DMPA (DEPOT MEDROXYPROGESTERONE- ACETATE) INJECTION EFFECT ON LEPTIN LEVELS AND BODY MASS INDEX

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KEYWORDS

DMPA
Leptin
BMI

ABSTRACT:

Introduction: MPA (depot medroxyprogesterone acetate) is an effective hormonal injectable contraceptive method, but some acceptors may experience side effects such as weight gain. This weight gain has been linked to increases in serum leptin levels.

Objectives: This study aims to analyze the relationship between leptin levels and Body Mass Index (BMI) in DMPA acceptors.

Methods: This study is an analytical observational study with a Prospective Cohort design. The sample consisted of 61 women with DMPA injection at the Health Center in Makassar. Statistical analysis used Kolmogorov-Smirnov and Wilcoxon test. DMPA acceptors (from the 6-12th month) was increase in BMI (obesity)

Results: Statistical analysis showed a significant relationship between the duration of DMPA use and BMI ($P < 0.001$). Serum leptin levels was increase after DMPA use (6-12th month). Statistical analysis showed a significant relationship between the duration of DMPA use and leptin levels ($p < 0.001$). A significant relationship was observed between BMI and leptin levels at the 12th month of DMPA use ($p < 0.001$), but not at the 6th month ($p > 0.05$).

Conclusions: The use of DMPA at the 12th month resulted in an increase in leptin levels and Body Mass Index (obesity)

1. Introduction

Indonesia has a large and growing population, with over 270 million people in 2020. The maternal mortality ratio (MMR) in Indonesia was 189 maternal deaths per 100,000 live births in 2020. [1] However, the MMR in Indonesia is still considered high compared to the global targets set by the World Health Organization. The high MMR in Indonesia remains a significant challenge that needs to be addressed immediately. [2,3]

Efforts to reduce the maternal mortality rate in Indonesia, such as through family planning programs and improving access to maternal health services, have shown some progress but not effective. One of them is the injecting hormonal contraceptive method. Injectable contraceptive (combination or progesterone only) is a contraceptive that is safe and effective and reversible, does not require daily use, simple, cheap, and can be accepted by many people. One of injectable contraceptive is progestin-only contraceptive depot medroxyprogesterone acetate (DMPA). [4]

DMPA is a synthetic progestin-only contraceptive that works by inhibiting gonadotropin-releasing hormone (GnRH) signaling and gonadotropin secretion, leading to a greater suppression of luteinizing hormone (LH) compared to follicle-stimulating hormone (FSH) and prevent ovulation. While DMPA is an effective contraceptive method, it has been associated with several side effects, including weight gain. This weight gain has been linked to increases in serum leptin levels, an appetite-regulating hormone [23]. The mechanism behind this weight gain and leptin increase is not fully understood but may involve the glucocorticoid-like effects of DMPA [5].

2. Objectives

This study aims to analyze the relationship between leptin levels and Body Mass Index (BMI) in DMPA acceptors.

3. Methods

This research was observational analytic research with prospective cohort design to determine the association between body mass index and leptin level in hormonal contraceptive users of Depo Medroxyprogesterone Acetate (DMPA). The research was conducted at Healthcare Makassar, while the data was taken from September 2023 until Augustus 2024. Acceptors who used hormonal drugs in the last 1 month, Smoking (active smoker), Consuming alcohol, diabetes mellitus, hypertension (≥140/90mmHg), cardiovascular disease and undergoing a weight loss program are excluded into sample. Samples in this research were 61 acceptors of Depo Medroxyprogesterone Acetate (DMPA) that met the research inclusion criteria and were selected by non-random selection method with consecutive sampling technique

4. Results

A total of 61 participants were involved in the study. Table 1 provides a comprehensive overview of various parameters related to study, including age distribution, parity, body mass index (BMI) at 6 and 12 months, and leptin levels. Among the 61 participants, a significant majority (68.9%) were aged between 20 and 35 years. The parity data shows that most participants were multiparous (88.5%). The average BMI at 6 months was 23.33, with a notable percentage classified as overweight (31.1%). By 12 months, the average BMI increased slightly to 24.62, with a higher proportion of participants categorized as obese (44.3%). Leptin levels also showed a marked increase from an average of 2.82 ng/mL at 6 months to 15.64 ng/mL at 12 months

The duration of DMPA use is associated with changes in BMI distribution, with a trend towards increased overweight and obesity over time. (Table 2) Statistical test results show that there is a significant relationship between the duration of DMPA use with BMI ($P < 0.001$).

Table 3 The relationship between the duration of DMPA (Depot Medroxyprogesterone Acetate) acceptor use and the weight change observed in the study participants. A statistically significant difference in weight change between the two DMPA use durations. Leptin levels (in ng/mL) measured at two different time points, 6 months and 12 months after administering DMPA. At the 6-month mark, leptin levels ranged from a minimum of 0.02 ng/ml to a maximum of 10.60 ng/mL with a mean of 2.82 ng/ml. While the 12-month use, the minimum leptin level increased to 1.13 ng/ml. The mean leptin level at this time was 15.65 ng/ml. A statistically significant difference in leptin levels between the two time points ($p < 0.001$) (Table 3)

Parameters	Frequency [n(%)]
Age	
20-35	42 (68,9)
>35	19 (31,1)
Parity	
Primiparous	7 (11,5)
Multiparous	54 (88,5)
IMT	
6-month BMI	23.33 ± 3.26
Underweight	3 (4.9)
Normal	25 (41.0)
Overweight	14 (23.0)

Obesity	19 (31.1)
12-month BMI	24.62 ± 3.36
Underweight	1 (1.6)
Normal	23 (37.7)
Overweight	10 (16.4)
Obesity	27(44.3)
Leptin [Mean ± SD, mg/dl]	
Leptin 6 months	2.82 ± 1.94
Leptin 12 months	15.64 ± 17.03

