Journal of Diabetes and Metabolism
ISSN: 2155-6156

Akkus et al., J Diabetes Metab 2012, 3:8
DOI: 10.4172/2155-6156.1000216

Research Article Open Access

Evaluation of Skin and Subcutaneous Adipose Tissue Thickness for Optimal Insulin Injection

Oktay Akkus, Aytekin Oguz, Mehmet Uzunlulu* and Muhammed Kizilgul

Department of Internal Medicine, Istanbul Medeniyet University, Goztepe Training and Research Hospital, Istanbul, Turkey

Abstract

Patient's skin and subcutaneous adipose tissue thicknesses are the primary criteria that determine the optimal insulin needle length in subcutaneous insulin treatment. The present study aims to measure skin thickness and subcutaneous adipose tissue thickness in patients with diabetes mellitus and to investigate the association of these measurements with waist circumference and body mass index. The study included 449 subjects (152 patients with DM and 297 healthy controls, mean age: 44.58 ± 14.25 year) aged 18 years or older. The primary endpoint was the time of comparison of skin thicknesses and subcutaneous adipose tissue thicknesses between patients with diabetes mellitus and healthy subjects and the secondary endpoint was the time of assessment of the relationship between skin and subcutaneous adipose tissue thicknesses and body mass index and waist circumference. Skin and subcutaneous adipose tissue thicknesses were measured by ultrasonography. Overall, average skin thickness values were 1.95 mm (1.05-3.92) for triceps, 2.35 mm (1.07-3.82) for anterior abdomen and 1.97 mm (1.12-3.12) for anterior thigh, while subcutaneous adipose tissue thicknesses were 6.42 mm (1.01-33.5) for triceps, 15.73 mm (1.04-39.3) for anterior abdomen and 7.92 mm (1.48-31.6) for anterior thigh. Triceps and anterior thigh skin thickness values were higher in the diabetes mellitus group compared to healthy controls ($p<0.01$ for both) while subcutaneous adipose tissue thicknesses were similar between the two groups. There was a positive correlation between body mass index and waist circumference and between skin and subcutaneous adipose tissue thicknesses ($p<0.01$ for both). The largest skin thickness measured in the present study was 3.92 mm, which supports the previous reports that short needle tips could be used safely in individuals with diabetes mellitus.

Keywords: Skin thickness; Subcutaneous adipose tissue thickness; Insulin needles; Diabetes mellitus

Introduction

Delivering the drug safely to the subcutaneous tissue without any leakage or discomfort and selecting the appropriate needle length to achieve these are the objectives of insulin injections in diabetic patients [1]. It is recommended that the choice of needle length should be on an individual basis with consideration to physical, pharmacological and psychological factors [2-4]. Long needles that are recommended for adults (e.g., 12.7 mm) have been associated with an increased risk of intramuscular injection while shorter needles were shown to be safer and better tolerated even in obese individuals [5,6]. It has been demonstrated that patients using shorter needles (4 mm, 5 mm and 6 mm) did not experience more insulin leakage, pain or lipohypertrophy, nor did they experience worsening of complications or diabetes mellitus regulation [5-11]. Injection site skin thickness has been shown to vary minimally in diabetic adults depending on some demographics, including body mass index (BMI). Ultrasonography is described as a reliable method for measuring skin and subcutaneous adipose tissue thickness [12].

The purpose of the present study is to compare skin and subcutaneous adipose tissue thicknesses between healthy controls and patients with type 1 and type 2 diabetes using ultrasound and to investigate the association of these measurements with waist circumference and body mass index.

Materials and Methods

The study was performed with patients with type 1 and type 2 diabetes aged 18 years or older, who were being followed-up by Istanbul Medeniyet University Goztepe Training and Research Hospital, Department of Internal Medicine and Diabetes Polyclinics, and healthy individuals as controls. Approval of the local ethics committee of the hospital and written informed consents from the subjects were obtained for the study.

The diabetics group included patients with type 1 or type 2 diabetes mellitus diagnosed according to the American Diabetes Association (ADA) criteria [13] and the control group included healthy individuals who presented to the hospital for routine health checks and whose history did not include any known relevant diseases.

Demographical and anthropometric data of the subjects who met the inclusion criteria and provided consents were recorded.

The primary endpoint of the study sought to compare skin and subcutaneous adipose tissue thicknesses between diabetic patients and healthy controls. Skin thickness and subcutaneous adipose tissue thicknesses were evaluated by the type of diabetes and by whether the patient was on insulin therapy. The secondary endpoint aimed to assess the relationship between skin and subcutaneous adipose tissue thicknesses and BMI and waist circumference, for which a correlation analysis was performed.

