Research Article

Incidence of Melasma, Breast Pain, and Depression in Users of Combination Hormonal and Progesterone-Only Contraceptives

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Abstract

Objective: To determine if there is a difference in the incidence of melasma, breast pain, and depression between a combination hormonal contraceptive (CHC) acceptors and a progesterone-only contraceptive.

Methods: This was a comparative analytical observational research with a cross-sectional design at Pakem Health Center, Yogyakarta. One hundred twenty subjects consisted of 60 progesterone-only contraceptive acceptors and 60 CHC acceptors aged 15-49 years, duration of use of hormonal contraceptives >6 months. In addition, measurements on melasma were clinically determined, breast pain using a Visual Analogue Scale (VAS) score, and depression using the Montgomery Asberg Depression Rating Scale (MADRS) questionnaire.

Results: Chi-square test results and logistic regression in CHC acceptors are likely to experience melasma (b=1.55; CI 95%=0.08-0.55; p=0.002), breast pain (b=2.32; CI 95%=0.02-0.34; p=<0.001), and depression (b=-1.02; CI 95%=1.15-6.74; p=0.023).

Conclusion: There were significant differences in the incidence of melasma, breast pain, and depression in CHC acceptors and progesterone-only contraceptives. The incidence of melasma and breast pain was higher in CHC acceptors, while depression was higher in progesterone-only contraceptive acceptors.

Keywords: breast pain, contraceptive, depression, melasma.

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INTRODUCTION

Hormonal contraceptives were first introduced in 1960, and the pill became the most widely used contraceptive method worldwide due to its ease of use [1,2]. Hormonal contraceptives consist of two options based on their content: progesterone-only contraceptives and combination hormonal contraceptives (CHC) containing the hormones estrogen and progesterone [3]. Progesterone works to prevent ovulation by inhibiting the development of ovarian follicles. It causes changes in the cervical mucus to become more viscous, making it difficult for sperm cells to penetrate [4,5].

Generally, side effects arise as a result of the hormones used. Side effects of using CHC include breast pain and increased scores of mental symptoms, including emotional, depressed mood, and anxiety [6,7]. Side effects that may arise due to the content of the hormone progesterone include fatigue, loss of libido, and depression [7,8.] While estrogen-related side effects commonly include nausea, headache, breast pain, and melasma [7]. Depression, a mental disorder characterized by persistent sadness and a lack of interest in daily activities, is also a noted side effect [9].

In a study of 302 patients in Brazil, it was found that factors that influence the onset of melasma include pregnancy (36.4%), oral contraceptives (16.2%), and sun exposure (27.2%) [10]. The skin of women who take oral contraceptives containing estrogen is more susceptible to hyperpigmentation. The effects of UV radiation rays can also increase the proliferation of melanocyte cells, thus exacerbating hyperpigmentation[11]. Melasma is influenced by many factors, including estrogen

and angiogenesis[12]. Two estrogenic receptors respond to estrogen, namely estrogenic receptors α and β. It was found that the expression of β-estrogenic receptors was dominant in the case of hyperpigmentation lesions due to melanocytes [13].

Histologically, melasma is characterized by the excessive deposition of melanin in the epidermis (epidermal type, 70%), in dermal macrophages (dermal type, 10%), or both (mixed type, 20%)[14]. The exact etiology of breast pain has yet to be determined. However, three factors are believed to be related to its onset: increased ovary secretion, reduced progesterone production, and hyperprolactinemia[15]. Breast pain is typically described as pain in one or both breasts [16].

Selecting an appropriate contraceptive method is crucial not only for individual health but also for broader public health goals, such as controlling population growth and addressing related societal issues[17]. Women who use or are considering the use of birth control often express concerns about its potential impact on their future fertility[18]. Consequently, it is essential to provide comprehensive education and counseling about the available contraceptive options, including their benefits and potential side effects. This information helps individuals make informed decisions. A lack of knowledge can lead to ineffective, inconsistent, and incorrect use of contraceptives[19,20]. The study aims to determine if there is a difference in incidence rates of melasma, breast pain, and depression between a CHC acceptor and a progesterone-only contraceptive.

