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Original Article

Insulin injection site and time interval administration for the postprandial glucose control in patient with diabetes type 2: A randomized clinical trial

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ABSTRACT

Background & Aim: insulin injection to the patients suffered from diabetes mellitus need to consider the dose, route, time and injection spot since it will affect to postprandial blood sugar. This study aimed to determine the effectiverness of insulin injection site and interval timing administration to the control of postprandial glucose in diabetes mellitus patients type 2.
Methods & Materials: The study was an experimental with Randomized Complete Block Design (RCBD). The population were patients with diabetes mellitus type 2 in dr. Moewardi Hospital Solo, Indonesia, consisted of 60 respondents taken from simple random sampling (allocate by inverse transform random variate generator and with Microsoft Excel), the respondents were divided into 4 blocks or groups (15 respondents/blocks). Injection used was Rapid-acting insulin with the dosage prescribed by the doctor. Injection was done in four (4) locations; abdomen, deltoid, thigh and gluteus. The administration were 0 minutes (along with meals), 10 minutes before meal, 20 minutes before meal and 30 minutes before meal. Two hour postprandial glucose levels were measured using a Glucometer. Data were then analyzed by SPSS 18 with Two-Way ANOVA and Tukey HSD.
Result: 55% of the respondents was male and 45% was female. All respondents were ≥ 40 years old, most of the respondents were in normal body weight and they have suffered the illness >10 years. There were differences in postprandial glucose levels in people with diabetes who obtained insulin injection at the site of the abdominal, deltoid, thigh and gluteus ($P < 0.05$). There were differences in postprandial glucose levels in people with diabetes who obtained insulin injections at 0, 10, 20 and 30 minutes before meal ($P < 0.05$). The location and the most effective time for insulin injection was in the abdomen at time 0 minute before meal ($P < 0.05$).
Conclusion: Injection of insulin made in the abdomen by the time of meals effectively controlled postprandial glucose levels in patients with diabetes mellitus type 2.

Introduction

Various studies discovered that people with diabetes who manage low plasma glucose levels indicated the incidence of micro vascular complications such as the onset of diabetic retinopathy, nephropathy, and neuropathy were lower compared to patients who did not manage the low plasma glucose levels (1). Therefore, controlling glucose levels in diabetics was very crucial, especially post-prandial glucose levels.

Administering proper insulin injection was one of the ways to manage postprandial glucose levels well controlled (2). Administering insulin injection by a nurse was more often performed in the deltoid area compared to other locations, but there were a few locations that can be done for such insulin injection in the abdomen, thigh and gluteus.

The theory stated that insulin worked faster when it was injected into the abdomen. Insulin would come into the body system longer if it was injected in the upper arm, leg or thigh and the slowest was in the buttocks (3). Previous research stated that, insulin should be given immediately before meals, it was done

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because the insulin worked better when the glucose from food entering the blood (4).

The previous research and theories above resulted in postprandial glucose levels that would vary in each injection location and administering time, therefore it was important to know the most effective location of injection and administering of insulin in controlling postprandial glucose levels, so that nurses will provide proper insulin inject and time of administration.

Methods

The research was experimental with Complete Randomized Block Design (RCBD) (5). RCBD is a randomized design by categorizing the experiment into homogenous blocks called groups and determining randomized treatment design in each group. All group obtained different types of treatments (6,7).

Patients suffered from diabetes mellitus type 2 in Dr. Moewardi Hospital Solo, Central Java, Indonesia were selected as the sample of the research. The sample size was determined for a difference in means based on the funding of Dahlan, 2010 (8). The diabetic patients should be 40 years old at least for both male and female to meet in inclusion criteria. Meanwhile, patients with complications (neuropathy diabetic, retinopathy diabetic, nephropathy diabetic); hyper osmolality ketoacidosis were part of exclusion criteria. The selected sample in inclusion criteria were then divided into 4 blocks through single blind by simple random sampling (9). The study finally obtained 60 respondents (15 respondents per group).

Insulin was randomly injected in 4 (four) different locations, namely in the subcutaneous abdomen, deltoid, thigh and gluteus, through insulin pens, all injections were conducted by the researcher (10). The time of administration were 0 minutes (along with meals), 10 minutes before meal, 20 minutes before meal and 30 minutes before a meal. Types of insulin administered was Rapid-acting insulin at a dose prescribed by the doctor. The respondents' activity was controlled into mild activity.

