# EFFECT OF LOW INTENSITY EXERCISE ON GLUCOSE INTOLERANCE IN THE DEPO MEDROXYPROGESTERONE ACETATE (DMPA) INJECTED RAT

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## ABSTRACT

*Progesterone and derivate of progesterone-only contraceptive, such as injectable depo Medroxyprogesteron acetate (DMPA) increased diabetic risk. Glucose intolerance and hyperinsulinemia were found in women who had been four until twelve month injected 150 mg DMPA. Exercise reduces glucose intolerance in a lot of diabetic patients but the effect of exercise in women who had injected DMPA remains controversial. This study was to measure the effect of low intensity exercise on glucose intolerance injected DMPA rat. Glucose tolerance was tested on 32 female rats which divided into four groups: group 1 was a group of control rats, group 2 had done low intensity exercise, group 3 was injected with 20 mg DMPA each week and the group 4 was DMPA injected rat which had done low intensity exercise for 12 weeks. It was found that plasma glucose rose significantly ($p<0.05$) after 30 minutes post glucose intraperitoneal (ip) challenge on group 3 and 4 but decreased on group 1 and 2. Plasma glucose delta were as follows: 37.500 ± 6.060; 35.500 ± 0.872; -27.25 ± 0,362; -25.875 ± 1.820. The result showed no differences between group 1 and group 2 also between group 3 and 4 ($p>0.05$). In conclusion, low intensity exercise did not reduce glucose intolerance on DMPA injected female rat.*

***Keywords:*** *DMPA, exercise, intolerance and glucose*

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## INTRODUCTION

Two epidemiological studies found progesterone only contraceptive use, such as depo *Medroxyprogesteron acetate* (DMPA) associated with increased incidence of type 2 diabetes. Glucose intolerance and hyper-insulinemia were found in women who had been four until twelve months injected with 150 mg DMPA. On the contrary, 80 percent of 284 diabetic Navajo women had used depo provera during lactation (Kahn et al. 2003; Kjos et al. 1998). BKKBN reported in October 2005, there were 601.454 new contraceptive acceptors which 65,49 percent used DMPA injected method. These suggested that DMPA injected method were preferable to be used for more than ten years and became more popular every next year. It would potentate to increase incidence of type 2 diabetes in Indonesian women.

Exercise reduces glucose intolerance in a lot of diabetic patients. Exercise increased glucose uptake stimulation and insulin sensitivity on the muscle, fat and the liver cells. The effect of exercise in women who had injected DMPA remains controversial because they had hyperinsulinemia, which did not occur in regular diabetic patient (Fueger 2004; Peres et al. 2004; Winder 2001). High intensity exercise is not recommended to diabetic patient because of acute hypoglycemic danger. Even well recommended minimal exercise intensity is also still questionable. This study aimed to measure the effect of low intensity exercise on glucose intolerance in the depo *medroxyprogesterone acetate* (DMPA) injected rat.

## MATERIALS AND METHODS

This study was an experimental research, which used a randomized posttest only control group design. Thirty-two female white rats were randomized into 4 different groups: group 1 was a group of control rats, group 2 had done low intensity exercise, group 3 was injected with 20 mg DMPA each week and the group 4 was DMPA injected rat which had done low intensity exercise. The treatment of each group was 12 weeks long. DMPA was administered 20 mg a week for 12-week intramuscularly. DMPA dose was mathematical conversion to the DMPA adult women dose and as large as another previous study. Exercised rats had to swim 30 minutes a day, 3 days a week for 12 weeks in a low intensity (50 percent of maximal performance).

In the end of 12th week treatment, every rat groups were tested for glucose tolerance (GTT). Blood sample were collected from supra orbital sinus for 3 times: fasting period, 30 minutes post intraperitoneal glucose challenge (2 g/kgBW) and 60 minutes post glucose challenge. Plasma glucose was measured by GOD PAP enzymatic method. The glucose tolerance was defined as the delta between plasma glucose of 30 minutes and 60 minutes post glucose challenge. The one-way ANOVA was used to compare the glucose tolerance between 4 different groups. P values below 0.05 were considered to indicate statistical significance.

## RESULTS

The result of glucose tolerance test (GTT) is shown in Table 1. Plasma glucose rose after 30 minutes post glucose challenge on group 3 and 4 but decreased on group 1 and 2. These phenomena are shown in Figure 1. Comparison of the delta glucose tolerance is shown in Figure 2.

Table 1. The description of glucose tolerance test (GTT)

| | Mean (mg/dl) | Standard deviation |
|---|---|---|
| Fasting plasma glucose | | |
| Group 1: control | 98.375 | 8.123 |
| Group 2: exercise | 97.500 | 8.751 |
| Group 3: DMPA | 89.000 | 14.303 |
| Group 4: DMPA+exercise | 98.000 | 11.161 |
| 30' plasma glucose challenge | | |
| Group 1: control | 196.875 | 25.648 |
| Group 2: exercise | 188.875 | 18.551 |
| Group 3: DMPA | 129.625 | 14.242 |
| Group 4: DMPA+exercise | 139.250 | 12.948 |
| 60' plasma glucose challenge | | |
| Group 1: control | 159.375 | 19.588 |
| Group 2: exercise | 153.375 | 17.679 |
| Group 3: DMPA | 156.875 | 14.604 |
| Group 4: DMPA+exercise | 165.125 | 11.128 |

## DISCUSSION

DMPA raised plasma glucose significantly ($p<0.05$) after 30 minutes glucose challenge. The delta glucose tolerance showed in negative result in group 3 and 4. This suggested that insulin sensitivity decreased in stimulating glucose uptake in the muscle, fat and liver cells. These findings were the same as those in another study that showed glucose intolerance on DMPA administered rats.

