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Diabetes & Metabolism 42 (2016) 374–377

Research letter

Skin and subcutaneous tissue thickness at insulin injection sites in Chinese diabetes patients: Clinical implications

1. Introduction

China is currently experiencing an epidemic of diabetes. Affecting 11.6% of its adult population [1], the country has one of the highest prevalences of diagnosed diabetes in the world. Nearly 10 million diabetes patients are already being treated with insulin, and that figure is expected to climb to 15 million by 2020. Nevertheless, until the present study, there were no data on the anatomical characteristics of insulin injection sites in Chinese patients.

Injections must be performed in a technically precise fashion to ensure that the insulin is deposited in neither the intradermal (ID) nor intramuscular (IM) tissues, but consistently in the subcutaneous tissue (SCT) layer instead. This requires a judicious choice of needle length and meticulous technique performed for every injection by every patient, whether in a private home, office or other setting. The future challenge in China is to achieve this in 10s of millions of people several times a day for perhaps up to a lifetime.

To determine what needle length(s) are most appropriate for China, as well as the proper technique to use, it is imperative to know the actual metrics of skin thickness (ST) and SCT thickness (SCTT) in Chinese patients with diabetes. Only then can Chinese healthcare professionals (HCPs) recommend the proper technique and devices to their patients. Given this objective, high-frequency ultrasonography (US) was performed in a large, representative group of Chinese adults to measure ST and SCTT at all the usual injection sites.

2. Methods

A total of 508 Chinese patients between the ages of 18 and 85 years were enrolled. For inclusion, patients could be insulin injectors or not, but all had to have a diagnosis of either type 1 (T1DM) or type 2 diabetes mellitus (T2DM) for at least a year. Patients were excluded if they were pregnant, or had active or recurrent skin disorders or cancer, for which they were currently undergoing treatment. Enrolled patients provided written informed consent, and the study was performed in accordance with the principles of the Declaration of Helsinki. The study protocol was approved by the Ethics Committee of the Peking University First Hospital.

For each patient, a clinical report form collected basic demographic characteristics, diabetes history and treatment, as well as weight and height. A physical examination was performed, including a visual inspection of the four most commonly used insulin injection sites: abdomen; upper outer thigh; back of the arm; and upper buttock. These sites were then evaluated using ultrasonography (US). Measurements were taken with a portable MyLabTouch^{TM} ultrasound device, using a 33-mm, 13.6-MHz probe (Esaote Biomedica Deutschland GmbH, Köln, Germany) at a single location selected for each injection site. The body sites used for evaluation were standardized. Measurements for the abdomen were taken midway between the umbilicus and iliac crest; those for the thigh were taken midway between the iliac crest and top of the patella, while those for the arm were taken in the upper third of the distance from the acromion to olecranon and, for the buttock, in the upper outer quadrant. The side of the body (left or right) was randomly assessed.

Three independent investigators measured the ST, SCTT and skin-to-myofascial thickness (SMFT) on each US image. The average of these three measurements was used as the final value for analysis. Data were analyzed using SPSS 20.0 software (IBM, Armonk, NY, USA). Group data were compared using either independent *t*-tests or one-way analysis of variance (Anova). Evaluation of the influence of different factors on ST and SCTT was assessed by linear regression.

3. Results

Demographic data (Table 1) showed that our patients were representative of typical T1DM and T2DM Chinese patients throughout the country. Patients with T1DM were younger and thinner than the T2DM patients, whereas the T2DM patients taking insulin were slightly older, and had a body mass index (BMI) that was about 1 kg/m^2 higher than T2DM patients not taking insulin ($P < 0.01$). Mean (SD) ST ranged from 1.91 (0.35) mm in the arm to 2.68 (0.53) mm in the buttock (Table 2). ST was

Abbreviations: BMI, body mass index; G, gauge (of needle); GDM, gestational diabetes; HCP, healthcare professional; ID, intradermal; IM, intramuscular; ITQ, Injection Technique Questionnaire; NPH, neutral protamine Hagedorn (Humulin® N, Novolin® N); PD, pharmacodynamic; PK, pharmacokinetic; SC, subcutaneous; ST, skin thickness; SCT, subcutaneous thickness; SD, standard deviation; SMFT, skin-to-myofascial thickness; T1DM, type 1 diabetes mellitus; T2DM, type 2 diabetes mellitus; US, ultrasonography.

http://dx.doi.org/10.1016/j.diabet.2016.04.010

Table 1
Demographics of the study population ($n = 503$) by diabetes type/insulin use.

