Comparison of the Effectiveness of Subcutaneous Insulin Injection between Upper Arm and Abdominal Sites in Type II Diabetes Mellitus Patients with Normal and Above Normal Body Mass Index

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ABSTRACT

Background. Type II Diabetes Mellitus (DM) has high morbidity and mortality. One of DM therapy is insulin. Insulin effectiveness is affected by the injection site and the thickness of the fat in the injection site. Several studies on the effectiveness of insulin injection sites have been conducted, but the results still vary.
Objective. To determine the difference in the effectiveness of subcutaneous insulin injections between the upper arm and abdominal sites on changes in capillary glucose levels in type II diabetes mellitus patients with normal and above-normal body mass index (BMI).
Methods. The research design used a quasi-experimental repeated measure design. The research subjects were patients diagnosed with type II DM, age ≥ 40 years, hospitalized in the ward of Dr. Sardjito Hospital Yogyakarta. The effectiveness of insulin injection is described by the difference between 2-hours postprandial glucose (2hPPG) minus fasting blood glucose (FBG) (Δ2hPPG-FBG). Δ2hPPG-FBG was taken on the site of the upper arm and abdomen. Patients were classified based on normal and above normal BMI. Statistical analysis was performed using paired T-tests.
Result. There were 14 patients with normal BMI and 11 patients with above normal BMI. Paired T-test showed a significant difference in Δ2hPPG-FBG between the upper arm and abdominal sites in normal BMI patients (p=0.028) with a mean of Δ2hPPG-FBG for the upper arm site of 26,14±38.18 mg/dL, and a mean of Δ2hPPG-FBG of the abdominal site -0.64±50,62 mg/dL. Paired T-test showed no significant difference in Δ2hPPG-FBG between the upper arm and abdominal sites in patients with an above-normal BMI (p = 0.239).
Conclusion. The effectiveness of subcutaneous insulin injection in the abdominal site was better than in the upper arm site in patients with normal BMI. There was no difference in the effectiveness of subcutaneous insulin injection between the upper arm and abdominal sites in patients with an above-normal BMI.

Keywords. Effectiveness of insulin injection, abdominal site, upper arm site, BMI

Abstrak

Latar Belakang. *Diabetes Mellitus (DM) tipe II memiliki morbiditas dan mortalitas yang tinggi. Salah satu terapi DM adalah insulin. Efektivitas insulin dipengaruhi oleh tempat suntikan dan ketebalan lemak di tempat suntikan. Beberapa penelitian tentang efektivitas tempat suntikan insulin telah dilakukan, namun hasilnya masih bervariasi.*
Tujuan. *Untuk mengetahui perbedaan efektivitas penyuntikan insulin subkutan antara lengan atas dan daerah abdomen terhadap perubahan kadar glukosa kapiler pada pasien diabetes melitus tipe II dengan indeks massa tubuh (IMT) normal dan di atas normal.*
Metode. *Desain penelitian menggunakan quasi-experimental repeat measure design. Subyek penelitian adalah pasien yang didiagnosis DM tipe II, usia 40 tahun, dirawat inap di ruang IRNA 1 RSUP Dr.Sardjito Yogyakarta. Efektivitas injeksi insulin digambarkan oleh perbedaan antara glukosa 2 jam postprandial (2hPPG) dikurangi glukosa darah puasa (FBG)*

(⊿2hPPG-FBG). 2hPPG-FBG diambil di lokasi lengan atas dan perut. Pasien diklasifikasikan berdasarkan BMI normal dan di atas normal. Analisis statistik dilakukan dengan menggunakan uji T berpasangan.

***Hasil**. Terdapat 14 pasien dengan IMT normal dan 11 pasien dengan IMT di atas normal. Uji T berpasangan menunjukkan perbedaan yang signifikan dalam 2hPPG-FBG antara lengan atas dan situs perut pada pasien BMI normal (p=0,028) dengan rata-rata 2hPPG-FBG untuk situs lengan atas 26,14±38,18 mg/dL, dan a rata-rata 2hPPG-FBG dari situs perut -0,64±50,62 mg/dL. Uji T berpasangan menunjukkan tidak ada perbedaan signifikan dalam 2hPPG-FBG antara lengan atas dan bagian perut pada pasien dengan BMI di atas normal (p = 0,239).*

