Expert Opinion

Insulin administration: selecting the appropriate needle and individualizing the injection technique

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Introduction: Patients with diabetes who receive insulin therapy often fail to meet their targets for metabolic control with insulin injections. Their inadequate glycemic control may be related to incorrect injection procedure.
Areas covered: This review examines the latest data related to insulin injection and needle characteristics, which play an integral role in patient satisfaction. Searches of Medline and Cumulative Index to Nursing and Allied Health Literature databases were conducted. Results show that optimal insulin injection can facilitate glycemic control in pediatric and adult patients. In general, needles shorter than 8 mm are appropriate for normal weight, obese pediatric and adult patients. However, body mass index, gender, race, age and injection site can influence the depth of subcutaneous tissue and thus, the desired needle size and injection technique. Although the abdomen, thighs and buttocks are all recommended injection sites, abdominal injections disperse insulin slightly more rapidly than thigh injections.
Expert opinion: Wider acceptance of needles shorter than 6 mm will occur with more evidence of their safety and efficacy, particularly in children. Development of shorter and thinner needles to make injections even easier and less burdensome may be expected in the future.

Keywords: diabetes, guidelines, injection technique, insulin, lipohypertrophy

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1. Introduction

Insulin injections are commonly used in the treatment of diabetes. For optimal glycemic control and reduction in the incidence of long-term microvascular complications, patients with type 1 diabetes are advised to follow an intensive insulin regimen administered by three or more injections or continuous subcutaneous (s.c.) insulin infusion daily, while patients with type 2 diabetes may require multiple doses of daily insulin injections [1,2]. Despite wide acceptance of the benefits of intensive insulin therapy, a large percentage of patients with diabetes fail to achieve their target hemoglobin A_{1c} (HbA_{1c}) treatment goals [3,4]. In the US, it is estimated that ~ 40% of patients with diabetes do not have adequate glycemic control [5].

Lack of knowledge of correct injection procedures is common among patients with diabetes [6-8] and may contribute to inadequate glycemic control [8-10]. A 2008 – 2009 survey by De Coninck *et al.* [11] of 4352 patients with type 1 or 2 diabetes in 16 countries discovered that patients reported receiving varying degrees of education on 14 injection topics, which included site of injection, depth of injection, making a skin fold, duration of injection, rotating the injection site and using a needle once. For only one of these topics, site of injection, did 80% or more of patients in all countries claim that they received training. For all other topics, there were fewer patients who reported that they received training [11]. In a study of

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Article highlights.

- Many patients with diabetes receiving insulin therapy lack knowledge of correct injection procedures, which may contribute to inadequate glycemic control.
- Selecting the optimal needle and instructing the patient in correct injection technique are important factors for reducing pain and fear associated with insulin injection.
- Patients show a preference for needles shorter than 8 mm with a small diameter designed with thin wall technology.
- The depth of subcutaneous (s.c.) tissue varies by body mass index, gender, race, age and injection site.
- The correct injection technique – angled or vertical insertion into a skin fold or flat skin – depends on the depth of s.c. tissue at the chosen injection site of the individual patient and the length of the needle being used.

This box summarizes key points contained in the article.

100 patients with type 1 or 2 diabetes injecting insulin regularly, 53 cases of local complications, such as skin hyperpigmentation and lipohypertrophy, were detected and attributed to poor injection technique [6]. Such complications due to improper insulin injection may impair patient adherence to their treatment and interfere with insulin absorption [6]. An incorrect choice of injection site combined with improper technique can increase the risk of hyperglycemia or nocturnal hypoglycemia [8]. Improper technique may also cause pain, causing patients to skip injections [12]. Optimal insulin injection is based on selecting an appropriate needle; identifying the appropriate injection site, which is determined by the type of insulin being used; and using the most suitable injection technique. Studies show that the correct injection technique can minimize perceived pain and improve glycemic control by maximizing insulin absorption [8,13].

The lack of patient knowledge about optimal injection technique may stem from inadequate training [11,12]. As shown by Strauss *et al.* [8], in a study of 1002 patient with diabetes, 70% of patients indicated a need for more information on correct injection procedure. The survey results of De Coninck *et al.* also indicated the general lack of education patients received about injection technique [11]. Attempts to improve education of people with diabetes about management of their condition, including HbA_{1c} target and injection technique, have been shown to improve glycemic control [14-17].

A barrier to educating patients with diabetes about proper injection technique may be the disparate nature of the scientific evidence supporting conventional recommendations. As demonstrated in a meta-analysis by Annersten and Willman [18], studies that have been carried out on s.c. insulin injection technique involve study designs that are heterogeneous and concerned with different aspects of injection technique, although several studies point out the importance of needle size and the depth of s.c. tissue in depositing insulin at the appropriate level.

Other efforts have been made, including recent ones, to establish comprehensive insulin injection recommendations for patients with diabetes [9,19-21]. This review article contributes to past efforts by examining the latest data and advice related to insulin injection to determine optimal techniques for individual patients. The discussion in this review includes an overview of needle characteristics, which play an integral role in patient satisfaction, and incorporates recently available data on skin and s.c. layer depths in patients with varying characteristics and the implications for needle selection, site of injection and injection technique.