Anthropometric measurements

Body weight, waist circumference and height measurements were

***Corresponding author:** Mehmet Uzunlulu, Department of Internal Medicine, Istanbul Medeniyet University, Goztepe Training and Research Hospital, Istanbul, Turkey, Tel: +90 216 4574385; Fax: +90 216 5655526; E-mail: mehmetuzunlulu@yahoo.com

Received August 14, 2012; **Accepted** September 17, 2012; **Published** September 21, 2012

Citation: Akkus O, Oguz A, Uzunlulu M, Kizilgul M (2012) Evaluation of Skin and Subcutaneous Adipose Tissue Thickness for Optimal Insulin Injection. J Diabetes Metab 3: 216. doi:10.4172/2155-6156.1000216

taken by the same person using standard measurement tools while the subjects were wearing hospital gowns, were on empty stomach and in standing position. Body weight was measured using conventional platform weighing machines. Waist and height measurements were taken using non-elastic measuring type with the patient in the standing position. Weight readings closest to 100 g and height readings closest to 1 cm unit were recorded. Waist circumference was taken as the narrowest diameter between arcus costarum and spina iliaca anterior superior. BMI was calculated using the Quetelet index as the patient's body weight divided by the square of his/her height (kg/m²).

Skin thickness and subcutaneous adipose tissue thickness for all subjects were measured by ultrasound at three different sites. Sites of measurement were the most widely preferred three sites for insulin injection: from the midpoint of the line extending from the posterior aspect of the upper arm triceps muscle, from 5 cm lateral of the umbilical point of the abdomen anterior, and from the anterior of the upper leg from the linear line centring the muscle extending from the quadriceps femoris muscle anterior on 1/3 area. MyLab™ Touch model (Esaote) portable, LCD touch-screen ultrasound device with 7.5-12 MHz range equipped with a linear probe and capable of recording the images and data to the memory were used for all measurements. When using the probe, care was taken to perform the measurement at the minimal pressure that enabled clear images. After taking skin thickness and subcutaneous adipose tissue thickness measurements in mm in all three sites described above, the data was recorded both on digital media and patient files.

Statistics

NCSS (Number Cruncher Statistical System) 2007 and PASS (Power Analysis and Sample Size Software) 2008 Statistical Software (Utah, USA) was used. In addition to descriptive statistical methods (mean, standard deviation), Kruskal-Wallis test was used for inter-group comparison of parameters without normal distribution and Mann Whitney U test was used to identify the group originating the difference while Mann Whitney U test was utilized for parameters without normal distribution for comparisons between the two groups. Chi-square test and Fisher's exact chi-square tests were used to compare qualitative data. Relationships between parameters were analyzed using Spearman's rho correlation coefficient. Statistical significance was set at $p<0.05$.

Results

The study included 449 subjects (141 males; 308 females; mean age: 44.58 ± 14.25). Demographic and anthropometric data of the whole study population is presented in table 1.

The diabetes group included 152 patients (16 with type 1 and 136 with type 2 diabetes) and the control group included 297 healthy individuals. In the diabetes group, there were 72 (47.4%) patients on insulin therapy with a mean therapy duration of 5.69 ± 5.76 years and a mean number of daily insulin injections of 2.74 ± 1.33 (3.80 ± 1.20 in patients with type 1 diabetes, 2.45 ± 1.22 in those with type 2 diabetes, $p<0.01$), and lipoatrophia was identified in 1 (1.4%). Two (2.8%) of the patients on insulin therapy were using 6 mm needles, 69 (95.8%) 8 mm needles and 1 (1.4%) 10 mm needles.

		Min-Max	Mean ± SD
Age (year)		18-80	44.58 ± 14.25
Waist circumference (cm)		60-135	92.46 ± 14.91
Body mass index (kg/m²)		16.85-66.20	28.83 ± 6.40
Skin thickness (mm)	Triceps	1.05-3.92	1.95 ± 0.38
	Anterior abdomen	1.07-3.82	2.35 ± 1.14
	Anterior thigh	1.12-3.12	1.97 ± 0.42
Subcutaneous adipose tissue thickness (mm)	Triceps	1.01-33.5	6.42 ± 5.97
	Anterior abdomen	1.04-39.3	15.73 ± 9.82
	Anterior thigh	1.48-31.6	7.92 ± 6.44

Table 1: Demographic and anthropometric data of the participants.