METHODS

This was a comparative analytical observational research with a cross-sectional design conducted at Pakem Health Center, Sleman, Yogyakarta, from August to October 2020. The study subjects were 60 progesterone-only contraceptive acceptors and 60 CHC acceptors, ages 15 - 49 years, with a more than six months duration[21]. The sampling technique used in this study is non-probability sampling with the purposive sampling method.

Inclusion criteria were hormonal contraceptive acceptors who have been more than six months, are willing to fill out questionnaires, and are willing to be examined. Exclusion criteria are women who take hormonal drugs other than contraceptives, previous history of depression, have abnormalities or diseases of the breast, including blistered nipples, have been diagnosed with breast cancer, lump the breast [15,22], have family members who have recently died 23, and have abnormalities in the limbs 24.

Measurements in melasma are clinically determined in the form of uneven macular lesions that are darker in color than the surrounding skin, symmetrical, and usually present on the face or place exposed to sunlight. Breast pain was assessed using the Visual Analog Scale (VAS) during the research visit when the patient reported pain. The VAS score was obtained based on direct anamnesis reflecting the patient's actual condition at the time of assessment. Subjects were considered to experience breast pain when they felt pain in the breast and had a VAS score >4 mm. Depression was assessed using the Montgomery-Asberg Depression Rating Scale (MADRS) questionnaire. If the subject gets a MADRS score >8, then the subject is considered depressed. If the MADRS score ≤8, it means the subject is not depressed.

Results were analyzed using the chi-square statistical test and multivariate logistic regression test using Statistic Product and Service Solution (SPSS).

RESULTS

Table 1. Characteristic Research Subjects

Characteristic	N	Min	Max	Mean	Standard Deviation
Age (years)	120	18	49	36.56	7.72
Weight (kg)	120	37	87	59.90	9.43
Height (cm)	120	126	169	153.33	5.55
Body Mass Index (kg/m2)	120	18	36	25.45	3.66
Duration of contraception use (Months)	120	6	240	66.02	56.61
Sports Duration/Week (Minutes)	120	0	420	28.37	60.87

Min: Minimal. Max: Maximum

Table 1 shows that out of 120 hormonal contraceptive acceptors, the acceptors' age was 18-49 years, with an average age of 36.56 years and a standard deviation of 7.72. Characteristic weight obtained a range of 37-87 kg with an average weight of 59.90 kg and a standard deviation of 9.43. Characteristic height ranges from 126-169 cm, with an average height of 153.33 cm and a standard deviation of 5.55. Characteristic BMI ranges from 18 to 36, averaging 25.45 and a standard deviation 3.66. The duration of contraceptive use ranges from 6-240 months, with an average usage of 66.02 months and a standard deviation of 56.61. Sports duration during the week ranges from 0-420 minutes, with an average time of 28.37 minutes and a standard deviation of 60.87.

Table 2. Bivariate Analysis of Melasma, Breast Pain, and Depression

Variable	Combination Hormonal Contraceptive		Progesterone-only Contraceptive		OR	*P-value*
	N	%	N	%		
Melasma						
Yes	32	71.1	13	28.9	4.13	0.001*
No	28	37.3	47	62.7		
Breast Pain						
Yes	19	79.2	5	20.8	5.09	0.002*
No	41	42.7	55	57.3		
Depression						
Yes	16	27.6	44	71.0	0.15	0.001*
No	42	72.4	18	29.0		

OR: Odd ratio
*Significant p<0.05

Table 2 shows chi-square test results of melasma, breast pain, and depression showed significant test scores (p<0.05).

