Original research

Ultrasound-guided measurement of skin and subcutaneous tissue thickness in children with diabetes and recommendations for giving insulin injections

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A B S T R A C T

Aim: To measure skin thickness (ST) and skin + subcutaneous layer thickness (SCT) by ultrasound and estimate the risk of intramuscular injection (IM) with different needle lengths across injection sites according to age group.

Method: Children recruited between 1 and 18 years with type 1 and 2 diabetes on insulin injections and divided into three age groups: 1–6 years, 7–12 years and 13–18 years. A portable ultrasound was used to measure ST and SCT at four injection sites on the abdomen, arm, thigh and buttock.

Results: Total 153 children enrolled for the study. The mean (SD) measurement of ST & SCT at four sites on abdomen, arm, thigh & buttocks were as follows; 4.33 mm (± 2.22), 5.55 mm (± 2.26), 5.83 mm (± 3.12), 6.48 mm (± 3.47) in 1–6 years old; 7.11 mm (± 3.68), 7.79 mm (± 4.54), 7.17 mm (± 3.62), 8.51 mm (± 3.65) in 7–12 years old; 8.94 mm (± 4.50), 8.42 mm (± 5.00), 8.61 mm (± 4.76), 9.76 mm (± 4.38) in 13–18 years old. Young children, 1–6 years have the highest risk of IM injection with all needle lengths, i.e. 4, 5, 6, 8 & 12.7 mm, while older children 7–12 & 13–18 years have a lower risk with shorter needles (4, 5 and 6 mm) as compared to longer needles (8 and 12.7 mm).

Conclusions: Children with diabetes on insulin therapy should be advised on the appropriate needle length accordingly to their age and BMI.

Introduction

Multiple-dose insulin injections are the mainstay of diabetes management in children and are given subcutaneously at four recommended sites with the prescribed technique. In recent years, the effectiveness of insulin therapy has improved tremendously with the availability of different needle lengths. Since injections are to be administered three to four times daily, the three most important points of the correct site, needle length and technique [1] are emphasised from the start to ensure delivery of insulin into the subcutaneous (SC) tissue and optimise insulin absorption. SC is the correct site for insulin administration as blood flow through this fat layer is slow and predictable in contrast to muscle wherein it is fast and ever-changing. If the injection becomes intramuscular, the absorption of insulin is rapid and can cause hypoglycaemia. Therefore, to avoid fluctuations in blood glucose, it is essential that injections are given consistently in the SC tissue.

Repeated injections at the same site over time can also lead to skin injuries such as hypertrophy, lipoatrophy and subcutaneous nodularity, thereby altering skin thickness [1]. Therefore, patients are advised to rotate and rest the sites as needed on a day-to-day basis. The technique to be used for insulin injections are part of standard diabetes education, and needle length depends on patient’s age [2]. But the most objective recommendation should be based on total skin and subcutaneous layer thickness (SCT) measurement across age groups [3–6]. Even among the different age groups ST and SCT will vary according to body mass index (BMI) which differs across ethnicity and gender. In children studies comparing this variability is lacking. However the adult study has shown that factors which influence ST at the abdomen and upper arms were gender and BMI whereas SCT at abdomen was gender and BMI, and SCT at upper arms was gender, BMI and age [5]. The studies done using ultrasonography to measure ST and SCT in children with type 1 diabetes showed that there is a progressive increase in thickness with age and also it varies at different sites (arm, thigh, abdomen and...
insulin in the SC [7]. These when using 6, 8, or 12.7 mm needle to ensure adequate delivery of up skin fold is not required for 4 or 5 mm needle but may be necessary old age group (20.2%) compared to 7–9 years (5.9%) and 10–12 years (4.6%). Additionally, the rate of intramuscular injection with the shortest needle (4 mm) was found to be five times more in the 1–6 years old age group (20.2%) compared to 7–13 years (4.6%) and 14–17 years (2.4%) with a non-pinch skin-fold [6]. Lean children with a thin layer of subcutaneous tissue may also need to pinch a skin fold when using 4 or 5 mm needles for injection over arms or thighs [1,5]. In adults, a pinch-subcutaneous tissue may also need to pinch a skin fold when using 4 or 5 mm needle but may be necessary when using 6, 8, or 12.7 mm needle to ensure adequate delivery of insulin in the SC [7].