***Kesimpulan.** Efektivitas injeksi insulin subkutan di daerah abdomen lebih baik daripada di daerah lengan atas pada pasien dengan IMT normal. Tidak ada perbedaan efektivitas injeksi insulin subkutan antara lengan atas dan bagian perut pada pasien dengan BMI di atas normal.*

***Kata kunci.** Efektivitas injeksi insulin, daerah perut, daerah lengan atas, IMT*

Introduction

Diabetes Mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia due to abnormalities in insulin secretion, insulin action, or both.[1] Epidemiological research shows a trend of increasing the incidence and prevalence of type II DM in various parts of the world. The International Diabetes Federation (IDF) predicts an increase in the number of people with diabetes in Indonesia from 9.1 million in 2014 to 14.1 million in 2035.[2,3] About 1.5 million deaths worldwide that were directly caused by diabetes in 2012.[4] One of the DM managements is insulin therapy.[3] The correct injection of insulin is essential to optimize the drug's effect and achieve the glycemic target. One of the factors that contribute to the effectiveness of insulin injection is the insulin injection location.[4] Recommended locations for subcutaneous insulin injections are abdomen, gluteal, upper arms, and thigh[5].

This research is a sub-analysis of a study that analyzes the comparison of the effectiveness of subcutaneous insulin injection between the upper arm and abdomen to changes in capillary glucose levels in patients with type II DM at Dr. Sardjito Hospital Yogyakarta. Vora's study in 1992 showed a positive correlation between the rate of insulin absorption and subcutaneous blood flow (SBF) and a negative correlation between body mass index (BMI), fat thickness, and insulin absorption rate.[6] Several researches have shown that the most effective sites for insulin injection are the abdominal site followed by the upper arm and thigh sites.[6,7,8] However, other research has shown no significant difference between these sites.[9] Research by Adams in 2005 showed a negative correlation between fat thickness and SBF (a study compared samples with various fat thicknesses in the abdominal site and their effect on SBF).[10] Alam and Chowdhury's research in 2016 showed that 100% of overweight and obese patients were central obesity, although 9% of normal BMI patients were accompanied by central obesity.[11] Based on these data, patients with overweight and obese status are most likely to have central obesity with a dominant fat thickness in the abdominal site, thus slowing insulin absorption in the abdominal site.

Based on the data above, it was conducted comparative analysis of Δ2hPPG-FBG between the upper arm and abdominal sites in patients with normal and above normal BMI. This research focuses on more effective insulin injection sites based on BMI. The purpose of this study was to determine the difference in the effectiveness of subcutaneous insulin injection between the upper arm and abdominal sites on the changes in capillary glucose levels in patients with type II DM with normal and above normal BMI.

Methods

The research design was a quasi-experimental repeated measure design. Samples were taken from in-patient unit (IRNA 1 ward) at Dr. Sardjito Hospital Yogyakarta. A comparison of the effectiveness of insulin in the upper arm and abdominal site was performed on each sample so that each sample received 2 types of treatment. The first treatment was measuring the effectiveness of insulin aspart in the upper arm site. The second treatment was measuring the effectiveness of insulin aspart in the abdominal site. Comparative analysis of the effectiveness of insulin in the upper arm and abdominal site was performed on samples with normal BMI (BMI 18.5-22.9 kg/(m^2)) and above normal BMI (BMI> 23 kg/(m^2)).

The research subject was patients diagnosed with type II DM, age ≥ 40 years, hospitalized in the IRNA 1 ward Dr. Sardjito Hospital, who met the inclusion and exclusion criteria. The inclusion criteria in this study were admitted patients with a diagnosis of type II DM, using aspart insulin, and in a stable condition (compos mentis, systolic blood pressure 90-140 mmHg, diastolic blood pressure 60-90 mmHg, pulse 60-100 times/minute, respiration rate 12-21 times/minute, temperature 36.5°C - 37.5°C). The exclusion criteria in this study were getting steroid therapy or therapy that increased sympathetic stimulation (such as norepinephrine, dopamine, and dobutamine), receiving oral antidiabetic therapy that affects prandial blood glucose (alpha-glucosidase inhibitor, acarbose; GLP-1/ incretin mimetic agonists, namely liraglutide, albiglutide, lixisenatide; and the DPP-4 inhibitors, namely sitagliptin, vildagliptin, saxagliptin, linagliptin), and receive insulin therapy with mixed preparations (e.g. human premixed insulin).