2. Methods

A literature search was conducted to locate information and data on insulin injection, including needle attributes, anatomical sites, guidelines and techniques. Relevant English-language articles published from 1980 until January 2011 were retrieved through searches of Medline and Cumulative Index to Nursing and Allied Health Literature databases. Search terms included the words 'needle', 'injection site', 'injection technique', 'insulin', 'lipohypertrophy', 'pain' and 'insulin guidelines'. References in retrieved articles provided additional sources of information and data for this review. Furthermore, as many studies concerning injection technique are not published in peer-reviewed journals due to their small scale and/or observational nature, relevant studies and documents known to the authors were also included. In-depth knowledge of devices used in diabetes therapy and extensive clinical experience treating patients with diabetes guided selection and analysis of the literature search results.

3. Selecting the appropriate needle characteristics

Evidence collected from clinical trials has revealed that selecting a needle acceptable to the patient is as important as the proper injection technique for reducing pain and fear associated with insulin injection among children, adolescents and adults with diabetes [22-28]. Fear of injection has been shown to interfere with initiation and intensification of, and adherence to insulin therapy, leading to poor glycemic control [29]. Although mechanical parameters of injection, such as the mechanical force of needle insertion, pressure needed for the injection button and the velocity of needle insertion, are associated with pain [28,30], the physical characteristics of the needle (i.e., diameter, length and bluntness) and how insulin is injected (i.e., technique) are easily individualized for the patient to reduce pain and fear, increasing the acceptance of insulin injection [22,23,28,30-35]. Needles with safety features, such as AutoShield™ Pen Needle (Becton, Dickinson and Co., Franklin Lakes, NJ, USA) and NovoFine Autocover® (Novo Nordisk, Bagsvaerd, Denmark), or novel attachment systems, such as NovoTwist® (Novo Nordisk), can reduce

the risk of needlestick injuries and increase patient satisfaction [36-40].

3.1 Needle diameter

Several studies have found a correlation between wider needle diameter (as measured by gauge; G) and frequency of painful injections [22,31,34]. In a study that examined frequency of pain with needles ranging from 23G (wide diameter, ~ 0.64 mm in outside diameter) to 32G (narrow diameter, ~ 0.23 mm in outside diameter), 54% of people injecting with the 27G needles registered pain compared with 31% injecting with 32G needles ($p < 0.0001$; **Figure 1**) [34]. Even small (1G) differences in needle tip diameter are perceived by patients as shown in two recent studies comparing thin needles. In a 2-week crossover study comparing NovoFine® (NF) 32G tip needles (Novo Nordisk) with MicroFine Plus® (MFP) 31G needles (Nippon Becton Dickinson Co. Ltd, Tokyo, Japan), study participants (n = 30) rated the NF 32G needles more satisfying ($p < 0.001$), less painful ($p < 0.01$) and less frightening ($p < 0.05$) to use than the MFP 31G needles [22]. In another study that tested patient comfort and preference when using MFP 32G needles compared with 31G needles, participants (n = 140) significantly preferred the 32G needle and rated it less painful ($p < 0.02$), as measured by the validated 150 mm visual analog scale (VAS) [31].

The increasing frequency of pain reported for needles with larger diameters may be influenced by an increase in visible bleeding. In a study by Egekvist *et al.* [28], more macroscopic bleeding was associated with insertions of 27G needles with an outer diameter of 0.4 mm than with 30G needles, which had an outer diameter of 0.3 mm. When needles were inserted with a computerized needle insertion device in healthy volunteers (n = 30), more injections with the 27G needles resulted in macroscopic bleeding than with the 30G needles (22.5 vs 17.8%, respectively, $p < 0.05$). Insertions with the 27G needles were also more frequently associated with pain (40.3 vs 30.8%, respectively; $p < 0.05$).

Other studies show that bleeding is less frequent with needles of narrower diameter [23,34]. For example, less bleeding occurred with a 33G needle (Nanopass®, Terumo Corp, Tokyo, Japan) compared with a MFP 31G needle in a 2-week crossover study of 40 patients with type 1 diabetes, who injected insulin four times daily and rated the needles on a VAS from -100 (worst) to +100 (best) (78.1 ± 20.7 vs 42 ± 40.6, respectively; $p = 0.001$) [23]. The overall patient satisfaction score was significantly higher for the 33G needle than for the 31G needle (73.1 ± 29 vs 37.5 ± 44.9, respectively; $p = 0.001$).

Although needles with decreased outer diameter cause less pain on insertion, they may increase insulin flow resistance, prolonging the time needed to inject and requiring more injection pressure. This effect may appear to risk inconvenience to the patient and, therefore, lead to dissatisfaction; however, patients have been observed to prefer needles with a smaller diameter despite increased injection button pressure, even when injecting doses above 40 units [25]. Needles designed with thin wall technology, which feature an increased inner diameter (bore width), can help reduce insulin flow resistance compared with standard needles of equal gauge [41], and patients have expressed a preference for these. In a 4-week crossover study, 78% of patients (n = 97) preferred a MFP 'thin wall' 31G needle over a 'regular-wall' 31G needle (Ypsomed Optifine, Ypsomed GmbH, Liederbach, Germany) [42]. The NF 32G tip needle has been manufactured using thin wall technology and has an internal diameter of 0.135 mm compared with 0.175 mm with NF 30G thin wall needles [25].