The data for Asian children are lacking and it remains uncertain whether previous findings could be generalised to our local population with diabetes since ST and SCT thickness could differ by race and ethnicity. Therefore, this study aims to establish recommendation of appropriate needle length for insulin injection among children with diabetes across different age groups in Singapore.

Materials and methods

Patient recruitment

Children between 1 and 18 years with diabetes on insulin injections recruited between 1st August 2013 and 30th June 2014 at KK Children’s & Women’s Hospital. They were divided into three groups according to their age: 1–6 years, 7–12 years and 13–18 years. Children excluded include those with secondary diabetes, duration of diabetes less than one year and hypertrophy/lipoatrophy/nodularity at insulin injection sites. Singhealth Centralized Institutional Review Board (CIRB) approved the study.

Data collection

Questionnaires were administered to patients more than age 13 years old and to the parents of patients less than age 13 years old to obtain participants’ demographics and medical history. The weight (kg) was measured using the digital weighing machine (Avacare Mechatronic, Singapore) and height (cm) using (Wall mounted Stadiometer) and BMI (kg/m²) calculated from these measurements. A capillary one millimetre’s blood sample was collected and tested for glycated haemoglobin (HbA1c) using clinical chemistry analyser (Bio- Rad Abbott Architect c8000, Unites States). Two trained Diabetes Nurse Educators did a measurement of ST and SCT in millimetres using portable M-Turbo® ultrasound system (Sonosite, United States) with 5–15 MHz transducer probe on four injection sites – arm, thigh, abdomen and buttocks on right or left side of the body. Standard procedures were adopted which include a selection of good sites, non-pinch (non-compressed) skin fold and transducer probe positioned perpendicularly to the marked area to obtain a clear and focused image to measure ST & SCT. The site of measurement was standardized using landmarks in order to reduce intersubject variability. The measurement site was mid-length directly inferior to the acromion process for the arms, greater trochanter for the thigh, 2 cm away from the umbilicus at the lateral abdomen and upper outer quadrant for the buttocks. No measurements were made over sites of lipohypertrophy. All measurements were calculated from an average of two readings obtained by each operator. Training for measurements was validated on two operators with inter-rater variability below 5%. The percentage of IM injection with different needle lengths (4 mm, 5 mm, 6 mm, 8 mm and 12.7 mm) across three age groups at four different injection sites was

Table 1
Baseline characteristics of patients.

| Boys + Girls | Boys only | Girls only |
|--------------|-----------|------------|
| 1–6 years (n = 12) | 7–12 years (n = 55) | 13–17 years (n = 86) |
| Gender (n, %) | p<0.003* | 0.26 |
| Boys | 11 (91.7) | 24 (43.6) | 34 (39.5) |
| Girls | 1 (8.3) | 31 (56.4) | 52 (60.5) |
| Ethnicity (n, %) | 0.40 | 0.030* | 0.072 |
| Chinese | 9 (75.0) | 34 (61.8) | 54 (62.8) |
| Malay/Indian/Others | 3 (25.0) | 21 (38.2) | 32 (37.2) |
| BMI-for-age percentile (n, %) | 0.78 | 0.61 | 0.23 |
| 3rd–25th | 0.027 | 12 (100) | 53 (96.4) | 72 (83.7) |
| 25th–75th | 0.51 | 11 (100) | 23 (95.8) | 31 (91.2) |
| 75th–97th | 0.23 | 0.078 | 0.61 | 0.78 |

1 Values are expressed as n (%).
2 Chi-square test conducted to compare different age groups; p < 0.05 taken to be statistically significant.
3 p < 0.05.

