Research Article

Changes of Body Mass Index and Lipid Profile in Injectable Depot Medroxyprogesterone Acetate and Levonorgestrel Implant Acceptors

Perubahan Indeks Massa Tubuh dan Profil Lipid pada Akseptor KB Suntik Depot Medroksi Progesteron Asetat dan Implan Levonorgestrel

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Abstract

Objective: To determine the comparison of body mass index (BMI) among acceptors of injectable depot medroxyprogesterone acetate (DMPA) with levonorgestrel implant acceptors for 1 year and comparison of lipid profiles between depot medroxyprogesterone acetate acceptors with levonorgestrel implants for 1 year.

Method: This study was conducted at dr. Wahidin Sudirohusodo hospital, Makassar and its satellite hospitals as well as family planning social service cooperation between the National Family Planning Coordinating Board with the Department of Obstetrics and Gynecology Hasanuddin University.

Result: The results showed the increase in BMI of levonorgestrel implant acceptors (1.25 kg/m^2) was greater than DMPA acceptors (0.74 kg/m^2). HDL cholesterol and triglycerides did not change significantly in either groups. LDL cholesterol was increased in DMPA acceptors (9.63 mg/dl) and decreased in implant acceptors (1.62 mg/dl). Total cholesterol increased in DMPA acceptors at 8.67 mg/dl) while in the levonorgestrel implant acceptors it was decreased by 5.37 mg/dl.

Conclusion: Weight gain occured among acceptors of DMPA and implant however the weight gain is more profound among the implant acceptors.

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Keywords: body mass index, DMPA, levonorgestrel implant, lipid profile

Abstrak

Tujuan*: Untuk mengetahui perbandingan indeks massa tubuh (IMT) antara akseptor KB suntik depot medroksiprogesteron asetat (DMPA) dengan akseptor implan levonorgestrel selama 1 tahun serta perbandingan profil lipid antara akseptor depot medroksiprogesteron asetat dengan implan levonorgestrel selama 1 tahun.*

Metode*: Penelitian ini dilaksanakan di rumah sakit pendidikan dr.Wahidin Sudirohusodo Makassar dan jejaring serta safari KB kerjasama antara Badan Koordinasi Keluarga Berencana Nasional dengan Bagian Obstetri dan Ginekologi Universitas Hasanuddin.*

Hasil*: Penelitian menunjukkan peningkatan IMT akseptor implan levonorgestrel (1,25 kg/m^2) lebih besar dibanding akseptor DMPA (0,74 kg/m^2). Kolesterol HDL dan trigliserida tidak mengalami perubahan yang bermakna pada kedua kelompok akseptor. Kolesterol LDL mengalami peningkatan pada akseptor DMPA (9,63 mg/dl) dan penurunan pada akseptor implan (1,62 mg/dl). Kolesterol total meningkat pada akseptor DMPA sebesar 8,67 mg/dl sedang pada akseptor implan levonorgestrel mengalami penurunan sebesar 5,37 mg/dl.*

Kesimpulan*: Peningkatan berat badan terjadi pada akseptor DMPA dan implan namun peningkatan berat badan lebih besar pada akseptor implan.*

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Kata kunci*: DMPA, implan levonorgestrel, indeks massa tubuh, profil lipid*

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INTRODUCTION

Indonesia is the fourth most populated country in the world with a considerably high population growth rate. Based on the Central Agency on Statistics, the population of Indonesia in 2010 is 237,641,326 people, meaning an increase of 31,373,731 people since year 2000. The population growth rate of Indonesia from 2000 to 2010 approximated 1.49% per year, which means that if family planning programs are not reinforced, the population of Indonesia is predicted to reach 368 million people by year 2020.[1]

Currently, the most commonly used contraceptive method is hormonal contraceptive methods, which includes depot medroxyprogesterone acetate (DMPA) injection, combined injectable contraceptives and subcutaneous contraceptive implants.[2]

DMPA is a synthetic progesterone that has similar chemical structure to progesterone that has glucocorticoid properties, while levonorgestrel implants have mineralocorticoid properties. This means that theoretically these contraceptive methods could cause an increase in body weight.[3]

A previous study by Fraser and Dennerstein reported weight gain in DMPA acceptors. However, a comparative study on long-term DMPA use by Surasak Taneepanichskul et al concludes that no significant difference in weight gain is observed between DMPA users and controls.[4]

Weight changes in implant acceptors have been reported by several clinical trials affirming that implant acceptors in America with 1-year period of utilization experienced weight gain at an average of 1.2 pounds.