3.2 Needle length

Another attribute of needles that can cause patient discomfort is needle length. Studies have shown that shorter needles (< 8 mm) are associated with less injection pain than longer (≥ 8 mm) needles [31,43,44]. In a 6-week crossover trial, patients with type 1 (n = 61) or type 2 (n = 103) diabetes were divided into two groups. One group used a 4 mm 32G needle for 3 weeks and then switched to a 5 mm 31G needle, while the other group switched from a 4 mm 32G needle to an 8 mm 31G needle [31]. Patients rated the 4 mm needle significantly less painful than either the 5 mm (mean difference -11.91; $p = 0.019$) or 8 mm needle (mean difference -23.26; $p < 0.001$) on a 150 mm VAS. In a similar 26-week crossover study, patients with diabetes (n = 52) used a 5 mm needle for 13 weeks and then switched to a longer needle (either 8 or 12 mm), or vice versa [44]. After 26 weeks, the 5 mm needle was associated with significantly less pain, bleeding and bruising ($p < 0.05$) than the 8 and 12 mm needles. Most patients preferred a 5 mm needle ($p < 0.05$). Another study demonstrated an overwhelming preference for shorter needles in obese patients (body mass index (BMI) > 30 kg/m^2; n = 62) who were randomized to use a 6 mm needle for 12 weeks before switching to a 12.7 mm needle or vice versa [35]. The 6 mm needle was preferred by 89% of patients ($p < 0.001$), with 76% having a 'strong', 'very strong' or 'extremely strong' preference compared with a 12.7 mm needle, even though no significant difference emerged between the different needle lengths regarding glycemic control, pain and leakage, convenience or ease of use.

A more important concern than reducing pain in determining the appropriate needle length is the need to reduce the risk of intramuscular injections. Injection of insulin in intramuscular tissue instead of s.c. tissue can cause inadequate insulin absorption, disrupt the timing between maximum glucose load and peak insulin effect, and ultimately lead to poor metabolic control with unexpected glycemic excursions [21]. It has been shown that uptake of rapid-acting insulin into the circulation can be 50% faster from intramuscular tissue than from s.c. tissue on the thigh [45]. However, although intramuscular absorption tends to be fast, it is irregular, and thus intramuscular injections are not recommended for daily injections [9,45,46]. In addition, exercise can increase absorption of insulin

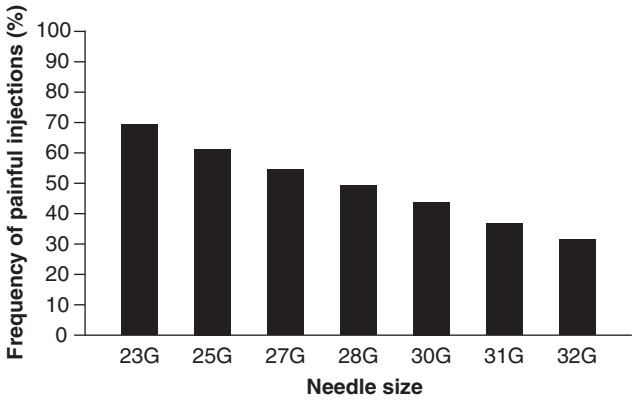

Figure 1. Frequency of painful injections according to needle gauge.

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deposited in muscle tissue, particularly in the thigh, thereby increasing the risk of hypoglycemia [47].

Intradermal injections are not recommended due to presumption that they may lead to local reactions, increased pain and insulin leakage [43]. However, there has recently been increased research interest in this route of administration using microneedles (1.5 – 2 mm) [48-50]. These studies showed that onset of the metabolic effect of insulin when it is absorbed from the skin is faster than when it is absorbed from s.c. tissue, and this may have clinical relevance for rapid-acting insulin formulations.

Knowledge of s.c. tissue depth can aid the selection of proper needle length. Generally, insulin injections should only reach s.c. tissue to avoid intramuscular injection and inconsistent insulin absorption in pediatric and adult patients [9,19-22,51,52]. Skin thickness has been shown to be similar at the four injection sites: abdomen, rear upper arm, anterior upper thigh and upper outer quadrant of the buttock [53]. The results of ultrasound measurements of skin and s.c. adipose layer thickness at these four injection sites in a study of 388 patients with type 1 and 2 diabetes and a wide BMI range (19.6 – 64.5 kg/m^2), who were diverse in race, age (range: 18 – 86 years) and gender, indicated that the mean skin thickness ranged from 1.87 ± 0.39 mm in the thigh to 2.41 ± 0.48 mm in the buttocks. No significant correlation was found between age and skin thickness ($p = 0.369$) [53], but it is possible that skin tissue may be slightly thinner in children than in adults at these locations [53,54]. More variability was discovered with mean s.c. tissue depth, which was shown to range from 10.35 ± 5.65 mm in the thigh to 15.45 ± 7.27 mm in the buttock. The following factors had significant associations with s.c. depth: injection site ($p < 0.001$), gender ($p < 0.001$), BMI ($p < 0.001$) and race ($p = 0.038$). **Figure 2** shows the mean s.c. depths for the four injection sites according to the categories of BMI, gender, race and age. It should be noted, however, that the authors measured s.c. tissue depth in the back of the arm and not the anterior. Thow *et al.* [55] measured s.c. layer thickness in the area commonly used as an injection site on the anterior arm and found it to be 5.8 ± 1.5 mm in men and 10.1 ± 2.4 mm in women.