Approved for publication by the Singapore Paediatric Society, the Singapore Paediatric Diabetes Group and the SingHealth Centralized Institutional Review Board (CIRB).
|                      | Boys + Girls | Boys only | Girls only |
|----------------------|--------------|-----------|------------|
|                      | 1–6 years (n = 12) | 7–12 years (n = 55) | 13–17 years (n = 86) |
|                      | 1–6 years (n = 11) | 7–12 years (n = 24) | 13–17 years (n = 34) |
|                      | 1–6 years (n = 1) | 7–12 years (n = 31) | 13–17 years (n = 52) |

**Skin thickness (ST)**

|          | Boys + Girls | Boys only | Girls only |
|----------|--------------|-----------|------------|
| Abdomen  | 1.57 ± 0.31† | 1.59 ± 0.31* | 1.78 ± 0.27* |
| Arm      | 1.33 ± 0.23† | 1.32 ± 0.24* | 1.51 ± 0.28* |
| Thigh    | 1.54 ± 0.19† | 1.54 ± 0.20* | 1.60 ± 0.27* |
| Buttocks | 1.65 ± 0.29† | 1.60 ± 0.24* | 1.87 ± 0.37* |

**Total skin and subcutaneous thickness (SCT)**

|          | Boys + Girls | Boys only | Girls only |
|----------|--------------|-----------|------------|
| Abdomen  | 4.33 ± 2.22† | 4.10 ± 2.18* | 6.59 ± 3.11* |
| Arm      | 5.55 ± 2.26† | 5.18 ± 1.96* | 7.38 ± 4.23* |
| Thigh    | 5.85 ± 3.12† | 5.02 ± 1.39* | 6.79 ± 3.08* |
| Buttocks | 6.48 ± 3.47† | 5.73 ± 2.58* | 8.00 ± 3.23* |

* Values are expressed as mean ± S.D. (in mm).
1 Based on one-way ANOVA; p < 0.05 was considered to be statistically significant.
2 Based on independent t-test to compare ST or ST + SC of 7–12 years old and 13–17 years old girls; p < 0.05 was considered to be statistically significant.
3 Based on independent t-test to compare ST or ST + SC of boys and girls from each age group; p < 0.05 was considered to be statistically significant.
4 Bonferroni post hoc test significantly different from 1 to 6 years old; p < 0.05 was considered to be statistically significant.
5 Bonferroni post hoc test significantly different from 7 to 12 years old; p < 0.05 was considered to be statistically significant.
6 Bonferroni post hoc test significantly different from 13 to 17 years old; p < 0.05 was considered to be statistically significant.
7 * p < 0.05.
analysed based on measurements of ST and SCT. We considered participants to have experienced intramuscular injection when needle length exceeded SCT measurement with the assumption of a non-pinch skin fold technique.

**Statistical analysis**

Differences across age groups were compared using Fisher’s exact test for categorical variables and one-way analysis of variance (ANOVA) for continuous variables. P < 0.05 was considered as statistically significant. All statistical analyses were performed using Statistical Package for the Social Sciences, Version 19.0 (IBM New York).

**Results**

**Baseline characteristics of patients**

A total of 153 children were enrolled in this study. They comprised 12 (8%) 1–6 years old, 55 (36%) 7–12 years old and 86 (56%) 13–18 years old children. Table 1 shows the comparison of participants’ characteristics across age groups. In the three age groups majority of children had type 1 diabetes (p = 0.027) and in the older age group 7–12 years and 13–18 years there were more female (p = 0.003) while there were more boys in the younger age group 1–6 years. There were no significant differences in ethnicity (p = 0.68) and HbA1C (p = 0.78) among the three groups. Among the boy’s majority of them have BMI in the 25th to 75th percentile across all age groups (p = 0.03).
Measurement of skin and subcutaneous thickness (ST & SCT)