The minimum time interval between the measuring effectiveness of insulin in the upper arm site and abdominal site is 24 hours, in accordance with the minimum time limit of the two treatments, which must exceed the duration of insulin aspart (duration of insulin aspart is 5 hours).[12] Samples were obtained by consecutive sampling methods.

The dependent variable in this study is the effectiveness of insulin injection which is represented by Δ2hPPG-FBG. The smaller Δ2hPPG-FBG, the more effective insulin injection is. The definition of the effectiveness of insulin injection (Δ2hPPG-FBG) in this study is based on the function and effect of insulin action in reducing blood sugar levels.[13] The definition of the effectiveness of insulin injection (Δ2hPPG-FBG) in this study is also an improvement of the previous study on the effectiveness of insulin injection by Santosa and Rosa in 2014 that measured the effectiveness of insulin injection through 2hPPG levels. The independent variable is the insulin injection location (the upper arm site and abdominal site). Baseline characteristics data included sex, age, BMI, the onset of DM, hypertension, macrovascular disease (coronary artery disease, stroke, and peripheral artery disease), impaired kidney function, breakfast calories, and insulin dose.

The series of measuring the effectiveness of insulin is that the patient is checked for FBG levels in the morning before the patient has breakfast. Aspart insulin was administered before consuming a certain number of calories. The number of calories and the dose of insulin administered during treatment in the upper arm site and abdominal sites were the same in one sample. Next, the 2hPPG levels were checked. The effectiveness of insulin injection was calculated based on Δ2hPPG-FBG.

The effectiveness of insulin injection between the upper arm site and abdominal sites was compared by statistical analysis.

Bivariate analysis of paired T-tests would be used to analyze the significance of the difference in the Δ2hPPG-FBG between the upper arm and the abdominal sites if the Δ2hPPG-FBG data were normally distributed. If the data distribution is not normally distributed, an analysis would be carried out using the non-parametric Wilcoxon test. A p-value <0.05 would be considered statistically significant.

Result and Discussion

This research was conducted from November 2020 to January 2021. There were 36 patients who met the research criteria, with 11 patients who dropped out due to returned discharge before the second treatment day, the routine dose of insulin changed, or the patient did not eat the same number of calories as during the first treatment. A total of 25 patients were included in the study.

One sample and another sample have different characteristics, such as insulin dose, breakfast calories, and BMI. However, these differences have been controlled by analyzing the data using the paired T-test method. The baseline characteristics of the samples treated on the upper arm site and the samples treated on the abdominal site were the same. This is because the research design used is a repeated measure design method.

The mean level of FBG level in the upper arm site in the whole sample was 157.20±55.46 mg/dL and the mean level of FBG in the abdominal site in the whole sample was 152.60± 53.03 mg/dL. The mean 2hPPG level in the upper arm site in the whole sample was 174.20±75.79 mg/dL and the mean 2hPPG level in the abdominal site in the whole sample was 162.20±60.57 mg/dL.

The mean Δ2hPPG-FBG in the upper arm site was 17.0±43.33 mg/dL, and the mean Δ2hPPG-FBG in the abdominal site was 9.6±44.62 mg/dL. Based on the calculation of the Shapiro-Wilk formula, the data distribution of Δ2hPPG-FBG for the upper arm site and the abdominal site was normal so it can be continued into the paired T-test (Table 2). The standard deviation (SD) number was greater than the mean, but the data were still normally distributed because the data ranges from -49 to 107 in the upper arm site, and between -77 to 88 in the abdominal site so the mean looks smaller than SD.

