
Research Article

The Correlation of Use of Depo Medroxy Progesterone Acetate (DMPA) Injections with Lipid Profile Levels in Rats

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ABSTRACT

Introduction: Family Planning is a national strategy of Indonesia government to manage the population growth. Depo Medroxyprogesterone Acetate (DMPA) is one of injectable contraceptives most widely used because it is simple and easy to obtain. However, it has various side effects causing imbalance of hormone estrogen, in turns to result in a decrease in HDL (High Density Lipoprotein) and an increase in LDL (Low Density Lipoprotein) which will result in an increase in total cholesterol. It will also affect changes in fat metabolism in human body due to hormonal influences. This results in dyslipidemia and atherosclerosis. **Method:** The method in this study is an experimental study with a pretest-posttest control group design. **Results:** The purpose of this study was to determine the relationship between duration of use of DMPA injections with lipid profile levels in mice. The data were analyzed by using the Paired t-test parametric test to compare between treatment groups. This study found that there were significant differences in HDL levels and total cholesterol levels between before and after administration of DMPA injections on the 14th and 35th days. There is a significant relationship between the duration of administration of DMPA injections with HDL levels and total cholesterol levels in mice. However, there was no difference in LDL levels and triglyceride levels between before and after administration of DMPA injection on day of 14 and day of 35, while, there was a significant difference between before and after the 35th day. There is no relationship between duration of administration of DMPA injections with LDL levels, while there is a relationship among mice triglycerides. **Conclusions:** Administration of DMPA injections for a long time lowers HDL.

Keywords: *DepoMedroxy Progesterone Acetate, Hypercholesterolemia, Hyperlipidemia, Lipid Profiles.*

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Background

Family Planning (KB) is a program in an effort to plan the birth of children, the ideal distance and age to give birth, regulate pregnancy through promotion, protection, and assistance in accordance with reproductive rights to create a quality family (5). Contraceptive methods have been used by most women of childbearing age (63%) in almost all of the world in 2017. Globally, 58% of women of childbearing age use modern contraceptive methods (10). Modern contraceptive methods consist of injections, pills, implants, IUDs, female operative methods (MOW), male operative methods (MOP), and emergency contraception (9). Data from the Indonesian Demographic and Health Survey (IDHS) in 2017 shows the trend in the prevalence of contraceptive use / Contraceptive Prevalence Rate (CPR) in Indonesia, an increase in contraceptive use from 61.9% (2012 IDHS) to 63.22% (Central Bureau of Statistics, 2018). The achievement of using modern contraceptive methods is 57% in Indonesia. Most (more than 80%) active family planning participants choose the type of injectable contraception, which is 62.77% (6).

Most of the modern contraception methods chosen were KB injections, which amounted to 210,610 participants (38.44%) (2). This method is used because it is considered the easiest and does not cause pain or fear. One method of injecting family planning that is widely used is Depo Medroxyprogesterone Acetate (DMPA). DMPA injectable contraception is a contraceptive in the form of a liquid containing only the hormone progesterone. DMPA is given in a single injection of 150 mg intramuscularly into a woman's body (periodically) every 3 months. 99% effectiveness in preventing pregnancy (3). DMPA injectable contraceptives have various side effects, including menstrual disorders, depression, vaginal discharge, acne, hair loss, weight gain, as well as long-term

use changes in serum lipids, headaches, and can cause vaginal dryness and decrease libido. (8). According to (7). DMPA injectable contraceptives have side effects, namely causing the hormone estrogen to be unbalanced, which results in a decrease in HDL (High Density Lipoprotein) and an increase in LDL (Low Density Lipoprotein) this will result in an increase in total cholesterol. It also affects changes in fat metabolism that occur due to hormonal influences, causing dyslipidemia disorders in long-term use which can be a risk factor for atherosclerosis (1). Atherosclerosis is one of the most common causes of increased cholesterol levels in the body which can lead to cardiovascular disease (4).

The use of injectable contraception which is in great demand by women of childbearing age cannot be prohibited because it is a person's right to make his/her choice. In addition, the target for the use of family planning must be in line with government programs in achieving national health targets. This study will see if it is true that the lipid profile will increase in DMPA users? And does it increase over time?