		Males (n=141)	Females (n=308)	*p*
Skin thickness (mm)	Triceps	1.99 ± 0.35 (1.94)	1.93 ± 0.40 (1.92)	0.079
	Anterior abdomen	2.35 ± 0.42 (2.31)	2.28 ± 0.42 (2.30)	0.183
	Anterior thigh	2.01 ± 0.35 (2.01)	1.95 ± 0.46 (1.92)	0.020
Subcutaneous adipose tissue thickness (mm)	Triceps	2.96 ± 2.35 (2.45)	8.01 ± 0.64 (4.86)	0.001
	Anterior abdomen	11.05 ± 8.44 (7.7)	17.87 ± 9.68 (17,6)	0.001
	Anterior thigh	3.65 ± 2.33 (3.05)	9.87 ± 6.77 (7.65)	0.001
Waist circumference (cm)		95.87 ± 10.65	90.91 ± 16.27	0.001
Body mass index (kg/m²)		27.56 ± 3.97	29.41 ± 7.18	0.001

Table 2: Skin thickness and subcutaneous adipose tissue thickness by gender.

Skin thickness and subcutaneous adipose tissue thickness measurements are presented in tables 2-4 by gender, BMI and insulin use. Anterior thigh skin thickness was higher in males than in females ($p=0.020$). Triceps, anterior abdomen and anterior thigh subcutaneous adipose tissue thicknesses were higher in females than in males ($p<0.01$ for all). Skin thickness and subcutaneous adipose tissue thickness increased with increasing BMI values for both genders. Skin thickness and subcutaneous adipose tissue thickness measurements did not differ significantly between patients who were using and who were not using insulin.

Waist circumference and body mass index were higher in patients with type 2 diabetes than in patients with type 1 diabetes and healthy controls ($p<0.01$ for both) (Table 5).

Skin thickness and subcutaneous adipose tissue measurements of the diabetes and control groups are shown by gender in tables 6 and 7. Triceps and anterior thigh skin thicknesses were higher in the diabetes group compared to healthy controls ($p<0.01$ for both). Triceps and anterior thigh skin thickness ($p=0.003$ and $p=0.015$, respectively) and anterior thigh subcutaneous adipose tissue thickness ($p=0.013$) measurements in diabetic males, triceps and anterior thigh skin thickness ($p=0.001$ for both) and anterior abdomen subcutaneous adipose tissue thickness ($p=0.004$) measurements in diabetic females were higher compared to healthy controls.

Skin and subcutaneous adipose tissue thickness measurements of patients with type 1 and type 2 diabetes are presented by gender in tables 8 and 9. In patients with type 2 diabetes, anterior abdomen subcutaneous adipose tissue thickness measurements were higher compared to type 1 diabetics ($p<0.01$). In women with type 2 diabetes, anterior abdomen subcutaneous adipose tissue thickness measurements were higher than in women with type 1 diabetes ($p=0.002$).

There was a positive relationship between BMI and triceps and anterior thigh skin thickness measurements in both men and women (in males: r: 0.257, $p<0.01$ and r: 0.235, $p<0.01$, respectively; in females: r: 0.270, $p<0.01$ and r: 0.436, $p<0.01$, respectively). BMI was positively correlated with triceps and anterior thigh subcutaneous adipose tissue thickness measurements (r: 0.292, $p<001$ and r: 0.462, $p<001$, respectively) in males, and with triceps, anterior abdomen and anterior thigh measurements (r: 0.322, $p<001$, r: 0.602, $p<0.01$ and r: 0.393, $p<0.01$, respectively) in females. Waist circumference was positively correlated with triceps (r: 0.264, $p<0.01$) and anterior