A needle length greater than 8 mm has been associated with an increased risk of intramuscular injections in several studies [56-59]. As studies show that using shorter needles (< 8 mm) reduces the risk of intramuscular injections, they are generally recommended instead of longer needles, particularly in the case of pediatric and lean adult patients [7,9,21,43,44,53,56,57,60-64]. In a study of pediatric and adult patients (n = 122 and 137, respectively), who received 976 and 1096 injections, respectively, of sterile air corresponding to 20 IU of insulin with 5 mm needles at 90° or 45° angles in the abdomen and thigh, with or without a pinched skin fold, injection depth was assessed each time via ultrasonography [43]. Only 5.5% of injections in children and 1.3% in adults were intramuscular. The authors of this study concluded that 5 mm needles could be reliably inserted into s.c. tissue, and recommended using an angled injection and pinched skin fold in children, while adults could choose an injection technique based on preference. In the previously mentioned study by Gibney *et al.* [53] examining s.c. layer thickness in 388 patients, the authors concluded that 4 and 5 mm needles when inserted at a 90° angle will enter s.c. tissue with minimal risk of intramuscular or intradermal injection in almost all adults regardless of the injection site.

Short needle lengths have not been associated with any increase in insulin backflow in several studies [31,43,63,65]. Although significant differences in insulin backflow were observed with shorter needle lengths in a study that tested needle lengths from 12 to 4.5 mm in an *ex vivo* model, all needle lengths resulted in backflow that was clinically insignificant and it appeared that the dose amount had a greater effect on insulin leakage than needle length [65]. None of the needle lengths in the study appeared to pose any threat to the safety of an insulin injection due to backflow [65]. In a study to determine the ideal injection technique among a range of patients when using 5 mm needles, only minimal leakage was observed when patients were injected with an insulin-free test medium equivalent to 20, 40 and 60 units of insulin [43]. When patients in a crossover study used 4 mm needles at least once a day to administer insulin for 3 weeks and a 5 or 8 mm needle for another 3 weeks, 1488 leakage events were reported with 838 (58%) occurring during use of a 5 or 8 mm needle. The mean subjective reported leakage for all needle sizes was < 1 unit of insulin, but no adverse clinical effect was observed for this leakage with any needle length [31]. In a trial with simulated injections of a test medium corresponding to 10 and 40 units of insulin with either a 4 or 6 mm needle in 32 lean adults, leakage with either needle length was negligible [63]. In this trial, patients counted to 10 before withdrawing the needle completely. Holding the needle in for 10 s after injection is a technique recommended by Annersten and Frid [66], who measured leakage when