Table 1. Baseline characteristics

Baseline characteristics		n(%) or mean±SD or median(min-max) (sample = 25)
Sex	Men	36 %
	Women	64 %
Age (years)		56.2 ± 6,02
BMI (kg/m²)		23.63 ± 4,67
DM onset (months)		36 (1-240)
Hypertension	Yes	32 %
	No	68 %
Macrovascular disease	Yes	24 %
	No	76 %
Impaired kidney function	Yes	8 %
	No	92 %
Breakfast calories (calories)		371.16 ± 57.87
Insulin dose (unit)		7.08 ± 3.32

Table 2. Comparative analysis of Δ2hPPG-FBG between the upper arm and abdominal sites in whole samples

Δ2hPPG-FBG	n	Mean ±SD	Median (min-max)	p
Upper arm site	25	17.0± 43.33	14 ((-49) – (107))	0.444
Abdominal site	25	9.6± 44.62	24 ((-77) – (88))	

Paired T-test results showed no significant difference in Δ2hPPG-FBG between the upper arm and abdominal site

(p=0.444). This showed that the effectiveness of insulin injection in the abdominal site was no better than in the upper arm site in the whole sample.

The possibility that causes the results of this study to differ from previous studies could be due to the excessive thickness of the fat in the abdominal site in certain samples (patients with central obesity) which led to the slow absorption of insulin in the abdominal site. Research conducted by Vora et al in 1992 showed that BMI and fat thickness have a negative correlation to insulin absorption rate[6]. Research by Adams et al in 2005 showed that the greater thickness of the fat causes the slower the subcutaneous blood flow (a study compared samples with various thicknesses of fat in the abdominal site and its effect on SBF).[10]

Table 3. Baseline characteristics of normal BMI samples

Baseline characteristics		n(%) or mean±SD or median (min-max) (sample = 14)
Sex	Men	21.4 %
	Women	78.6 %
Age (years)		57.0 ± 6.03
BMI (kg/m²)		20.49 ± 1.39
DM onset (months)		48 (3-240)
Hypertension	Yes	28.6 %
	No	71.4 %
Macrovascular disease	Yes	14,3 %
	No	85,7 %
Impaired kidney function	Yes	0 %
	No	100 %
Breakfast calories (calories)		373,07 ± 40,12
Insulin dose (unit)		6,85 ± 3,61

Furthermore, a comparative analysis of Δ2hPPG-FBG between the upper arm and abdominal site in patients with normal BMI was performed to reduce the confounding excess fat thickness in the abdominal site that might be found in patients with a BMI above normal. The total sample with normal BMI was 14 samples.

The mean FBG level in the upper arm site in samples with normal BMI was 161,07±65,45 mg/dL and the mean FBG level in the abdominal site in samples with normal BMI was 160±58,02 mg/dL. The mean 2hPPG level in the upper arm site in samples with normal BMI was 187,21±83,98 mg/dL and the mean 2hPPG level in the abdominal site in samples with normal BMI was 159,85±65,13 mg/dL.

In patients with normal BMI, the mean 2hPPG-FBG in the arm site was 26,14±38,18 mg/dL, and the mean Δ2hPPG-FBG in the abdominal site was -0,64±50,62 mg/dL. Based on the calculation of the Shapiro-Wilk data distribution formula, the data distribution of Δ2hPPG-FBG for the upper arm site and the distribution of Δ2hPPG-FBG data for the abdominal site is normal, so it can be continued into the paired T-test.

Table 4. Comparative analysis of Δ2hPPG-FBG between the upper arm and abdomen in a sample with normal BMI

Δ2hPPG-FBG	n	Mean± SD	Median (min-max)	p
Upper arm site	14	26.14± 38.18	32 ((-30) – (76))	0.028
Abdominal site	14	-0.64± 50.62	-11.5 ((-77) – (78))	

The paired T-test showed a significant difference in Δ2hPPG-FBG between the upper arm and abdominal site in samples with normal BMI (p = 0.028) with a smaller Δ2hPPG-FBG in the abdominal site. This showed that insulin injection in the abdominal site was more effective in lowering blood glucose compared to the upper arm site patients with normal BMI.