Table 1. Characteristics of the Study Sample

5. Discussion

Our study shows majority samples opting for injectable DMPA are age range of 20 to 35 years. This demographic aligns with previous research that identifies this age group as optimal for childbirth. Health professionals advocate for birth control acceptors who have recently given birth to their first child to consider spacing their pregnancies during this period. While women over 35 years, especially after having two children, are recommended to consider long-term contraceptive methods, such as intrauterine devices. This guidance is rooted in medical recommendations that suggest women over 35 should avoid further pregnancies due to health-related concerns and other high risk of pregnancies. [6,7]

The present study demonstrates a significant correlation between the duration of DMPA (Depot Medroxyprogesterone Acetate) use and body mass index (BMI). These findings are consistent with the research conducted by Beksinska et al. (2021), which reported an increase in the baseline BMI among women who utilized DMPA injections for a duration of 12 months. Furthermore, a study by Suciana et al. (2017) revealed that among DMPA contraceptive acceptors, 20.5% of those who had used the method for 3 to 18 months were classified as obese, whereas the prevalence of obesity rose to 59% among those who had been using DMPA for more than 18 months. These results underscore the potential impact of prolonged DMPA use on weight gain and obesity among users. Another literature reported there was an increase in body weight of about 3.01 kg and significant weight gain after 12 months of DMPA use. [8,9,10]

Our study investigated the impact of DMPA (depot medroxyprogesterone acetate) contraceptive use on circulating leptin levels. The results demonstrate a significant increase in mean leptin concentrations among women who utilized DMPA for 12 months compared to those using it for 6 months. These findings are consistent with previous research conducted by Mayniar et al. (2017), which reported elevated leptin levels in 87.2% of DMPA injectable contraceptive acceptors. Furthermore, a recent study by Wahyuni et al. (2023) using a rodent model corroborated the current observations, revealing increased leptin synthesis following DMPA administration. [11,12] Leptin function is regulated by the hypothalamus through a feedback mechanism via sensory signals regulated from adipose tissue mass, the hypothalamus as the center of sensory reception and integration of leptin signals through leptin receptors (LR), the effector pathway includes the sympathetic system that regulates energy balance and energy expenditure. We assume that this increase is due to increased synthesis, even if the number of cells does not increase due to adipose cell hypertrophy. [10] Leptin has functions such as fertility through the Hypothalamus-Pituitary Gonadal-Axis system via regulation of gonadotropin-releasing hormone (GnRH) and contributes to the regulation of energy and body mass index through neuroendocrine mechanisms. The factor that regulates leptin production is adipocytes.

Obesity also causes an increase in leptin levels because in obesity there is an increase in serum triglyceride levels. [13,14] Increased serum triglycerides can lead to expansion of adipose tissue, which can further increase serum leptin concentrations. [11,15]

The present study is not without limitations. Firstly, leptin levels were not assessed prior to the initiation of DMPA contraceptive use, precluding the ability to analyze changes in leptin in relation to baseline values. Additionally, the duration of DMPA exposure was limited to 12 months to more comprehensively evaluate the impact on body mass index and leptin concentrations. Furthermore, the current study did not account for potential differences in obesity attributable to fluid retention. Finally, a few confounding factors, such as physical activity patterns and dietary habits, which may have influenced the observed outcomes, were not evaluated. Future research would benefit from addressing these methodological considerations to provide a more robust characterization of the metabolic effects associated with long-term DMPA use.

6. Conclusion

The use of DMPA injectable contraceptives for 12 months can lead to a significant increase in both BMI and serum leptin levels, potentially contributing to the development of obesity in this population.

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Ethical approval

The study protocol was approved by the [Hasanuddin University, Faculty of Medicine] ,Approval Number: [560/UN4.6.4.5.31/PP36/2023]). Participants' confidentiality and anonymity were ensured, and informed consent was obtained from all participants before data collection.

Conflicts of interest

The authors declare no conflict of interest.Table 2. Association between the length of use of DMPA acceptors with BMI

	DMPA	BMI				P
		Underweight	Normal	Overweight	Obesity	
		n (%)	n (%)	n (%)	n (%)	
Time	6 months	3 (4,9)	25 (41,0)	14 (23,0)	19 (31,1)	<0,001*
	12 months	1 (1,6)	23 (37,7)	10 (16,4)	27 (44,3)	

**Fisher exact test (P<0.05)*

Table 3. Relationship between the duration of DMPA acceptor use and the weight Change and Leptin serum levels

	DMPA	Weight change (kg)				p	Leptin levels (ng/mL)				P
		N	Min	Max	Mean ± SD		N	Min	Max	Mean ± SD	
Time	6 months	61	0,00	7,5	2,13 ± 1,54	< 0,001	61	0,02	10,60	2,82 ± 1,94	<0,001
	12 months	61	-3.00	11.00	5.17 ± 3,61		61	1,13	73,35	15,65±17,03	

Wilcoxon test (P<0.05)

Table 4. Relationship between BMI and leptin levels

IMT	Leptin levels (ng/mL)				p
	N	Min	Max	Mean ± SD	
6 months					
Underweight	3	0,37	0,90	0,69 ± 0,28	
Normal	25	0,20	5,96	2,68 ± 1,73	0,116
Overweight	15	0,02	10,60	3,34 ± 2,57	
Obesity	19	0,66	7,42	2,94 ± 1,67	
12 months					
Underweight	1	1,52	1,52	1,52 ± 0,00	
Normal	23	1,13	59,58	10,62 ± 13,87	0,003
Overweight	10	2,32	50,19	10,24 ± 14,50	
Obesity	27	1,49	73,35	22,45 ± 18,56	

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