Characteristics	Type 1	Type 2/no insulin	Type 2/insulin
Subjects (*n*)	26	220	257
Gender, male	9 (34.6)	68 (31.3)[a]	117 (45.7)[b]
Age (years)			
Mean (SD)	44.7 (16.3)	57.3 (12.0)	63.9 (9.6)
Min/max	18/73	26/81	35/84
Age groups (years)			
18–39	10 (40.0)	20 (9.1)	4 (1.6)
40–59	8 (32)	100 (45.5)	80 (31.5)
60–85	7 (28)	100 (45.5)	170 (66.9)
Missing values (*n*)	1	0	3
BMI (kg/m^2)			
Mean (SD)	21.9 (3.0)	24.3 (3.1)	25.2 (3.1)
Min/max	17.2/30.1	17.6/32.7	18.3/34.9
BMI category			
BMI < 24	20 (76.9)	97 (44.1)	95 (37.0)
BMI ≥ 24 but < 28	5 (19.2)	99 (45.0)	114 (44.4)
BMI ≥ 28	1 (3.8)	24 (10.9)	48 (18.7)

Data are presented as *n* (%) unless otherwise stated.
BMI: body mass index
[a] Missing values for three patients.
[b] Missing values for one patient.

thinnest at the arm, with increasing values at the thigh, abdomen and buttock, in that order (data not shown), and men had slightly thicker STs than women at all injection sites (data not shown). ST measurements slightly > 4 mm were found in 2.2% (11/508) of the patients, but only for the buttock; 10 of these 11 were men. Subsequent enquiries into these 11 patients revealed no particular occupational, familial or pathological causes for their relatively increased STs in the buttock.

All patients were divided into three subgroups by BMI, and age, gender, BMI, type of diabetes and insulin/non-insulin use were transformed into categorical variables. Multivariate analysis demonstrated statistically significant and independent effects on the STs at all four sites for gender ($P < 0.01$) and BMI ($P < 0.01$). Age showed statistical significance only for the thigh ($P < 0.01$), and no statistical significance at the other three sites. Type of diabetes and insulin use showed no statistical significance at any of the sites.

Mean (SD) SCTT ranged from 7.23 (3.58) mm in the arm to 12.14 (4.90) mm in the abdomen (Table 2). The thinnest SCTT was in the arm, and increased in the thigh, buttocks and abdomen, in that order (Fig. 1). Female patients had thicker SCTTs than male patients at all injection sites by around 2–3 mm (Fig. 2). The mean (SD) SMFT ranged from 9.17 (3.72) mm in the arm to 14.53 (4.94) mm in the abdomen (Table 2).

Multivariate analysis of age, gender, BMI, type of diabetes and insulin/non-insulin use demonstrated a statistically significant and independent effect on SCTTs at all injection sites, and again for gender ($P < 0.01$) and BMI ($P < 0.01$). Age and insulin use showed no statistical significance at any site, whereas type of diabetes showed a statistical difference only for the arm ($P < 0.01$).

Estimates for the frequency of SCT, intradermal (ID) and intramuscular (IM) insulin delivery (using a 90° insertion angle) at each site with different needle lengths (and a 45° angle for 8-mm needles) are shown in Table 3. The overall percentage of SCT delivery with 4-mm needles was nearly 99%, but only 75% with 8-mm needles (with a 90° insertion angle). The risk of IM delivery was lowest with 4-mm needles (0.6%). Also, the IM

Table 2
Skin thickness (ST), subcutaneous tissue thickness (SCTT) and skin–myofascial thickness (SMFT) by body site.

Site	*n*	ST (mm)	95% CI	SCTT (mm)	95% CI	SMFT (mm)	95% CI
Arm	508	1.91 ± 0.35	1.88–1.94	7.23 ± 3.58	6.91–7.54	9.17 ± 3.72	8.84–9.49
Thigh	508	2.10 ± 0.39	2.06–2.13	7.37 ± 3.62	7.05–7.68	9.45 ± 3.66	9.13–9.77
Abdomen	508	2.47 ± 0.42	2.43–2.50	12.14 ± 4.90	11.71–12.56	14.53 ± 4.94	14.10–14.96
Buttock	508	2.68 ± 0.53	2.64–2.73	10.48 ± 4.34	10.10–10.86	13.17 ± 4.33	12.79–13.54

Data are presented as means ± SD.
95% CI: 95% confidence interval.

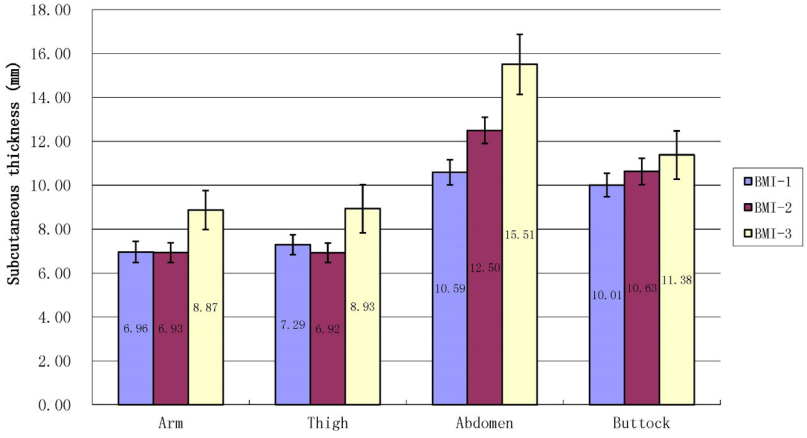

Fig. 1. Subcutaneous tissue thickness (means and 95% CI) by injection site and according to body mass index (BMI) group.