch technique may still be required in very thin subjects [23]. In the transition from a longer needle to a shorter one, there might be differences in insulin absorption, therefore monitoring blood
glucose levels is recommended under these circumstances [24,25].

Subcutaneous tissue thickness varies significantly depending on sex, body mass index, age, ethnicity, diabetes type, morphology of the diabetic individual, as well as, on pressure exerted during injection [8,11,14]. The risk of intramuscular injections depends on that and has been estimated to be 15.3% with 8 mm, 5.7% with 6 mm and 0.4% with 4 mm needles [14,26-28].

Injection site rotation within large surfaces, needle disposal after each shot and 45° angle pinch technique utilization with needles >6 mm are essential factors to ensure optimal insulin absorption and prevent skin injury [11,15,22,29-34].

With the advent of insulin analogues, absorption varies much less both between and within individuals and is therefore more predictable and easier to handle by the patient [30]. However, despite technological advances allowing newer and newer insulin analogue availability, certain absorption/ action affecting factors still remain, such as exercise, counter-regulatory hormones, high dosage, incorrectly mixed preparations or even the habit to pull out needles from the skin too early after pen needles reaching their end stroke positions [29,30]. Another example of how the injection technique may affect insulin pharmacokinetics is given by glargine [31]: Its long acting effect is based on its ability to precipitate within the subcutaneous tissue at pH 7, and cannot be exploited in case of intramuscular injections, which thus cause unexpected hypoglycaemic episodes [30].

Insulin absorption does not vary as a function of how deep it reaches into the subcutaneous tissue. However, the use of the same anatomical region for shots performed at the same time of day and the choice of abdomen before meals [24] are recommended only for different types of human insulin preparation [6-8], which also of course require to regularly inject the drug at a distance of about 2 cm from previous shots within each region in order to avoid repeated traumas.

So, to summarize all the above, the choice of delivery devices and needle length has been proven to affect insulin absorption and, independently of using pens or syringes, the needle influences correct techniques the most. Nowadays insulin syringes with needles less than 8 mm are not available in our country and their use without pinching the skin and injecting at a 45° angle increases the risk of intramuscular injections. Therefore we suggest using pens with short needles (4 mm) just to minimise the risk of intramuscular injections. Also needle gauge (G) and sharpness are important factors in terms of patient acceptance and satisfaction [32-35]. 4 mm × 32G needles provide both obese and non-obese patients with comparable degrees of metabolic control as 5 mm × 31G and 8 mm × 31G needles but are perceived as less painful and better accepted [34,36-39].

Injecting insulin by shorter and thinner pen needles (4 mm and 32G) with triple bevels, in compliance with the UNI EN ISO 7864 standards, cause less pain and discomfort [14,36,39-40] and ensure better therapy acceptance and adherence. In fact, the greater the outer diameter, the greater the resistance the needle has to face to penetrate the skin and, vice versa, the smaller the outer diameter, the less the feeling of discomfort at injection.

One of the most common complications of such treatment is the development of cutaneous lipodystrophy, also described with continuous insulin infusion systems [41-43]. Its exact aetiology is not entirely clear yet, although several causative factors are implicated, such as repeated traumas into very limited areas, needle re-use, insulin per se as a growth factor, especially at a high doses, and old protaminated/human insulin [22,44]. The risk of lipohypertrophy is 31% higher in subjects using the same needle several times than in the others [11].

Lipodystrophies are widespread. Vardar and Kızılçığ [45] reported a prevalence of 48.8% in 215 Turkish patients treated with insulin for at least two years; according to Hauner et al. [46], in 233 German patients with DMT1 the prevalence was 28.7%. More recently, Blanco et al. [11] documented lipodystrophy in as many as 64.4% investigated patients, with a strong relationship to incorrect site rotation habits. In addition, 39.1% patients with lipohypertrophy showed unexplained hypoglycaemia and 49.1% had high glycaemic variability. Several studies show that insulin absorption from lipodystrophic areas can be delayed or become unpredictable [47-50], thus representing a potential factor of worsening glycaemic control [50-58], while the use of very short needles is preferred by patients [35,37,38] and is less traumatic per se [39,42].