Injected DMPA increased plasma progesterone that affected the insulin-glucose metabolic changes. High plasma progesterone level redistributed (phosphotydil-inositol 3 kinase) PI-3 kinase in muscle cells. PI-3 kinase was not activated by insulin receptor substrate IRS-1 as normally, but, in the contrary, PI-3 kinase phosphorilated IRS-1. IRS-1 were inactivated and degenerated very slowly. These changes inhibited glucose transporter (GLUT 4) translocation to the muscle membrane and decreased glucose uptake stimulation (Campbell 2001; Gonzales et al. 2000; Shao et al. 2002)

High plasma progesterone level increased progesterone receptor (PR) stimulation in beta cells of pancreas. Beta cells became highly proliferated and hyperplasia. It increased very high insulin secretion after glucose challenge. This phenomenon could be seen in group 3 and 4 that their 30 minutes of plasma glucose level were not as high as that in group 1 and 2. Hyperinsulinemia raised glucose uptake stimulation on liver cells but not on muscle and fat cells because liver glucose uptake had a different mechanism within muscle and fat cells (Picard et al. 2002; Tamura et al. 2005).

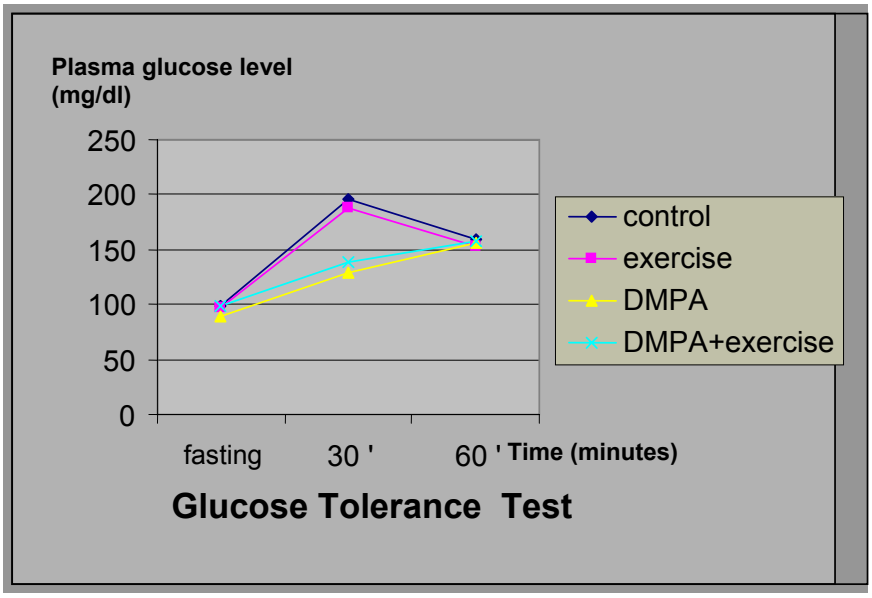


Figure 1. The mean of plasma glucose in 4 different groups

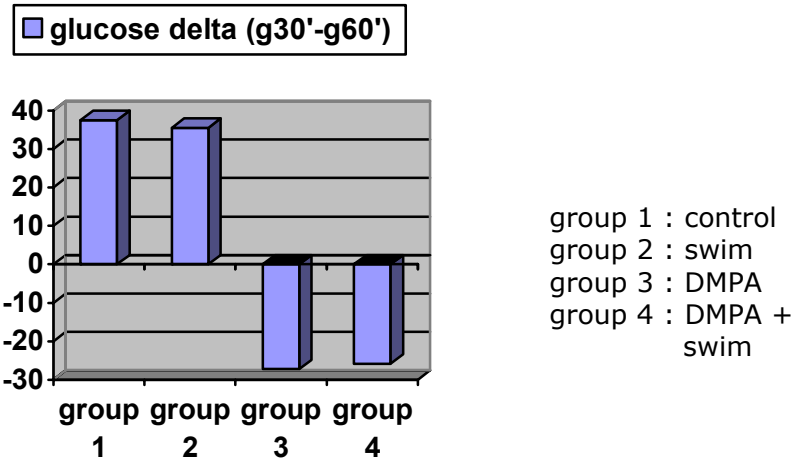


Figure 2. The comparison of glucose delta tolerance in 4 different groups

Low intensity exercise influenced very low changes in glucose tolerance. There was no significant difference between group 1 and 2 or between group 3 and 4 ($p>0.05$). These findings were different from another study that showed positive effect on glucose uptake stimulation (Fueger 2004; Peres et al. 2004). This difference may be due to lower intensity exercise that treated to the normal and DMPA administered rats. A higher intensity perhaps could increase glucose tolerance. It activated another glucose uptake signaling pathway that was not influenced by plasma insulin level.

## CONCLUSION

Low intensity exercise cannot repair glucose intolerance on DMPA injected rats

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