Methods

Experimental research with pretest-posttest control group design (Pocock, 2008). The research subjects were female mice with the Sprague dawley strain. During the initial 2 weeks, the mice were collected, then pre-test blood was taken for examination of the lipid profile through the orbital vein as much as 0.5 cc, then examined in the laboratory using the spectrophotometric method. After that, the mice in the treatment group were given DMPA injection of 38 mg every day for 14 and 35 days.

Results and Discussion

The results of the research conducted are as follows:

Table 1. Average levels of lipid profile in mice before and after injection of Depo Pedroksi Progesterone Acetate (DMPA)

Profil Lipid	Pre Test	Post Test 14 days	Post Test 35 days
HDL	56,63	36,28	28,98
LDL	21,13	21,71	28,10
Trigliserida	105,75	91,25	84,13
Cholesterol Total	103,91	114,13	120,01

The mean value of HDL cholesterol levels was higher pre-test (56.63) and the mean post-test day 14 (36.28) decreased as well as the mean post-test day 35 (28.98). Likewise, the

value of Triglycerides decreases over time. In contrast to the mean value of LDL cholesterol and Total Cholesterol, the longer the DMPA injection, the higher the dose.

Table 2. Significance Test Paired t Test High Density Lipoprotein (HDL) Levels Before and After Injection of Depo Medroxy Progesterone Acetate (DMPA)

	mean	Std.dev	t	Sig. (2-tailed)
Pre test – Post test 14 days	20,35	9,858	5,839	0,001
Pre test – Post test 35 days	27,65	7,351	10,639	0,000
Post test 14 days – Post test 35 days	7,300	4,073	5,070	0,001

The pre-test value with the post-test on day 14 was stated to be 0.001 smaller than 0.05, which means that there is a significant difference in HDL levels between before and after DMPA injection, where the levels are decreasing. If we look at the significance value between

posttest day 14 and posttest day 35, which is 0.001 it can be interpreted that there is a difference in HDL levels after administration for 14 and 35 days, which means that there is a relationship between duration of administration and HDL levels in mice.

Table 3. Significance Test Paired t Test Low Density Lipoprotein (LDL) Levels Before and After Injection of Depo Medroxy Progesterone Acetate (DMPA)

	mean	Std.dev	t	Sig. (2-tailed)
Pre test – Post test 14 days	-0,59	8,30	-0,200	0,847
Pre test – Post test 35 days	-2,25	10,32	-0,617	0,557
Post test 14 days – Post test 35 days	-1,66	5,20	-0,904	0,396

All of the above significance values are greater than 0.05, which means that there is no difference in LDL levels after injection for 14

days or 35 days. But if it is seen the longer the value of the significance is getting smaller.

Table 4. Significance Test Paired t Test Triglyceride Levels Before and After Depo Medroxy Progesterone Acetate (DMPA) Injection

	mean	Std.dev	t	Sig. (2-tailed)
Pre test – Post test 14 days	14.50	23.15	1.772	0.120
Pre test – Post test 35 days	21.63	25.71	2.379	0.049
Post test 14 days – Post test 35 days	7.13	21.11	0.955	0.372

Judging from the value above, the significance value between the pre-test and post-test on day 14 was 0.120, greater than 0.05, which means that there was no significant difference in triglyceride levels after DMPA injection was given. Likewise between the post test day 14

and day 35. But between the pretest and post test day 35, the significance value is 0.049, which is smaller than 0.05, which means that there is a significant difference. Judging from this value, it can be stated that the longer DMPA injection will reduce triglyceride levels.

Table 5. Significance Test Paired t Test Cholesterol Total Levels Before and After Depo Pedroxyl Progesterone Acetate (DMPA) Injection

	mean	Std.dev	t	Sig. (2-tailed)
Pre test – Post test 14 days	-10.21	5.68	-5.085	0,001
Pre test – Post test 35 days	-16.10	7.78	-5.850	0,001
Post test 14 days – Post test 35 days	-5.88	3.54	-4.699	0,002

The table above shows a significant value where the value is smaller than 0.05, which means there is a difference in total cholesterol levels between before and after DMPA injection. Likewise with the duration of administration, the longer the total cholesterol level will increase.

Discussion

High Density Lipoprotein (HDL) is cholesterol that serves to clean excess cholesterol that makes harm in the blood and bring it back to the liver to be removed from the body. Therefore, HDL is also known as the 'good cholesterol'. In addition to helping to remove excess bad cholesterol, HDL also functions to prevent damage to blood vessel walls due to fat accumulation and keep them healthy. So that HDL cholesterol levels actually need to be increased considering its function is needed by the body.