The demographic data were collected through interview and medical records. The research instrument was Glucometer. The blood sugar test was belonged to the hospital which was YSI 2300 STAT Plus Glucose Lactate Analyzer (11). The blood glucose checked was blood glucose level in 2 hours postprandial. The data 2–h postprandial glucose, were then analyzed by SPSS 18 program package with Two Way ANOVA and Tukey HSD formulas (12,13).

The study was registered in Ethics Committee University of Muhammadiyah Yogyakarta with the number of: 441/EP-FKIK UMY/2015. Besides, it was listed in Iranian Registry of Clinical Trials with the number of: IRCT2017062134690N1. Informed consent was given to all of the respondents before the treatment.

Results

The demography data presented that 55% respondent was male and 45% was female. Furthermore, the respondents were in ≥ 40 years old, the body weight of the patients were in normal category at most and they suffered the illness mostly >10 years (Table 1).

The study showed different results in postprandial blood glucose levels at each site of injection and time injection administration. Patients obtained abdominal insulin injection showed the lowest postprandial glucose levels compared to injection in the deltoid, thigh and gluteus. Patients who obtained insulin on time with meals or 0 minutes showed the lowest postprandial glucose levels compared to the injection time of 10, 20 and 30 minutes before meal.

Injection site in the abdomen affected best postprandial glucose levels with an average score of 156.2 mg / dl, while the injection time at 0 min or concurrently

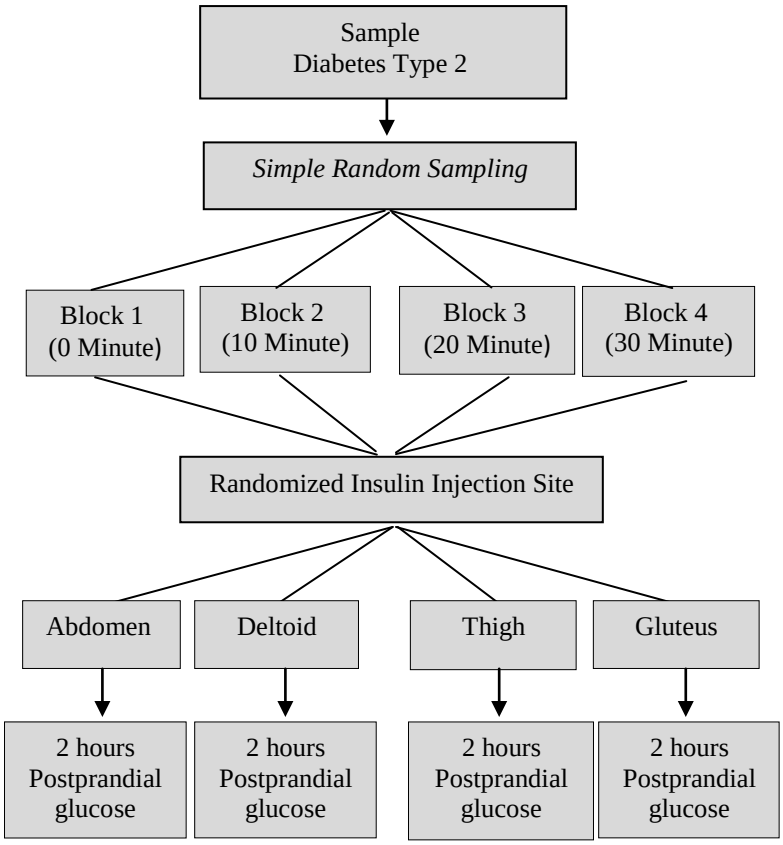

Figure 1. Schematic of the Study Design. Patients with type 2 diabetes were included in the inclusion criteria and then divided into 4 blocks of the timing of injection (block 0 minute, 10 minutes, 20 minutes and 30 minutes before a meal) by simple random sampling, then it was injected at 4 locations (abdominal, deltoid, thigh and gluteus) and measured its postprandial glucose level. Daily insulin dosage obtained by the doctor to the respondent was approximately 8.3UI, while the number of calories obtained by nutritionist was approximately 1876 MPA/ day. There were 71 respondents who participated in the study, however 11 respondents were drop-outs due to various factors. Therefore, 60 respondents (15 respondents per group) were only analyzed.

with a meal resulted in proper postprandial glucose levels with a mean score of 160.8 mg / dl. The trend rose in every interval injection of postprandial glucose levels. Trend line of postprandial glucose levels at each site of injection and timing of injections could be seen in (Figure 2).