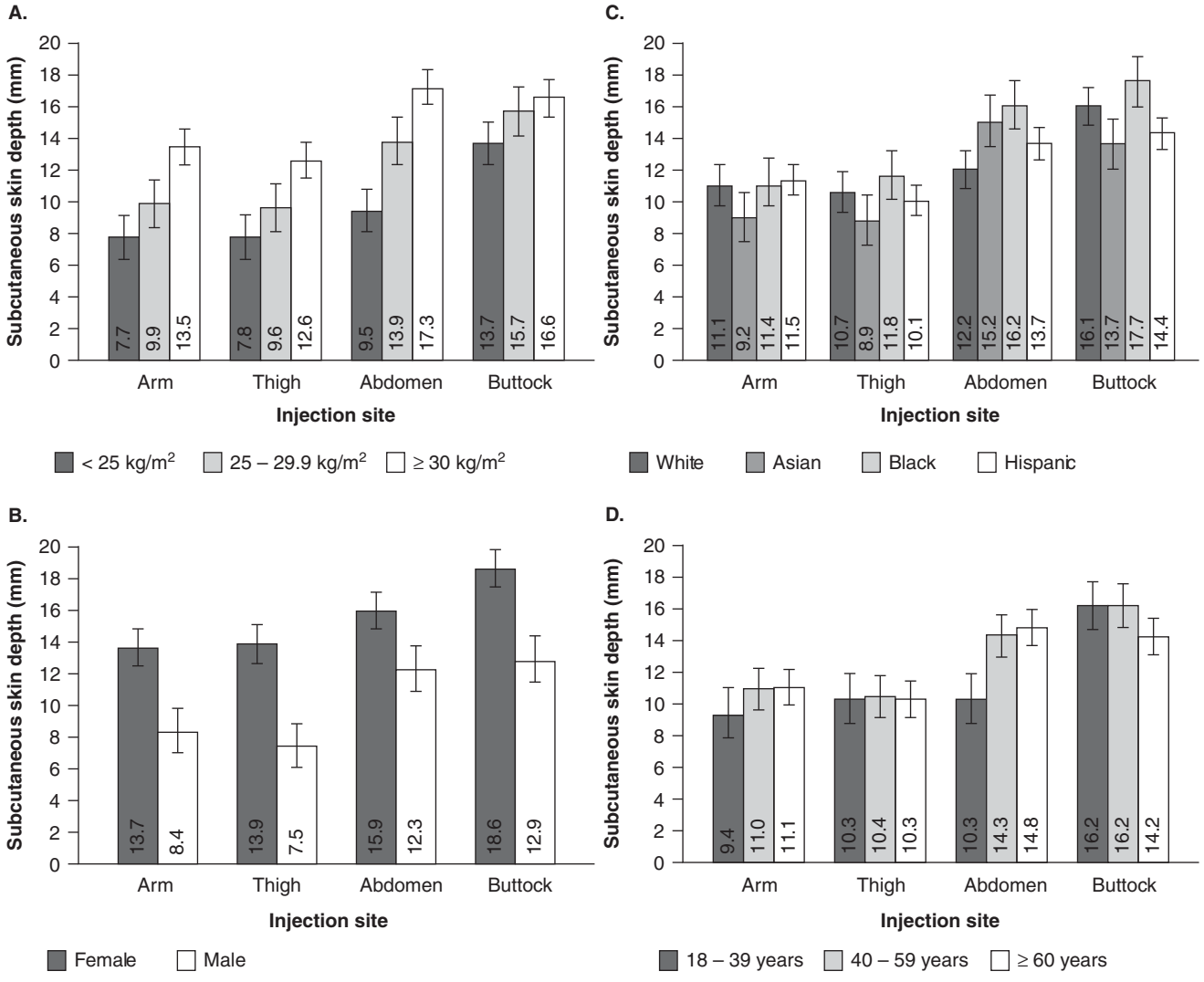

Figure 2. Subcutaneous skin depth in patients with type 1 and 2 diabetes according to injection site (arm, thigh, abdomen, buttock) categorized by: A. body mass index; **B.** gender; **C.** race; and **D.** age.
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needles were withdrawn 1, 3, 5 and 7 s after injection of sterile saline in 20 volunteers.

3.2.1 *Needle length and glycemic control*

An overlooked barrier to widespread use of shorter needles is the concern that they adversely affect glycemic control because they do not deposit insulin as deep within the s.c. tissue as longer needles, particularly in obese patients. However, several studies have shown that short needles versus longer needles provide equivalent glycemic control without any difference in hypoglycemic events, even in patients who are obese [31,35,67]. In the previously mentioned 6-week crossover trial in which one group (n = 83) used a 4 mm 32G needle for 3 weeks and then switched to a 5 mm 31G needle, while the other group (n = 80) switched from a 4 mm 32G needle to an 8 mm 31G needle, 52% of patients were obese with a BMI > 30 kg/m^2 and baseline mean fructosamine was 301 ± 55.1 µmol/l [31]. Percent absolute changes in fructosamine were calculated to determine changes in glycemic control when patients switched pen needle lengths. The mean percent absolute change in fructosamine in patients in the first group was 4.9% (95% CI 3.8, 6) and 5.5% (95% CI 4.3, 6.4) in the second group. These small changes in fructosamine (median changes 11 – 13.5 µmol/l) were nonsignificant and did not correlate with BMI in either group. The number of patients who experienced hypoglycemia was also comparable when using the three needle lengths: 36 (20.8%) of 173 with the 4 mm needle, 21 (23.6%) of 89 with the 5 mm needle and 22 (26.2%) of 84 with the 8 mm needle. In another crossover study, 62 obese patients with type 1 or 2 diabetes were randomized to insulin treatment with 6 mm 31G or 12.7 mm

Table 1. Injection technique for different needle lengths and patient types.

Weight	Needle length	Injection angle	Skin fold
Normal (BMI < 25)	4 mm	90°	None
	5 mm	90°	Lifted skin fold
	6 mm	90°	Lifted skin fold
	8 mm	45°	Lifted skin fold
Overweight (BMI > 25)	4 mm	90°	None
	5 mm	90°	Abdomen: no skin fold Thigh: lifted skin fold
	6 mm	90°	Abdomen: no skin fold Thigh: lifted skin fold
	8 mm	90°	Lifted skin fold

BMI: Body mass index.

29G for 12 weeks before switching to the other needle length for a further 12 weeks [35]. After 24 weeks, no difference in glycemic control was observed between the needle lengths. The most common adverse event was injection site bruising (51% for the longer needle vs 34% for the shorter needle, a nonsignificant difference). A more recent crossover study examining the influence of needle length on glycemic control in 130 obese patients with type 1 and 2 diabetes who were randomized to use a 5 or 8 mm needle for 3 months before switching to the other needle for another 3 months detected a small difference [67]. Within the two treatment groups, there were no observed changes in HbA_{1c}, fructosamine, hypoglycemic events or bruising, but when data from all 126 patients who completed the study were pooled, with the 5 mm needle, HbA_{1c} was 7.47 ± 0.9%, and with the 8 mm needle it was 7.59 ± 1% ($p = 0.02$). The results of these studies show that even obese patients can use shorter needles and maintain the metabolic control achieved with longer needles.