From the stated theoretical framework and previous studies, we find it necessary to do a study on the BMI changes in DMPA acceptors in comparison with implant acceptors.

METHODS

This study is carried out at Dr. Wahidin Sudirohusodo Hospital and several teaching hospitals in Makassar, as well as participants of mobile family planning services provided by the National Family Planning Coordinating Board in collaboration with the Obstetrics and Gynecology Department Hasanuddin University. The duration of the study spans from December 2011 until December 2012.

We performed a prospective comparative observation by comparing BMI and lipid profiles in DMPA injection acceptors and levonorgestrel implant acceptors. The sample in this study is women accepting DMPA contraceptives or levonorgestrel implants who subsequently had quarterly weight and height measurement as well as blood sample collection for a period of one year.

The population we target in this study are acceptors of injectable DMPA contraceptives and levonorgestrel implants in the family planning clinic of teaching hospitals in Makassar as well as the mobile family planning program. The inclusion criteria is women accepting injectable DMPA contraceptives or 2-capsule levonorgestrel implant who have signed the informed consent.

The data collected was analyzed using bivariate analysis in the form of independent and "before/after" t-test to test the average from two populations that are independent of each other and which the researcher has no information on the variability of the population. Independent means that one population is not influenced by or related to the other population.

RESULTS

In Table 1 we can see that the age of DMPA and implant acceptors ranged between 20-35 years old with most DMPA acceptors falling in the age range of 30-34 years old (13 people; 61.9%) and for implant acceptors most fall into the age range of 20-24 years old (9 people; 81.8%).

Table 1. Baseline Characteristics of DMPA and Implant Acceptors.

No	Characteristic	Total			
		DMPA		Implant	
		N	%	N	%
1	Age (years)				
	20-24	2	18.2%	9	81.8%
	25-29	6	50.0%	6	50.0%
	30-34	13	61.9%	8	38.1%
	35	3	75.0%	1	25.0%
2	Education Level				
	Elementary	9	64.3%	5	35.7%
	Junior high school	9	50.0%	9	50.0%
	Senior high school	6	37.5%	10	62.5%
3	Occupation				
	Private employee	2	100.0%	0	0.0%
	Housewife	22	47.8%	24	52.2%

Regarding education levels, DMPA acceptors were dominated by samples with elementary school education (9 people; 64.3%) and junior high school education (9 people; 50%) while implant acceptors were dominated by samples with senior high school education (10 people; 62.5%). For occupational status, almost all of our samples were housewives, while only two were private sector employees.

Table 2 illustrated the change in BMI experienced by the 24 DMPA acceptors as measured quarterly. At month 0, the average weight of DMPA acceptors was 55.15 kg with average BMI of 22.76 kg/m2 with a drop in weight at the third month of 0.16 kg with BMI of 22.70 kg/m^2. Starting from month 6, DMPA acceptors experienced an increase in weight and BMI. Furthermore, at month 9 they experienced a significant gain in weight (p=0.014) and BMI (p=0.010). In general, comparing month 0 to month 12 in DMPA acceptors, there was a significant gain in body weight (p=0.001) and BMI (p=0.000).

Table 2. Quarterly BMI Changes in DMPA and Implant Acceptors in a One Year Period.

Month	Mean							
	DMPA (N=24)				Implant (N=24)			
	weight (kg)	p	BMI	p	weight (kg)	p	BMI	p
0	55.15		22.76		49.98		21.31	
		0.517		0.587		0.395		0.299
3	54.99		22.70		50.34		21.49	
		0.073		0.077		0.179		0.116
6	55.71		22.99		50.93		21.61	
		0.014		0.010		0.008		0.005
9	56.23		23.20		52.24		22.29	
		0.001		0.000		0.002		0.001
12	56.94		23.50		52.90		22.56	

Furthermore, Table 2 also shows that at the first measurement, the average body weight of implant acceptors was 49.98 kg with average BMI of 21.31 kg/m^2 and there was a significant gain in body weight (p=0.008) and BMI (p=0.005). Comparing the first and last measurements in implant acceptors, there was a significant increase of body weight averaging 2.92 kg (p=0.002) with an average BMI of 22.29 kg/m^2 (p=0.001).