In this study, seen from the results above in the treatment group after being given DMPA injections in mice, their HDL cholesterol decreased, the longer the administration decreased. As is known, the content of DMPA injections is progesterone with a failure rate of <1%. Hormonal contraceptives are injected intramuscularly once every 3 months as much as 150 mg. The hormone progesterone works by stimulating the appetite control center in the hypothalamus which causes appetite to increase. If the increase in appetite is not matched by body movement, it will cause an increase in body fat which is the result of the metabolism of carbohydrates and fats consumed. So it is very important for DMPA users to pay attention to the food they eat and exercise regularly so that glycogen stored as body fat from food consumption can be metabolized again.

In this study, mice were given the same standard diet, but their movement was restricted in the cage, this possibility also caused the decrease in HDL cholesterol levels of mice.

As is known, the function of HDL is to reduce the oxidation of LDL and VLDL. If HDL decreases, there will be an increase in LDL and VLDL because the role of HDL as a thrombotic is not able to prevent fibrosis and calcification, which causes disruption of the elasticity of blood vessels. If this continues for a long time, atherosclerosis will occur. From this study, it was also found that the duration of administration of DMPA injections caused HDL levels to decrease.

From the results of the above study, HDL cholesterol levels before were different from HDL cholesterol levels after DMPA injection on day 14, as well as levels after injection on day 15. The results of the significance test also showed that there was a significant difference between the pre test and post test on day 15. The 14th and 15th days. This means that there is an effect of giving DMPA injections to HDL levels in the blood of mice and also the effect of the duration of DMPA injections. The longer the DMPA injection, the lower the HDL level in the blood.

Low Density Lipoprotein (LDL) is the bad cholesterol that can cause the buildup of cholesterol in the blood throughout the body. LDL serves to carry cholesterol from the liver into the blood vessels, while HDL functions to carry cholesterol from the blood vessels to the liver to be removed from the body. So if the state of LDL cholesterol increases it will result in a lot of cholesterol in the blood because a lot of it transports cholesterol from the liver to the blood vessels. On the other hand, if HDL decreases, it will not be able to return the excess cholesterol carried by LDL to the blood vessels because the amount is less. So that cholesterol in the blood increases. An increase in LDL levels is a barometer of an increase in total cholesterol levels in the blood.

This study showed an increase in LDL cholesterol levels in the treatment group after

DMPA was injected and increased if injected for a longer time. The same study was also found by Yadav (2011), that various synthetic progesterone used as contraception can affect lipid and lipoprotein fractions. Total cholesterol (TC) and LDL-C levels were significantly higher in DMPA users compared to those not using DMPA, so the use of DMPA can induce changes in lipid metabolism that will increase the risk of cardiovascular disease. (11).

The results of this study indicate a significant number for the duration of DMPA injection, which is 0.041 where the longer the administration, the higher the LDL level in the blood.

Triglycerides are a type of fat that are often found in the blood. Triglycerides are produced in the liver, but most of them come from food. Fat obtained from food will be broken down and then converted into triglycerides. Excess and unused fat will become triglycerides which are stored in fat cells. If needed the body will convert it in the form of energy. If there are too many triglycerides in the blood, it can lead to thickening of the walls of blood vessels.

In this study, mice given DMPA injection did not experience a significant increase in triglyceride levels. However, there was a significant difference between the pretest and posttest group on day 35 with a value of 0.049. This value is not very different, probably due to standard food provided and not foraging freely.

Total cholesterol is a fat compound in the body that is produced by various body cells, and the most cholesterol produced by the body is produced by the liver. In other words, the body still needs cholesterol to stay healthy. Total cholesterol is a combination of HDL, LDL and triglycerides in the blood.

The results of this study showed that the total cholesterol levels of mice given DMPA injections tended to increase. As is known, DMPA contains artificial progesterone or synthetic steroids that can stimulate the acceptor to eat so that it stimulates hunger and eats more. In

addition, progesterone also causes carbohydrates and sugars to easily accumulate into fat. According to Zainatul (2019), there is a significant relationship between the duration of contraceptive use at Depo Medroxy Progesterone Acetan and the incidence of hypertension.

Conclusion

DMPA injections decreased HDL and triglyceride levels for both 14 days and 35 days, but increased LDL and total cholesterol levels in mice.

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