Table 2. Bivariate Analysis of Melasma, Breast Pain, and Depression

Variable	b	95% C.I		*P-value*
		Lower	Upper	
Melasma	1.55	0.08	0.55	0.002*
Breast Pain	2.32	0.02	0.34	<0.001*
Depression	-1.02	1.15	6.74	0.023*

*Significant p<0.05

Combined hormonal contraceptive acceptors are 1.55 times higher than a progesterone-only contraceptive acceptor (b=1.55; CI 95%=0.08 to 0.55; p=0.002). The CHC acceptors were 2.32 times higher than a progesterone-only contraceptive acceptor (b=2.32; CI 95%=0.02 to 0.34; p=<0.001). Combined hormonal contraceptive acceptors are 1.02 lower than progesterone-only contraceptive acceptors (b=-1.02 CI 95%=1.15 to 6.74; p=0.023).

DISCUSSION

Hormonal contraceptive acceptors are more prone to melasma, breast pain, and depression than non-hormonal contraceptive acceptors and women who do not use contraceptives. This is because the content of estrogen and progesterone hormones in hormonal contraceptives can affect the condition of the body acceptors. Estrogen hormones tend to cause increased melanogenesis in the skin, resulting in melasma. In contrast, the hormone progesterone that has been studied can cause a decrease in monoamine neurotransmitter levels in the body that causes the mood of the acceptor to drop so that the acceptor tends to experience symptoms of depression[11,25]. These two hormones can also cause an imbalance in the body's estrogen/progesterone ratio, causing the onset of breast pain [26]. In this study, CHC acceptors were 4.13 times more likely to experience melasma than progesterone-only contraceptive acceptors. These results align with previous research, which states that melasma incidence tends to be more found in hormonal contraceptives containing estrogen and progesterone than in contraceptives containing only progesterone [27]. In addition, estrogen use is likely to cause the risk of melasma in the face and skin to become darker5. Another study also state that skin contraceptive acceptors containing estrogen are more susceptible to the process of melasma occurrence[11]. The skin susceptibility

to CHC acceptors to melasma is thought to be due to stimulation by the hormone estrogen in several proteins related to melanogenesis, namely Tyrosinase-Related Protein-1 (TRP-1), Tyrosinase-Related Protein-2 (TRP-2), PDZK1, and Melanocyte Inducing Transcription Factor (MITF)[12]. Estrogen can also increase RNA levels in melanocortin receptor type 1 (MRC-1), resulting in increased keratinocyte activity, which causes more melanin production than usual [28].

Combined hormonal contraceptive acceptors were 5.09 times more likely to experience breast pain than progesterone-only contraceptive acceptors. The cyclic properties of breast pain may be caused by the effects of estrogen [29.] There have been no studies comparing the incidence of breast pain between contraceptive types. Still, breast pain is often mentioned as a side effect arising from the use of hormonal contraceptives.

A progesterone-only contraceptive acceptor was 0.15 times more likely to have depression than CHC acceptors. This is in line with previous research stating that using progesterone-only contraceptives can increase the risk of depression, whereas CHC is not [25]. A study in Denmark with a total of 1,061,997 subjects said that there was a link between hormonal contraceptive use and relative risk in progesterone-only contraceptive users was higher at 1.34 on progesterone pills, 2.0 in implant users, 2.7 in Depo Medroxyprogesterone Acetate (DMPA) injectable users, and 1.4 in IUD-LNG users, while in combined oral contraceptive (COC) pills of 1.23[30]. External progestin is thought to increase levels of monoamine oxidase more effectively than endogenous progesterone. Therefore, progestin has the potential to lower serotonin levels faster and thus improve symptoms of depression and irritability. At the same time, estrogen increases serotonin levels and other antidepressant neurotransmitters, resulting in protective effects against the incidence of depression [25].

The limitations of this study include the inability to control obesity, pre-existing melasma, and frequent sunlight exposure as confounding factors. These factors may have influenced the observed relationships. Future studies are recommended to consider obesity, pre-existing melasma, and sunlight exposure as exclusion criteria or include them as covariates in the analysis to improve the validity and accuracy of the results.

CONCLUSIONS

There were significant differences in the incidence of melasma, breast pain, and depression in CHC acceptors and progesterone-only contraceptives. The incidence of melasma and breast pain was higher in the CHC acceptors, while depression was higher in the progesterone-only contraceptive acceptors.

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