Table 3 shows that average HDL levels of DMPA acceptors was 47.29 mg/dl at the first month, which was within normal levels (>40 mg/dl). On the third month, there was a rise in HDL levels of 3.37 mg/dl although it was insignificant. On the 6th and 9th month, HDL levels show a tendency to decline which continues until the level reach 46.29 mg/dl on the last measurement.

Likewise, average HDL levels in implant acceptors were within normal limits. On the third month, HDL level was reduced by 1.63 mg/dl but was continued by a rise starting from month 6 to the end of the study. However, this change in HDL level was found to be insignificant.

Average LDL level in DMPA acceptors on the first measurement was 117.37 mg/dl, which was higher than the normal level of 100 mg/dl. On the third month, average LDL level fell by 3.87 mg/dl but increased on the sixth month and showed to be steady until the 12th month.

Among implant acceptors, LDL levels on first measurement averaged 112.62 mg/dl. On the third and sixth month, the trend was found to be increasing but fell on the 9th and last month. The changes in LDL among DMPA and implant acceptors showed a significant rise on month 12 with p=0.028.

Furthermore, triglyceride levels in DMPA acceptors were found to be within normal limits (<150 mg/dl). On the first measurement, triglyceride level was 121.67 mg/dl and showed a downward trend until the 9th month but experienced a climb on the last month. This change in triglyceride level did not reach statistical significance. The average triglyceride level of implant acceptors on the first measurement was within normal limits (122.25 mg/dl). The fluctuation in triglyceride level in implant acceptors was similar to DMPA acceptors. However, the rise in triglyceride level in the last month did not surpass the measurement in month 0.

Total cholesterol levels at month 0 in both groups were within normal levels (<200 mg/dl). In DMPA acceptors, total cholesterol experienced a rise starting from the 6th month with a total increase of 8.67 mg/dl in total cholesterol. However, the increase was not found to be statistically significant. In contrast, average total cholesterol showed a tendency to decrease until the final measurement although a spike of 5.13 mg/dl was

observed at month 6. On the last month, the drop in total cholesterol was 5.37 mg/dl in comparison with the first month. The difference in total cholesterol change between DMPA and implant acceptors was found to be statistically significant (p=0.035).

DISCUSSION

This study shows that the increase in body weight and BMI was more pronounced in implant acceptors compared to DMPA acceptors. We hypothesize this is caused by the mineralocorticoid properties of levonorgestrel, leading to fluid retention. However, further studies are needed to investigate the effect of levonorgestrel on weight changes until the end of implant use. Other factors that may influence weight gain but were not studied include genetic patterns, psychologic factors, physical activity, eating habits, alcohol consumption and smoking. Some people have a habit of eating more as a response mechanism towards negative psychological conditions such as sadness, boredom or anger. However, some others have the opposite response. Aside from the factors listed previously, specific medical conditions or medications may cause weight gain.[5]

A study by Marcia Pantoja et al found an increase of BMI as much as 1.78 kg/m^2 in DMPA acceptors after 1 year of usage. Another study reported 5% increase in body weight after 6 month usage of DMPA or a monthly increase of approximately 0.35 kg. A study by Balogun in Nigeria showed the increase of body weight in levonorgestrel contraceptive implant acceptors is 1.3 kg and 2.4 kg in the 6th and 12th month after implant use respectively.[6,7]

HDL cholesterol has protective effects from coronary disease. High HDL levels can be found in individuals who are physically active and not obese.[8] In this study, HDL levels in DMPA acceptors fell starting from the 6th month until the end of the study, with a total decrease of 1 mg/dl from the first measurement. In implant acceptors, HDL levels declined on the third month, but increased in the following months. In the final measurement, total HDL levels underwent a decrease of 0.46 mg/dl compared to the first measurement. However, the changes in HDL levels in DMPA or implant acceptors were not found to be statistically significant.

Levonorgestrel concentration in the blood is approximately 80 g/24 hours after implant insertion which persists until the 6th month and declined to 30 r/24 hours thereafter. HDL was found to increase starting from the 6th month in accordance to the fall in levonorgestrel concentration in blood.

LDL cholesterol is a lipoprotein responsible for transporting serum cholesterol into the cells. This function of LDL allows it to mark the development of cardiovascular diseases, such as coronary heart disease.[9]

In DMPA acceptors, the rise in LDL until the 12th month was 6.5 mg/dl from the first measurement. In implant acceptors, LDL level was elevated to a maximum level on the 9th month but fell until the 12th month so that it had an overall reduction of 1.62 mg/dl from the first month. The change in LDL was significantly different in DMPA and implant acceptors (p=0.028), which indicates the tendency of DMPA acceptors to experience a rise in LDL levels in the long term compared to implant acceptors.