The analysis showed that insulin injection location and timing of the injection affected on postprandial blood glucose levels in patients with type 2 diabetes mellitus ($p < 0.05$) (Table 2).

The study discovered that insulin injection site in the abdominal area was the most effective injection site compared to the deltoid area, thigh and gluteus, (Table 3).While the timing of insulin was the most effective at 0 minutes or coincide with meal times (Table 4).

Discussion

The study discovered that changing of the location of the injection from abdomen to another place, the postprandial glucose concentrations increased by 18.2 mg / dl - 60.6 mg / dl (Table 2). The data indicated that there was a difference in absorbed insulin at each site of injection (3,14). The analysis proved that the injected insulin into the abdomen was 100% absorbed by the body, whereas the deltoid just absorbed 75%. The injected insulin into the thigh was 50% absorbed by the from the abdomen to other locations would reduce the dose of insulin administered (14). The dose of insulin given to patients were varied in this study, depending on the daily dose that the doctor prescribed, however the doses that

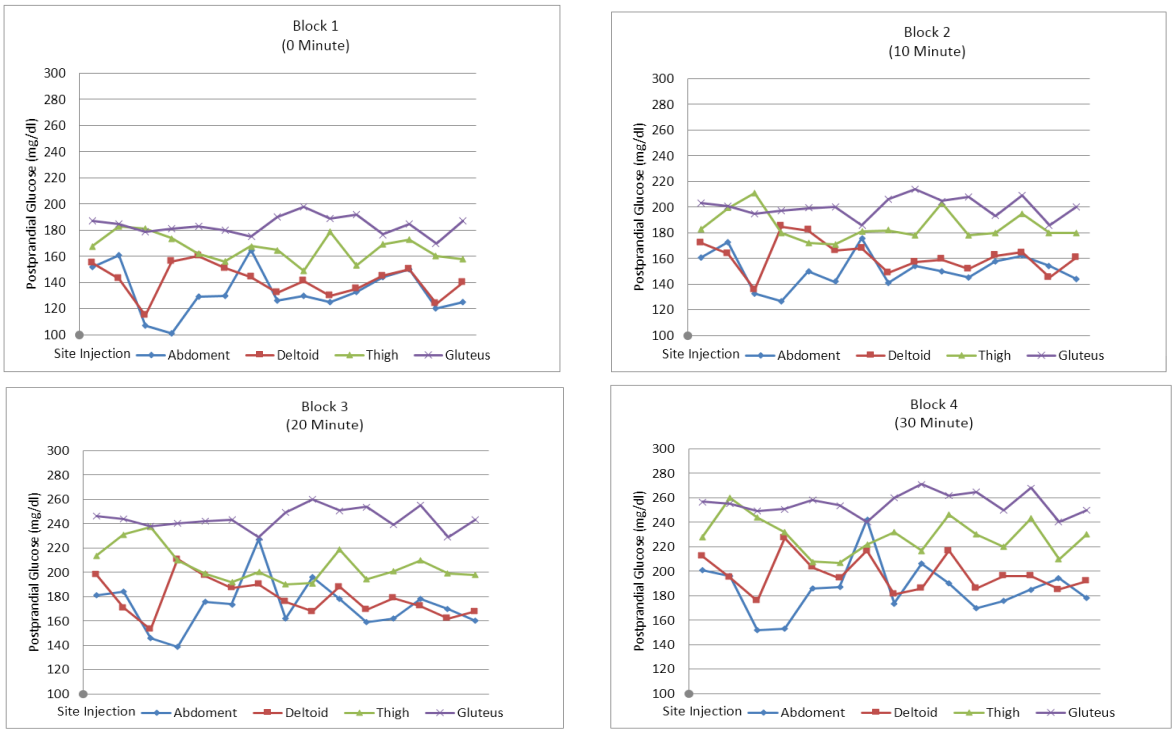

Figure 2. Trend line postprandial glucose levels at each site of injection and timing of insulin injections in patients with diabetes mellitus type 2. Block 1: Insulin administration with meals or 0 minutes, Block 2: Insulin administration conducted 10 minutes before a meal, Block 3: Insulin administration conducted 20 minutes before meal, and Block 4: Insulin administration conducted 30 minutes before meal. The graph above showed differences in postprandial blood glucose levels at each site of injection and at each time interval injection administration.