Education

Insulin therapy is a long-lasting patient commitment day after day putting them at risk for more and more careless and incorrect habits in the absence of any proper and consistent educational support. As a consequence of that glycaemic variability and poor metabolic control are expected to increase [10].

Appropriate education on injection techniques is obviously essential, nevertheless it is often lacking [4], as shown by the high rate of skin lesions caused by incorrect injecting habits [11,36,38-50].

Diabetes care teams must promote patient empowerment to let people understand what is best for them day by day. In particular, insulin self-administration requires specific skills to be acquired to perform injections correctly.

Patients need to understand the close relationship between injection technique and metabolic control [59], as well as, changes in pharmacokinetics expected to occur with incorrect injection techniques and consequent increased risk of chronic complication onset/acceleration [10,11,14,15].

All patients starting injections should be accurately educated on proper techniques [23,32,54-56]. Education should also be regularly reinforced and healthcare professionals are expected to perform inspection and palpation interested sites on a regular, systematic basis in all subjects on injection therapy [26,36,48,54,58,60-62] and
especially in those facing repeated unexplained hypoglycaemic episodes [11]. Education should not be limited to treatment start, it should rather go on throughout the whole follow-up period with timely reinforcements [63], put special emphasis on the negative effects of getting into the muscle tissue or into altered skin areas.

People with diabetes should also learn that self-monitoring blood glucose has to be intensified when moving from longer to shorter needles and/or from healthy to altered skin areas [8,11,50,51].

An appendix on insulin appears in an attachment in “AMD Algorithms Online - The personalisation of therapy in type 2 diabetes” and can be consulted on the AMD website: at http://www.aemmedi.it/pages/linee-guida_e_raccomandazioni/.

Training of healthcare providers

Diabetes teams should follow systematically the simple procedure for the diagnosis of lipohypertrophy reported in a previous paper from our group and try to get it further implemented and progressively refined in large scale studies.

Briefly it can be summarized as follows: The health care professional should (i) inspect each interested area first, using direct and tangential light against a dark background; (ii) touch the skin at the beginning and progressively increase finger pressure thereafter; (iii) fine-tune palpation by performing slow circular and vertical fingertip movements followed by repeated horizontal attempts on the same spot; and (iv) perform the pinch maneuver when perceiving a harder skin by comparing suspected spot to surrounding areas in terms of thickness.

This would have a major impact on education not only in terms of correct injection technique per se but also to allow patients to identify lipodystrophic areas themselves early and easily enough to avoid them and thus prevent poor metabolic outcomes [58-64].

Summary and future outlook

To summarize all of the above, in insulin-treated patients a number of actions have to be implemented to minimize the risk of lipodystrophy due to incorrect injection techniques, which are hereby listed in the shape of a set of personalized practical hints:

- For insulin pen users:
  1. 4 mm/32G needles should be preferred regardless of BMI, age, sex, and race;
  2. The pinching technique should be used in extremely thin patients or in young children;
  3. Needles should be changed at each injection, “one needle, one injection”;
  4. Each injection should always be made at least 2 cm apart from the previous one;
  5. Injection sites should be constantly rotated within and among different locations (arms, thighs, abdomen, buttocks).
- For insulin syringe users:
  1. The shortest available needles should be chosen (currently 8 mm);
  2. The pinching technique should always be used at each site;
  3. Points 3, 4, and 5, for pens users also apply to syringe users.
- For CSII users:
  1. Shorter needles are mostly preferred;
  2. Needle insertion at 45° angle is also preferred;
  3. Each needle should not be kept there longer than three days;
  4. Points 4, and 5, for pens users also apply to CSII users.
- For any patients using any devices:
  1. It is essential to start structured education before starting insulin and have patients attend periodic follow-up refresher courses;
  2. Health care providers should make patients understand the need for proper injection techniques;
  3. Patients should learn how to perform careful skin self-examination prior to each injection systematically in order to skip any lipodystrophic area.

For the future we envisage the following actions to be taken:

- Unmeet needs
  1. EBM indications on proper injection techniques should be included in all guidelines when it comes to insulin therapy;
  2. Further studies are needed to define the best possible educational follow-up strategies;
  3. Further studies are warranted to define the risk of local injection-related side effects for all other injecting drugs meant for diabetes treatment.

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