			Body mass index (kg/m²)				*p*
			<25	25-29.9	30-39.9	≥ 40	
Males	Skin thickness (mm)	Triceps	1.82 ± 0.29	2.01 ± 0.28	2.13 ± 0.45	-	0.001
		Anterior abdomen	2.29 ± 0.36	2.37 ± 0.39	2.39 ± 0.52	-	0.836
		Anterior thigh	1.92 ± 0.27	2.65 ± 0.96	4.16 ± 4.14	-	0.002
	Subcutaneous adipose tissue thickness (mm)	Triceps	2.30 ± 0.72	2.65 ± 0.96	4.16 ± 4.14	-	0.001
		Anterior abdomen	8.24 ± 7.76	11.10 ± 8.29	13.84 ± 8.64	-	0.002
		Anterior thigh	2.68 ± 0.82	2.23 ± 1.39	5.38 ± 3.55	-	0.001
Females	Skin thickness (mm)	Triceps	1.81 ± 0,37	1.89 ± 0.41	2.03 ± 0.38	2.09 ± 0.44	0.001
		Anterior abdomen	2.21 ± 0.45	2.28 ± 0.36	2.35 ± 0.43	2.33 ± 0.42	0.084
		Anterior thigh	1.77 ± 0.51	1.90 ± 0.33	2.07 ± 0.36	2.27 ± 0.64	0.001
	Subcutaneous adipose tissue thickness (mm)	Triceps	5.87 ± 4.01	6.73 ± 5.05	9.62 ± 7.38	13.44 ± 8.90	0.001
		Anterior abdomen	10.61 ± 7.47	17.62 ± 8.31	22.45 ± 8.12	26.87 ± 9.10	0.001
		Anterior thigh	7.30 ± 5.45	8.59 ± 5.35	11.78 ± 7.31	15.69 ± 7.09	0.001

Table 3: Skin thickness and subcutaneous adipose tissue thickness by body mass index values in genders.

		Insulin users (n=72)	Non-insulin users (n=80)	*p*
Skin thickness (mm)	Triceps	2.11 ± 0.47 (2.08)	2.08 ± 0.38 (2.15)	0.931
	Anterior abdomen	2.35 ± 0.41 (2.32)	2.31 ± 0.44 (2.23)	0.477
	Anterior thigh	2.19 ± 0.49 (2.15)	2.06 ± 0.31 (2.03)	0.100
Subcutaneous adipose tissue thickness (mm)	Triceps	7.15 ± 7.03 (3.93)	7.19 ± 6.59 (4.01)	0.757
	Anterior abdomen	16.85 ± 10.12(16.9)	17.01 ± 10.08(16.5)	0.688
	Anterior thigh	8.43 ± 6.91 (5.42)	8.32 ± 6.97 (4.67)	0.564

Table 4: Skin thickness and subcutaneous adipose tissue thickness by insulin usage.

	Type 1 Diabetes (n=16)	Type 2 Diabetes (n=136)	Healthy control group (n=297)	*p*
Body mass index (kg/m²)	26.51 ± 5,5	32.43 ± 5.61	28.83 ± 6.40	0.001
Waist circumference (cm)	87.25 ± 16.14	102.67 ± 11.53	92.46 ± 14.91	0.001

Table 5: Comparative body mass index and waist circumference measurements between the type 1 and type 2 diabetes patients and healthy control groups.

		Diabetes group (n=152)	Healthy controls group (n=297)	*p*
Skin thickness (mm)	Triceps	2.09 ± 0.42 (2.09)	1.87 ± 0.34 (1.86)	0.001
	Anterior abdomen	2.32 ± 0.42 (2.31)	2.30 ± 0.43 (2.30)	0.768
	Anterior thigh	2.12 ± 0.41(2.08)	1.89 ± 0.41 (1.87)	0.001
Subcutaneous adipose tissue thickness (mm)	Triceps	7.13 ± 6.78 (3.95)	6.06 ± 5.49 (3.75)	0.197
	Anterior abdomen	16.91 ± 10.09 (16.9)	15.18 ± 9.65 (14)	0.097
	Anterior thigh	8.31 ± 6.90 (4.90)	7.72 ± 6.19 (5.0)	0.248

Table 6: Comparative skin thickness and subcutaneous adipose tissue thickness between the diabetes and healthy control groups.

thigh skin thickness (r: 0.240, p<0.01) measurements in males, and with triceps (r: 0.249, p<0.01), anterior abdomen (r: 0.124, p<0.05) and anterior thigh (r: 0.419, p<0.01) skin thickness measurements in women. Waist circumference was positively correlated with triceps (r: 0.253, p<0.01), anterior abdomen (r: 0.400, p<0.01) and anterior thigh (r: 0.484, p<0.01) thickness measurements in males, and with triceps (r: 0.282, p<0.01), anterior abdomen (r: 0.580, p<0.01) and anterior thigh (r: 0.334, p<0.01) subcutaneous adipose tissue thickness measurements in females. Age was positively correlated with BMI and waist circumference in both men and women in the multiple regression analysis (p<0.01 for both).