Table 2 shows the measurements of ST and SCT at abdomen, arm, thigh and buttocks across the age groups. ST measurements over four sites across the three age group vary significantly and are higher in 13–18 years compared to 1–6 and 7–12 years (p < 0.001). Overall ST at all sites does not differ between boys and girls except that the ST at abdomen in the age group of 7–12 years is more in girls as compared to boys (p = 0.047). While SCT also varies at different sites across the age groups, in girls is it higher in 13–18 years at all sites as compared to the boys (p ≤ 0.001). Fig. 1 scatter plot and Fig. 2 bar chart shows SCT measurement across age groups at different sites and Fig. 3 & Fig. 4 shows SCT measurement in relation to BMI percentile.

Percentage of intramuscular (IM) injection using different needle lengths

Table 3 shows the estimated percentage of IM injection risk with varying needle lengths across three age groups at the four different injection sites based on measurements of ST and SCT assuming a non-pinch injection technique and Table 4 shows IM risk across BMI percentile. In 1–6 years there is a high risk of IM injection with all needle lengths over four sites. Interestingly the risk of IM injection with 4 mm needle was highest at abdomen for 1–6 years (66.7%) & 7–12 year (21.8%) as compared to other sites, but for 13–17 year it was more at arm (11.6%) and thigh (9.3%) vs abdomen (7%). The risk of IM injection proportionately increases with the length of the needle in all age groups at four sites. The 8 mm and 12.7 mm needle carries a high risk of
IM infections of more than 50% in 7–12 years and 75–100% in 1–6-year-old age group. In the 13–18 years old even with thicker SCT, IM risk is still prevalent on all sites, with 8 mm is about 50%, and with 12.7 mm it is more than 70%. Interesting to note that in boys in the age group of 13–18 years have a higher risk of IM injection as compared to girls at all sites with 5, 6, 8 & 12.7 mm needle. With regards to BMI, boys with BMI between 25th–75th percentile are at higher risk of IM injection with 4,5,6,12.7 mm needle at the abdomen,with 5 & 8 mm needle at the arm, with 5,6,12.7 mm needle at thigh and 5,6,8,12.7 mm at buttoc. Fig. 5 shows the risk of IM injection in different age groups at four sites with four needle length and Fig. 6 shows the risk against the BMI percentile.

Discussion

The ST and SCT measurements are important factors in determining the needle length for insulin injection and its subsequent absorption. Our study reported a progressive increase of ST and SCT across all age groups with age, body mass index (BMI) and sites of injection (buttock > thigh > arm > abdomen). Our findings were consistent with other pediatric studies which showed a similar correlation between ST and SCT with age, BMI and sites of injection (3–6, 8).

Children with diabetes can experience day-to-day variation in insulin absorption rate where accidental intramuscular insulin injection is one of the factors [4], commonly causing hypoglycaemia which is an acute complication reported in many studies [3,4,9]. Hypoglycaemia can be a significant factor causing morbidity and mortality in patients with diabetes [10,11]. Subcutaneous layer is the ideal site for insulin administration as blood flow through this fat layer is slow and predictable. The blood flow to the muscle is faster and ever-changing, depending on the state of muscle activity and therefore the risk of hypoglycaemia is high with IM injection [6].

In children, it is crucial to avoid hypoglycaemia and erratic fluctuations in blood glucose as it has an immediate effect on their function and concentration. Therefore, the clinical question in caring for children with daily insulin injection is how to avoid hypoglycaemia which depends on balancing food, insulin doses and avoiding intramuscular injections during insulin administration. The objective is to deliver insulin safely into the subcutaneous layer without any leakage or discomfort and avoid IM injection by selecting needle of appropriate length, and this will impact on insulin absorption and ultimately glycaemia control. In addition to the choice of needle length, a pinch-up skin fold may be helpful to avoid intramuscular injection.