3.3 Needle bluntness

Although it appears possible that the sharpness or bluntness of the needle would influence the amount of pain associated with injection, studies have not indicated a significant connection [30,68]. When unused needles were compared with needles that were blunted, by penetrating the rubber seal of a vial five times prior to injection or used up to five times previously, patients did not give significantly higher pain scores to the latter needles [30,68], although a slight trend may have appeared when needles were intentionally blunted on a rubber seal [30]. Even if there is no difference in pain associated with new versus used needles, needles should always be changed after each use to prevent dosing error and lipohypertrophy [8,21].

4. Selecting the appropriate injection site

Understanding insulin absorption is the basis for selecting the proper injection technique for a patient. In addition to the depth at which insulin is deposited (s.c., intramuscular or intradermal tissue), insulin absorption is influenced by the injection site, presence of lipohypertrophy, type and amount of insulin injected, and other variables.

4.1 Anatomical location

The recommended sites for insulin injection of both rapid- and long-acting insulin analogs are the abdominal region, front of the upper arm, front of the thigh and buttocks [69-73]. The upper arm is not recommended by the Danish Nurses association as an injection site for self-injections, because in most of the frontal area there is often only minimal distance from skin to muscle, and the risk of intramuscular injection is high [19]. Injections in the back of the patient's arm where the s.c. layer is sufficiently thick can be given by caregivers and nurses. If an injection in the arm is performed by a self-injecting person, it should be done only in the lower third of the area between elbow and shoulder using short needles (4 – 5 mm).

Limiting injection to one anatomical area has been shown to improve the stability of insulin absorption between injections. In a crossover study in which 22 individuals with type 1 diabetes were randomized to receive regular insulin in the abdomen one morning and in the thigh another morning, abdominal injections produced a 29% lower postprandial glucose peak ($p < 0.001$) and a 38% higher peak in serum insulin ($p = 0.017$) compared with the thigh injections [74].

However, repeated injections into precisely the same anatomical area can lead to lipohypertrophy. Lipohypertrophy is a complication of insulin injection therapy characterized by the swelling of fatty tissue and is estimated to affect between 28.7 and 65% of people with type 1 diabetes and between 3.6 and 35% of people with type 2 diabetes who self-inject [6,8,9,11,75-78]. Lipohypertrophy hinders glycemic control by altering and/or delaying insulin absorption and can result in unexpected hypoglycemia [79-81]. It is caused by multiple injections in the same area and, in ~ 31% of cases, by needle re-use [8]. To prevent lipohypertrophy, when confining injections to one anatomical area, injection sites should be rotated within the area and separated by at least 3 cm [78,82]. Using a new needle with every injection can also help reduce the risk of this condition developing [8,78].

4.2 Type and amount of insulin

Insulin absorption varies for different types of insulin as well as the amount of insulin injected [83-90]. The differences in insulin type and amount may help in selecting an injection site. As insulin absorption is faster from the abdomen than another location, it is more suitable for deposition of rapid-acting insulins to provide prandial control in adult and pediatric patients [19,52,74]. Abdominal injections are recommended in the area ~ 4 cm below the navel and extending 12 cm to the right and left, because s.c. tissue tends to be thickest there [19]. Conversely, longer-acting insulins, which are designed to give consistent basal insulin coverage, and intermediate-acting insulins, which cover insulin needs for half the day or overnight, are appropriately injected in the thigh in pediatric and adult patients, because absorption is