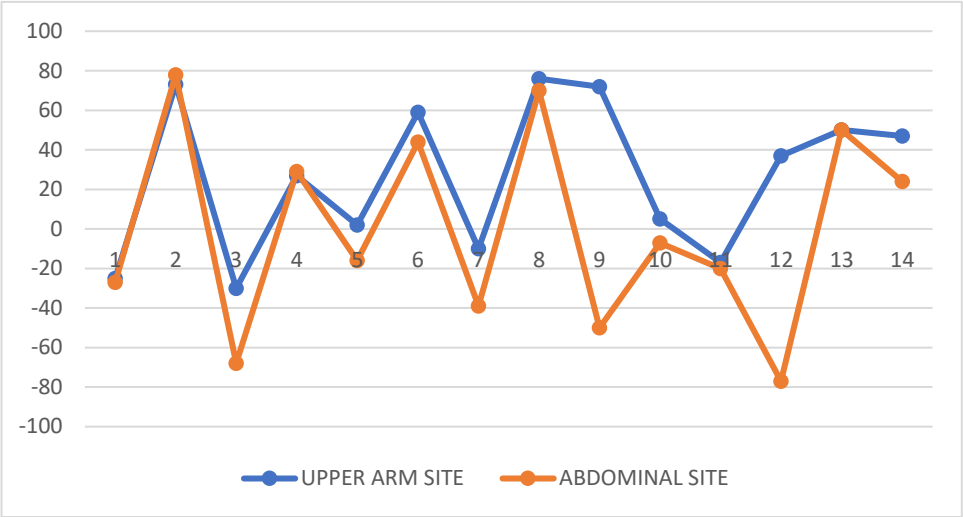

Figure 1. Δ2hPPG-FBG between the upper arm and abdominal sites in samples with normal BMI

Specificity of the group of patients with a normal BMI may reduce confusion in the study results caused by the excessive fat thickness of the abdominal site in patients with BMI above normal. The better effectiveness of insulin injection in the abdominal site is associated with a greater absorption rate in the abdominal site than the upper arm site, and that is associated with a greater SBF in the abdominal site. The results of this research support previous research by Vora et al. in 1992, Ter Braak et al. in 1996, and Santosa and Rosa in 2014 who stated that the insulin absorption rate in the abdominal site was faster than in the upper arm site.[6,7,8] However, in this research, the superiority of SBF in the abdominal site was only found in patients with normal BMI.

Further analysis was conducted on the group of patients with an above-normal BMI (overweight and obese). The mean FBG level in the upper arm site in the sample with a BMI above normal was 152,27±42,00 mg/dL and the mean FBG level in the abdominal site in samples with a BMI above normal was 142,54±46,64 mg/dL. The mean 2hPPG level in the upper arm site in samples with BMI above normal was 157,63±63,88 mg/dL and the mean 2hPPG level in the upper arm site in samples with BMI above normal was 165,18±57,22 mg/dL.

In patients with an above normal BMI (overweight and obese), the mean Δ2hPPG-FBG for the upper arm site was 5,36±48,42 mg/dL, and the mean 2hPPG-FBG in the abdominal site was 22,63±34,09 mg/dL. Based on the calculation of the Shapiro-Wilk data distribution formula, the data distribution of Δ2hPPG-FBG for the upper arm site and the distribution of Δ2hPPG-FBG data for the abdominal site were normal. Thus, it could be continued into the paired T-test.

Table 5. Comparative analysis of Δ2hPPG-FBG in samples with above normal BMI (overweight and obese)

Δ2hPPG-FBG	n	Mean± SD	Median (min-max)	p
Upper arm site	11	5.36 ±48.42	7 ((-49) – 107))	0.239
Abdominal site	11	22.63 ±34.09	27 ((-29) – (88))	

The Paired T-test results showed no significant difference in Δ2hPPG-FBG between the upper arm and abdominal site in

patients with a BMI above normal (p = 0.239). This can be due to the dominant thickness of fat in the abdominal site, which caused a decrease in SBF and caused a decrease in insulin absorption rate.[6,7] Research by Frayn and Humphreys in 2012 showed that in obese patients there was a decrease in SBF.[14] In normal patients, there is an increase of SBF after meals, and this is impaired in obese patients. The mechanism underlying this downregulation is due to decreased responsiveness to adrenaline in the fat tissue of obese patients.[15,16] Another thing that causes the low SBF in sites with excess fat thickness is adipocyte hypertrophy which is not supported by a sufficient increase in vascular growth.[10]

Conclusion

This study concludes that there is a significant difference in the effectiveness of subcutaneous insulin injection between the upper arm and the abdominal sites in samples with normal BMI, with better effectiveness in the abdominal site compared to the upper arm site. In samples with a BMI above normal, there is no significant difference in the effectiveness of subcutaneous insulin injections between the upper arm and the abdominal sites. In further research, it is necessary to measure the thickness of the fat in the upper arm and abdominal site and to measure the circumference of the upper arm and abdomen.

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