Skin thickness in children is less than in adults and increases with age. Ultrasonography is rapidly evolving with high-frequency transducers readily available for measurement of ST and SCT [8]. Many studies on skin and subcutaneous thickness measurements were done by either computed tomography (CT) or ultrasonography to project visualisation of insulin into the subcutaneous layer. A study using ultrasonography visualisation reported 86% intramuscular location of insulin deposits in children despite appropriate pinch-up skin fold technique when using longer needles (12.7 mm) [12]. A similar ultrasound study on children with diabetes of mean age 10.4 ± 2.3 years with BMI 17.6 ± 2.3 kg/m² visualised the location of air injected using angled or pinch-up skin fold technique with 6 mm or 8 mm needle length and also demonstrated intramuscular delivery with increased incidence over thigh as compared with abdomen [9]. On the contrary, variations in pinch-up skinfold thickness and insulin absorption may partly explain the well-known inter-individual variation in insulin absorption [13]. The pinch-up skin fold only expands a modest degree in children and IM injections during insulin administration. The objective is to deliver insulin safely into the subcutaneous layer without any leakage or discomfort and avoid IM injection by selecting needle of appropriate length, and this will impact on insulin absorption and ultimately glycaemia control. In addition to the choice of needle length, a pinch-up skin fold may be helpful to avoid intramuscular injection.

| Table 3 Percentage of intramuscular (IM) injection in children from different age groups due to different needle length. |
|---------------------------------|
| **Site** | **Boys + Girls** | **Boys only** | **Girls only** |
|        | 1–6 years | 1–6 years | 1–6 years |
|        | 7–12 years | 7–12 years | 7–12 years |
|        | 13–17 years | 13–17 years | 13–17 years |
|        | (n = 12) | (n = 11) | (n = 1) |
|        | (n = 55) | (n = 24) | (n = 31) |
|        | (n = 86) | (n = 34) | (n = 52) |
| **Needle length** | **Abdomen** | **Arm** | **Thigh** |
| 4 mm | 8 (66.7) | 12 (21.8) | 6 (7.0) |
| 5 mm | 9 (75.0) | 21 (38.2) | 16 (18.6) |
| 6 mm | 10 (83.3) | 27 (49.1) | 30 (34.9) |
| 8 mm | 11 (91.7) | 36 (65.5) | 49 (57.0) |
| 12.7 mm | 12 (100) | 52 (94.5) | 68 (79.1) |
| **Needle length** | **Arm** | **Thigh** | **Buttocks** |
| 4 mm | 4 (33.3) | 7 (12.7) | 10 (11.6) |
| 5 mm | 8 (66.7) | 16 (29.1) | 24 (27.9) |
| 6 mm | 8 (66.7) | 25 (45.5) | 39 (45.3) |
| 8 mm | 9 (75.0) | 41 (74.5) | 55 (64.0) |
| 12.7 mm | 12 (100) | 46 (83.6) | 68 (79.1) |

1 Values are expressed as n (%)

* Chi-square test or fisher’s exact test comparing boys and girls, p < 0.05

** Chi-square test or fisher’s exact test comparing boys and girls, p < 0.01

*** Chi-square test or fisher’s exact test comparing boys and girls, p < 0.001
Table 4  
Percentage of intramuscular (IM) injection in children from different BMI-for-age percentile\(^2\) due to different needle length.\(^1\)

| Site          | Boys + Girls | Boys only | Girls only |
|---------------|--------------|-----------|------------|
|               | 3rd–25th percentile (n = 24) | 25th–75th percentile (n = 86) | 75th–90th percentile (n = 24) |
|               | 90th–97th percentile (n = 19) | 25th–75th percentile (n = 46) | 75th–90th percentile (n = 7) |
| 3rd–25th percentile (n = 7) | 90th–97th percentile (n = 13) | 25th–75th percentile (n = 40) | 75th–90th percentile (n = 17) |
| 3rd–25th percentile (n = 14) | 90th–97th percentile (n = 14) | 25th–75th percentile (n = 17) | 75th–90th percentile (n = 14) |