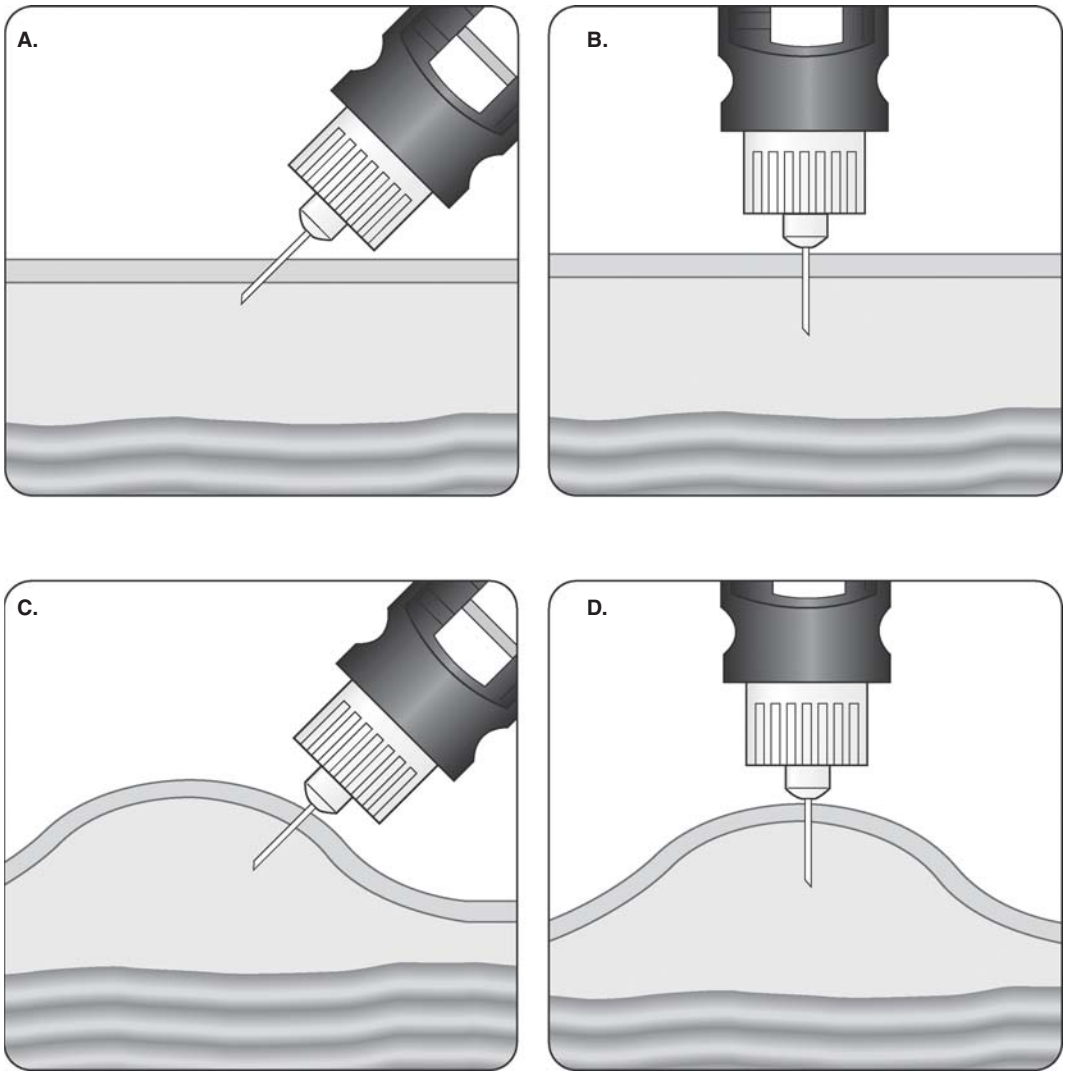

Figure 3. Needle insertions at 45° and 90° angles without and with a skin fold: A. 45° angle without skin fold; **B.** 90° angle without skin fold; **C.** 45° angle with skin fold; and **D.** 90° angle with skin fold.

slower from this location than from the abdomen [19,52,73]. Premixed insulin formulations, which are available in various combinations of rapid-acting and intermediate-acting insulins usually taken twice a day, are normally recommended for administration in the abdomen in the morning and in the thigh in the evening [19].

A larger insulin dose will enter the circulation more slowly than a smaller dose when insulin is injected into s.c. tissue. It is recommended to split doses larger than 40 IU into two doses to optimize absorption and prevent lipohypertrophy [19].

Other factors can influence the absorption of insulin and patients should be aware of these. Exercise, massage and high body temperature may increase the rate of insulin absorption, thus increasing the risk of hypoglycemia, while lower body temperature and smoking may decrease the rate of absorption [9,52,61].

5. Injection technique

The depth of s.c. tissue at the chosen injection site and the needle length will dictate which injection technique to use: at what angle the needle should be inserted and whether or not a lifted skin fold should receive the needle. Correct technique will ensure that the insulin is deposited in s.c. tissue and not the intramuscular or intradermal layer.

Needles are recommended to be inserted either at a 90° or 45° angle, depending on needle length and thickness of the s.c. tissue (**Table 1**). Usually, needles 8 mm or longer should be inserted at a 45° angle with a skin fold while needles 6 mm or shorter can be inserted at a 90° angle without a skin fold (**Figure 3**) [9,20,35,56,60,63,91]. However, in children, adolescents and lean adults, particularly when injection in the thigh is desired, a 45° insertion of 6 and 5 mm needles may help to

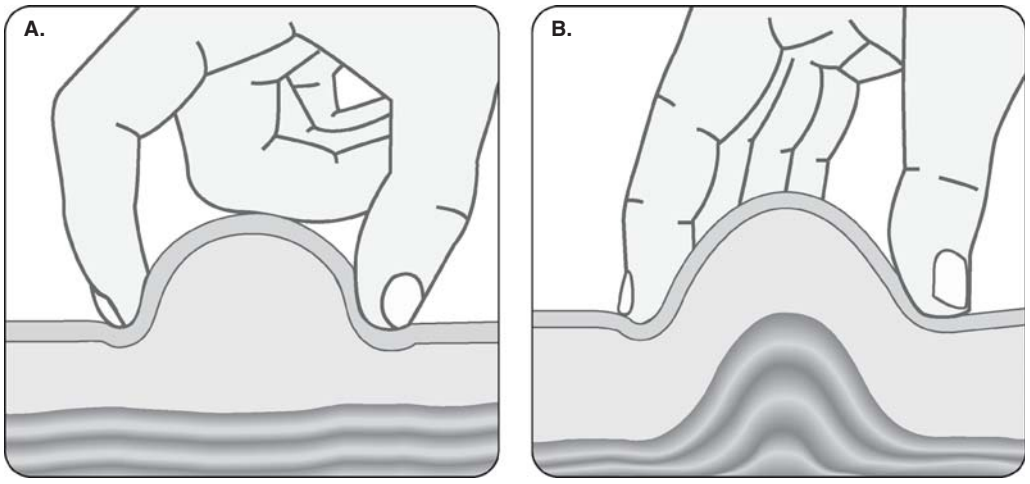

Figure 4. Lifting fold of skin between two fingers: A. correct method and **B.** incorrect method, in which muscle fascia is picked up when skin is lifted using several fingers.

reduce the risk of intramuscular injection (**Figure 3**) [9,31,43,53]. In most pediatric and adult patients, 4 mm needles can be inserted at a 90° angle without an elevated skin fold, even if the thigh is the injection site [53,63].