Discussion

The results of the present study demonstrated higher skin and, more markedly, subcutaneous adipose tissues thicknesses in subjects with higher waist circumference and body mass index. The largest skin thickness measured in the present study was 3.92 mm, which supports the previous reports that short needle tips could be used safely in individuals with diabetes mellitus.

Although 8 mm needles are usually preferred for insulin injections in daily practice, 6 mm and 12 mm needles based on the individual's BMI and adipose tissue reserve are also being recommended and the physicians tend to prefer longer needles with increasing severity of obesity. In a study by De Coninck et al. 63% of the subjects who were on insulin therapy used 8 mm or longer needles [14]. In most countries, 8 mm or longer needles are recommended for obese patients [15,16].

In the present study, average skin thickness values were 1.95 mm (1.05-3.92) for the arm, 2.35 mm (1.07-3.82) for the abdomen and 1.97 mm (1.12-3.12) for the leg. The finding of the present study that the highest skin thickness value for the participants was 3.92 mm may suggest that needles shorter than the conventional ones (6.8 mm and 10 mm length) are capable of completely penetrating through the skin. In addition, intramuscular injection resulting from the needle penetrating

			Diabetes group (n=152)	Healthy controls group (n=297)	*p*
Males	Skin thickness (mm)	Triceps	2.12 ± 0.39 (2.12)	1.92 ± 0.31 (1.86)	0.003
		Anterior abdomen	2.35 ± 0.43 (2.31)	2.36 ± 0.42 (2.32)	0.769
		Anterior thigh	2.11 ± 0.37 (2.08)	1.97 ± 0.33 (1.94)	0.015
	Subcutaneous adipose tissue thickness (mm)	Triceps	2.81 ± 1.16 (2.48)	3.03 ± 2.77 (2.45)	0.469
		Anterior abdomen	9.83 ± 6.67 (7.93)	11.68 ± 9.19(7.45)	0.605
		Anterior thigh	3.97 ± 2.76 (3.16)	3.48 ± 2.35 (2.84)	0.013
Females	Skin thickness (mm)	Triceps	2.08 ± 0.44 (2.05)	1.85 ± 0.35 (1.86)	0.001
		Anterior abdomen	2.31 ± 0.42 (2.30)	2.27 ± 0.43 (2.30)	0.610
		Anterior thigh	2.12 ± 0.43 (2.08)	1.86 ± 0.44 (1.86)	0.001
	Subcutaneous adipose tissue thickness (mm)	Triceps	9.14 ± 7.36 (6.80)	7.44 ± 5.87 (4.53)	0.081
		Anterior abdomen	20.19 ± 9.73(20.8)	16.71 ± 9.46(15.7)	0.004
		Anterior thigh	10.33 ± 7.39(7.81)	9.64 ± 6.44 (7.65)	0.592

Table 7: Skin thicknesses and subcutaneous adipose tissue thicknesses of diabetic patients and healthy controls by gender.

		Tip 1 diabetes (n=16)	Type 2 diabetes (n=136)	*p*
Skin thickness (mm)	Triceps	1.99 ± 0.33 (2.06)	2.11 ± 0.43 (2.10)	0.303
	Anterior abdomen	2.33 ± 0.38 (2.31)	2.33 ± 0.43 (2.30)	0.988
	Anterior thigh	1.94 ± 0.43 (1.96)	2.14 ± 0.41 (2.08)	0.098
Subcutaneous adipose tissue thickness (mm)	Triceps	4.72 ± 3.70 (3.16)	7.46 ± 7.01 (4.12)	0.194
	Anterior abdomen	10.76 ± 7.8 (8.08)	17.66 ± 10.07 (17.43)	0.009
	Anterior thigh	6.54 ± 4.87 (4.12)	8.58 ± 4.87 (4.12)	0.341

Table 8: Skin thicknesses and subcutaneous adipose tissue thicknesses of patients with type 1 and type 2 diabetes.