| Needle length | Abdomen | Arm | Thigh | Buttocks |
|---------------|---------|-----|-------|----------|
| 4 mm          | 8 (33.3) | 15 (17.4) | 2 (8.3) | 0 (0.0) |
| 5 mm          | 10 (41.7) | 30 (34.9) | 4 (16.7) | 2 (12.5) |
| 6 mm          | 15 (62.5) | 44 (51.2) | 6 (25.0) | 2 (10.5) |
| 8 mm          | 20 (83.3) | 62 (72.1) | 12 (50.0) | 2 (10.5) |
| 12.7 mm       | 22 (91.7) | 81 (94.2) | 20 (83.3) | 9 (47.4) |
| Needle length | 4 mm     | 5 mm | 6 mm | 8 mm |
| 12.7 mm       | 22 (91.7) | 23 (95.8) | 23 (95.8) | 23 (95.8) |

BMI, Body mass index.
\(^1\) Values are expressed as n (%).
\(^2\) With reference to CDC Growth Charts 2000.
\(^*\) Chi-square test or fisher's exact test comparing boys and girls, p < 0.05.
\(^**\) Chi-square test or fisher's exact test comparing boys and girls, p < 0.01.
\(^***\) Chi-square test or fisher's exact test comparing boys and girls, p < 0.001.
IM injections [6], but this is limited to individual’s capacity in visualising an angled approach when injecting insulin.

Our study evaluates the measurements of ST and SCT layer using a non-pinch skin fold. The minimum SCT thickness is at abdomen (4.33 mm) in 1–6 years old and maximum at buttocks (9.76 mm) in 13–18 years old group. Young children between 1 and 6 years old have the highest risk with 5 mm, 6 mm, 8 mm, and 12.7 mm needle from 58.3% to 100% at all four injection sites. The 4 mm needle has a lower risk of IM injection across all age groups, and 8 mm and 12.7 mm needle lengths are not recommended due to the high percentage of IM injection at all four sites across all three age groups. The most appropriate needle for insulin injection in 1–6 years old according to our study is 4 mm needle which corresponds to SCT layer measurement at the abdomen, arm, thigh, buttock (4.33, 5.55, 5.83, 6.48 mm) respectively. But even with 4 mm the risk of IM injection is high at abdomen (66.7%) & buttock (41.7%). When stratified against BMI the risk of IM injection in the 25th-75th BMI percentile is higher in boys versus girls. Sites over abdomen and thigh remain at risk of IM injection across all BMI despite the shortest needle used. Therefore, we recommend a pinch-up skin fold for SC insulin injection at abdomen and thigh sites regardless of BMI percentile. Similar studies on the use of 4 mm needles were reported to be safer for all children in avoiding intramuscular delivery, more so when used in children aged 2–6 years old [6,8]. Another study analyzed the use of 4 & 5 mm needle for the abdomen and 4 mm for the arm to avoid the risk of intramuscular injection [5].

Conclusion

Although skin thickness increases with age, the risk of intramuscular injection is still high. The shorter needle of 4 mm is considered safest for children of all age groups, followed by 5 mm and 6 mm needle. The 8 mm and 12.7 mm needle carries a high risk of intramuscular injections in all age groups, therefore, should generally not be used in Pediatrics. If there are concerns of an intramuscular injection in young children or in children with low BMI, ultrasonography is a useful and quick office tool to measure ST and SCT to recommend appropriate needle length.
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Conflict of interest

Ms Lim STJ and all authors declare no conflict of interest.

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Fig. 6. Bar chart of mean total skin and subcutaneous thickness (SCT) at (a) abdomen, (b) arm, (c) thigh, and (d) buttocks of children from different body mass index (BMI)-for-age percentile groups (with reference to CDC Growth Chart 2000).
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