Table 3.   Quarterly Change in HDL, LDL, Triglyceride and Total Cholesterol in DMPA and Implant Acceptors.

Month	Mean (mg/dl)											
	HDL			LDL			Triglyceride			Total cholesterol		
	DMPA	Implant	p	DMPA	Implant	p	DMPA	Implant	p	DMPA	Implant	p
0	47.29	50.54	0.265	117.37	112.62	0.580	121.67	122.25	0.806	183.70	181.37	0.820
3	50.66	48.91	0.756	113.50	116.79	0.680	120.96	111.50	0.805	184.17	180.12	0.652
6	48.41	51.66	0.357	121.62	119.67	0.795	116.46	110.45	0.993	193.41	186.50	0.493
9	48.08	51.42	0.370	128.79	114.46	0.062	101.79	92.83	0.655	188.54	178.79	0.239
12	46.29	51.00	0.142	127.00	111.00	0.028	112.33	107.33	0.481	192.37	176.00	0.035

LDL reached its maximum level faster in implant acceptors, which was at week six. We hypothesize that this is coupled with the concentration of levonorgestrel, which was highest in the 6th month with subsequent decline until the 12th month. In DMPA acceptors, the concentration of medroxy-progesterone acetate tends to be stable causing constant suppression of endogenous estrogen. Endogenous estrogen suppression by progestin causes an increase in the excretion of VLDL in the liver. LPL will subsequently mediate the lipolysis of VLDL into VLDL remnant or commonly known as IDL. Hepatic lipase activity will convert IDL into LDL. The consequence of this chain of events is the increase of LDL concentration in the blood.

Carrie et al found no significant change of LDL levels in DMPA acceptors. In contrast, Araujo et al reported a slight decrease in LDL concentration in the first year of levonorgestrel implant use.[9]

Previously, the role of triglycerides is often neglected but current evidence shows the contribution of triglycerides on the pathogenesis of coronary heart disease. In our study, the triglyceride levels in DMPA acceptors shows a tendency of decreasing. The maximum drop in triglyceride concentration was found in the 9th month at 92.83 mg/dl. Both DMPA and implant acceptors experience the greatest decline on month 9. Although this fall in triglyceride concentration was found in more implant acceptors, it was not found to be statistically significant.

Triglyceride concentration reduction was less pronounced in implant acceptors than DMPA acceptors, which may be caused by the younger age of the implant group. With addition of age, physical activity tend to decrease leading to a decline in metabolic rate. Consequently, triglyceride levels tend to increase with age.[8] Another factor influencing triglyceride level is diet and eating habits, eventhough it was not investigated in this study. Kaunitz et al did not find a significant change in triglyceride level in DMPA acceptors after 96 weeks of use.[10]

Total cholesterol level of DMPA acceptors was 183.7 mg/dl on the first measurement and the trend seems to be increasing on the following month. On the final measurement, the rise in total cholesterol level was as much as 8.67 mg/dl. Implant acceptors started with a total cholesterol of 181.37 mg/dl and reached its maximum level on month 6. After that, total cholesterol tend to fall until the 12th month with a total drop of 5.37 mg/dl. We can see a significant difference in overall total cholesterol changes between DMPA and implant acceptors (p=0.035).

Theoretically, the total cholesterol increase in DMPA and implant acceptors was caused by induction of pre-adipocyte differentiation, LPL activity and triglyceride synthesis, which increase visceral adipose.[11]

CONCLUSION

Both DMPA and implant acceptors experience an increase in BMI, but it was more pronounced in implant acceptors. HDL reduction occurred in both contraceptive methods but in implant acceptors it only occurred in the third month and bounced back until the last month. LDL concentration in DMPA acceptors increased until month 12, while in implant acceptors it increased until month 9 before falling at the last measurement. Triglyceride concentration showed a non-significant decrease in both groups. Total cholesterol showed an increasing trend in DMPA acceptors which was observed until the last measurement. Meanwhile, in implant acceptors, the rise in cholesterol was only observed until the 6th month and continued to fall for the following months.

Further investigation is needed on the weight and lipid profile changes in DMPA and implant acceptors until the end of effective contraceptive duration. Investigation on other hormonal contraceptive methods is also needed to increase the knowledge of clinicians involved in family planning.

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