			Type 1 diabetes (n=16)	Type 2 diabetes (n=136)	*p*
Males	Skin thickness (mm)	Triceps	1.95 ± 0.27 (1.93)	2.15 ± 0.40 (2.16)	0.164
		Anterior abdomen	2.45 ± 0.45 (2.38)	2.33 ± 0.43 (2.24)	0.548
		Anterior thigh	1.94 ± 0.38 (2.02)	2.14 ± 0.36 (2.10)	0.328
	Subcutaneous adipose tissue thickness (mm)	Triceps	2.92 ± 0.63 (2.98)	2.79 ± 1.24 (2.45)	0.373
		Anterior abdomen	11.18 ± 8.11(8.46)	9.60 ± 6.48 (6.61)	0.627
		Anterior thigh	4.86 ± 3.26 (3.72)	3.82 ± 2.08 (3.12)	0.343
Females	Skin thickness (mm)	Triceps	2.02 ± 0.38 (2.10)	2.09 ± 0.45 (2.03)	0.764
		Anterior abdomen	2.22 ± 0.32 (2.15)	2.33 ± 0.43 (2.31)	0.484
		Anterior thigh	1.95 ± 0.48 (1.71)	2.15 ± 0.42 (2.08)	0.176
	Subcutaneous adipose tissue thickness (mm)	Triceps	6.12 ± 4.51 (4.16)	9.47 ± 7.50 (7.09)	0.174
		Anterior abdomen	10.44 ± 8.04(6.09)	21.14 ± 9.34(21.6)	0.002
		Anterior thigh	7.86 ± 5.47 (4.68)	10.64 ± 7.51 (8.6)	0.248

Table 9: Skin thicknesses and subcutaneous adipose tissue thicknesses in patients with type 1 and type 2 diabetes by gender.

beyond the subcutaneous adipose tissue common with other needles may be less likely with shorter needles. As a matter of fact, most of the needle lengths recommended for adults (e.g., 12.7 mm) and paediatrics (e.g., 8 mm) are now abandoned since these needles resulted in intramuscular injections. Shorter needles are safer and better tolerated. Comparable efficacy, safety and tolerability between shorter needles (5 mm and 6 mm) and longer needles (8 mm, 12.7 mm) have been shown even in studies with obese individuals. There is no evidence to suggest an increased incidence of insulin leakage, pain, lipohypertrophy or deteriorated diabetes regulation or complications in patients using shorter needles (4 mm, 5 mm, 6 mm) [1].

In the present study, average subcutaneous adipose tissue thickness was 6.42 mm (1.01-33.5) in the arm, 15.73 mm (1.04-39.3) in the abdomen and 7.92 mm (1.48-31.6) in the leg. There was a positive correlation between increasing BMI and waist circumference values and subcutaneous adipose tissue thickness. It should be noted that the present study included diabetic patients as well as healthy individuals, and that wider ranges were used for BMI (16.85-66.20 kg/m^2) and waist circumference (60-135 cm). It was also interesting that there were subjects with subcutaneous adipose tissue thicknesses as low as 1.01 mm in proportion to lower BMI and waist circumference. Remarkably, there were subjects whose combined skin and subcutaneous adipose tissue thickness was even lesser than 5 mm in our population, in which the thickest skin was measured as 3.92 mm. It is known that patients with type 1 diabetes in particular have low BMIs and therefore administration with conventional needle lengths (6 mm, 8 mm, 10 mm) without pinching the skin and/or with an angle of 90° may result in penetration to the muscular zone. This indicates that care should be taken when training these patients on the injection technique, but since there are no criteria or standardization as to which specific technique should to be recommended to certain groups of patients, this may also be interpreted as a challenge of administration and inadequacy on the

part of the needles. With shorter needles, on the other hand, it may be possible to perform injections without pinching the skin and directly with an angle of 90°.

Female subjects' subcutaneous adipose tissue thicknesses in all three sites were higher compared to those in male subjects. This may suggest that insulin injections resulting in intramuscular exposure may be more likely in males.

Subcutaneous adipose tissue thicknesses of diabetic patients were higher compared to healthy individuals. This may be associated with higher amount of adipose tissue due to insulin resistance in type 2 diabetes.

Lipoatrophia and hypertrophy are well-known complications of insulin treatment [17]. However, these do not represent a common disorder of skin and subcutaneous adipose tissues but are rather local complications. In the present study, diabetic patients using and not using insulin did not differ significantly in terms of skin thickness and subcutaneous adipose tissue thickness measurements. This result indicated that changes in skin thickness and subcutaneous adipose tissue thickness with insulin treatment in time is not to be expected and that the needle preferred at the start of treatment may still be used safely during the later stages of the disease process.

Study population has a wide age ranges in our study. In the multiple regression analysis, age was positively correlated with BMI and waist circumference in both man and women. Therefore age factor should also be taken into consideration while making comment.

Conclusion

Skin and more markedly subcutaneous adipose tissue were thicker in subjects with higher waist circumferences and body mass indices. The finding that the largest skin thickness measured among our patients was 3.92 mm supports the previous reports that shorter needle tips could be used safely in individuals with diabetes mellitus.

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