Injection into a lifted skin fold helps avoid intramuscular injection by increasing the distance from skin to muscle, which is particularly useful in children and lean adults with diabetes [43,52,57,92]. The lifted skin fold technique involves pinching up an s.c. skin fold between the thumb and index finger (**Figure 4**) [93], and injecting in this raised s.c. tissue, keeping the skin lifted for the entirety of the injection [8,33]. Once the injection is complete, the lifted skin fold is released, and the needle is withdrawn half-way out and held for 6 – 10 s depending on the pen used, before being withdrawn completely to ensure that all insulin is delivered and leakage is avoided [19,63,94-96].

6. Conclusion

Correct insulin injection technique can facilitate glycemic control by maximizing insulin absorption and minimizing patient pain associated with injection, thus improving treatment adherence. Optimal insulin injection involves selecting an appropriate needle; identifying the desired injection site, which can be influenced by the type of insulin being used; and using the most suitable injection technique. A needle with a narrow diameter designed with thin wall technology and shorter than 8 mm can reduce patient pain and increase treatment satisfaction. In general, needles shorter than 8 mm are appropriate for both normal weight and obese pediatric and adult patients, and are preferred by them. However, optimal needle length can vary depending on the depth of the patient's s.c. tissue, which is affected by BMI, gender, race, age and injection site. Optimal needle length can also be influenced by patient and physician preferences. Depending on the chosen needle size and depth of the s.c. tissue, injections should be given with either a 90° or 45° angle, with or without a lifted skin fold, so that the insulin is deposited in s.c. tissue. The recommended injection sites are abdomen, thighs and buttocks, and the type of insulin being used may help determine which injection site is preferable. Abdominal injections result in slightly more rapid dispersal of insulin, while thigh injections tend to disperse insulin more slowly. By assisting patients with diabetes in selecting needles suitable to them and teaching them correct injection procedures, healthcare professionals may help reduce discomfort related to injection, improve treatment adherence and enable better glycemic control.

7. Expert opinion

Over recent years, an increasing number of needles with lengths shorter than 8 mm and narrower diameters than in the past have been made commercially available. Clinical data have been published to support the safety, convenience and reduced pain when using these short and thin needles compared with the conventional 8 – 12 mm needles. Results from studies in both pediatric and adult patients with varying BMI suggest that these short needles can deliver insulin into the s.c. tissue with low risk of intramuscular injections and little backflow irrespective of a patient's age and adiposity.

Studies that have visualized insulin depositions from different injection techniques have provided useful data for making recommendations regarding optimal injection techniques for different groups of patients. These data have been supplemented by recent comparisons of insulin pharmacokinetics in the skin and s.c. layers, which challenge past assumptions about the s.c. layer being the only suitable recipient for insulin deposition. Altogether, the new findings are useful for assessing the safety and efficacy of current and future short needles

in ways that were previously not possible. In the future, these findings may provide a basis for tailoring recommended injection depths to the type of insulin injected. The ultimate goal is to develop individualized, evidence-based injection technique recommendations to optimize metabolic control in all patients with type 1 or 2 diabetes. At present, the variability of body composition, treatment regimens and patients' responses to therapy still present a challenge for defining ideal, individualized injection techniques.

Although published studies show that patients of all ages prefer short needles, wider acceptance of short needles in clinical practice may require more evidence-based guidance. The impact of backflow on long-term glycemic control, particularly in patients who are taking small doses with short needles, should be investigated further to establish a more rigorous body of evidence. It will be interesting to see the impact that recently developed needle designs have on treatment adherence in different patient groups, ranging from adolescents to adults with type 2 diabetes, who initiate insulin treatment.

Even shorter and thinner needles than those now available can be expected in the years to come which will aim to make injection even easier and less burdensome for patients. At the same time, the likelihood of unintended intradermal insulin delivery can be expected to increase with needles shorter than 5 mm. Before these needles can be implemented in daily clinical practice, it is critical that clinical studies are performed to measure their efficacy and safety in different patient groups. In this respect, the newest research of intradermal microneedles is promising as it may provide useful data that are applicable to short needles in general.

Declaration of interest

B Hansen has been a member of Advisory Boards and received speaker's fees from Novo Nordisk. I Matytsina is an employee of Novo Nordisk A/S. The authors are grateful to Watermeadow Medical PLC (Witney, United Kingdom) for manuscript development, comment collaboration and editorial assistance, supported by Novo Nordisk A/S.

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