Table 1. Demographic Characteristic

Demographic Characteristic	N (%)
Sex	
Male	33 (55%)
Female	27 (45%)
Age	
< 40 years old	-
≥ 40 years old	60 (100%)
Long illness	
< 10 Tahun	17 (10.2%)
≥ 10 Tahun	43 (25.8%)
Weight	
Thin	17 (28.3%)
Normal	35 (58.3%)
Fat	8 (13.3%)

Tabel 2. Effect of Insulin Injection Site and Time Interval Administration for the Postprandial Glucose Control (mg/dl)

Site	Time Interval				Overall, mean	n	(SD)	F	p value
	0	10	20	30					
Abdomen	133.2	141.4	166.5	183.8	156.2	60	36.1	2.813	0.004
Deltoid	151.3	161.5	184.8	200.1	174.4	60			
Thigh	172.8	179.2	205.6	244.1	200.1	60			
Gluteus	186.0	197.5	228.6	255.3	216.8	60			
Overall, mean	160.8	169.9	196.4	220.0	187.0	240			

Two-Way ANOVA Test

Tabel 3. Multiple Comparison to the effectiveness of controlling postprandial glucose levels to injected location in Abdomen, Deltoid, Thigh and Gluteus

Variabel		Mean Difference (I-J)	p value
(I) Site Injection	**(J) Site Injection**		
Abdomen	**Deltoid**	-18.22	0.002
	Thigh	-44.22	0.000
	Gluteus	-60.62	0.000
Deltoid	**Abdomen**	18.22	0.002
	Thigh	-26.00	0.000
	Gluteus	-42.40	0.000
Thigh	**Abdomen**	44.22	0.000
	Deltoid	26.00	0.000
	Gluteus	-16.40	0.008
Gluteus	**Abdomen**	60.62	0.000
	Deltoid	42.40	0.000
	Thigh	16.62	0.008

Tukey HSD Test

Tabel 4. Multiple Comparison to the effectiveness in controlling postprandial glucose level to injection administration of 0, 10, 20 and 30 minutes before meals.

Variabel		Mean Difference (I-J)	p value
(I) Time Administration	**(J) Time Administration**		
0 Minute	10 Minutes	-9.1	0.003
	20 Minutes	-35.58	0.000
	30 Minutes	-60.03	0.000
10 Minutes	0 Minute	9.1	0.003
	20 Minutes	-26.48	0.000
	30 Minutes	-50.93	0.000
20 Minutes	0 Minute	35. 58	0.000
	10 Minutes	26.48	0.000
	30 Minutes	-24.45	0.000
30 Minutes	0 Minute	60.03	0.000
	10 Minutes	50.93	0.000
	20 Minutes	24.45	0.000

Tukey HSD Test

patients obtained from the beginning to the end was still the same on a single respondent. The study revealed no significant relationship between the dose of insulin and injection location (p> 0.05).An Injected insulin in abdomen was the most effective in controlling postprandial glucose levels, then the deltoid was on the next, thigh and gluteal had no effect by insulin dose prescribed. The result presented that the small dose of insulin injected to the respondents and the location was on the abdomen, then the postprandial glucose produced would be higher, yet deltoid, thighs and gluteus remained higher than the abdomen. When respondents obtained a large insulin doses and it was injected in abdomen, the glucose produced in 2 hours would be low, however it would remain high when the injection was in deltoid, thighs and gluteus. Several studies on time variable of injection showed that the addition of injection time from 0 minutes to 10, 20 and 30 minutes before meal would increase postprandial blood glucose concentration 9.1 mg / dl - 60 mg / dl when administered at 10 , 20, and 30 minutes (table 3). To a normal person, insulin in the body would increase along with the consumption of food and it would be back to normal within 2 hours after a meal (15). Insulin would work immediately after injected into the body, if insulin was not administered with a meal, it would not work accordingly with the body's metabolic processes (16), causing glucose levels were higher in 2 hours after a meal (17,18). The previous studies, discovered that

insulin injection immediately before a meal was more effective in lowering glucose levels compared with injections immediately after the meal (16,19). Insulin injections were performed at 0 minutes, postprandial glucose levels showed 10 mmol / L (180 mg / dl), while the injection done 30 minutes before meal obtained postprandial glucose levels by 14 mmol / L (255 mg / dl). Insulin injection in the abdomen in the time of meals administration was the most effective in controlling postprandial glucose levels in patients with diabetes mellitus type 2.

The study applied Rapid-Acting insulin, if another type of insulin applied, the result would be different. The researcher then required to conduct the follow up study with HbA1c level indicator.

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Conflict of interest: None

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