

EFFECT OF DURATION OF USE OF DEPOT MEDROXYPROGESTERONE ACETATE AND PSYCHOLOGICAL STRESS ON THE FEMALE SEXUAL FUNCTION

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Abstract. Depot medroxyprogesterone acetate (DMPA) injectable contraceptive has side effects. One of the side effects of progestin-only hormonal is sexual dysfunction. This study aimed to analyze the factors that influence the incidence of sexual dysfunction in women who use DMPA injectable contraception. This study used a quantitative correlative design with a cross-sectional approach. This study used convenience sampling to select 75 respondents that met the inclusion criteria. In this study, female sexual function index was the dependent variable, while the age, occupation, parity, last delivery, length of use, sexual traumatic experience and psychological stress were independent variables. A questionnaire was used to collect demographic data while the Female Sexual Function Index (FSFI) was used to measure the female sexual function. Data were analyzed using Chi-square and logistic regression. The results showed that there was a relationship between last delivery ($p=0.041$), length of DMPA use ($p<0.001$) and psychological stress ($p=0.009$) with the female sexual function, while age ($p=0.441$), occupation ($p=0.308$), parity ($p=0.708$) and sexual traumatic experience ($p=0.502$) had no relationship with the female sexual function. Multivariate analysis showed that length of use of DMPA injection as birth control ($p=0.008$) and stress ($p=0.043$) affect the occurrence of sexual dysfunction; DMPA injection users for 1-2 years and >2 years

had a greater risk of experiencing sexual dysfunction when compared to those who used DMPA less than 1 year. Respondents who experienced stress were at greater risk of experiencing sexual dysfunction. This study shows that the length of DMPA use is most dominantly associated with the sexual dysfunction of women.

Keywords: contraception, depot medroxyprogesterone acetate, female, sexual dysfunction

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INTRODUCTION

Sexual function is an important component of sexual health that determines the general well-being of a person. There is a strong association between sexual well-being and overall life satisfaction of individuals over time, and sexual problems have negative impacts on emotional well-being (Stephenson and Meston, 2015). Female sexual dysfunction (FSD) is defined as psychophysiological changes and disturbances in sexual desire, which cause marked distress and interpersonal difficulty (Cayan *et al*, 2016). FSD which is the decrease in sexual desire arousal, or the presence of dyspareunia and difficulty/inability to achieve orgasm, can cause personal distress.

An estimation of the prevalence of sexual dysfunction in women is difficult, because the parameters of female sexual dysfunction are not very clear. Female sexual problems are highly prevalent worldwide. The prevalence of FSD ranges from 27 to 70% (Ramezani Tehrani *et al*, 2014). Based on survey among the female population in Italy, low sexual satisfaction was reported by 65.0% of the sample; low libido, dyspareunia,

and arousal disorder were reported by 29.0%, 24.0%, and 19.7% of the female sample (De Rose *et al*, 2019).

The etiology of FSD is often multifactorial and may include psychological problems such as depression or anxiety, relationship conflict, fatigue, stress, issues relating to prior physical or sexual abuse, medications, and physical problems. Female sexual function is influenced by several biological, psychological, and social factors. Sexual dysfunction has been especially linked to emotional intimacy and sexual hormone. There was a high prevalence of and a strong association between hormonal contraception and FSD (Butt *et al*, 2019). Mood and sexual related-side effects significantly generate problems to acceptor users of hormonal contraceptives in women of reproductive age due to hormonal change.

Worldwide, 922 million women of reproductive age (or their partners) are contraceptive user and 8% of them, used injectable contraceptive (United Nations, 2019). As of 2017, injectable contraceptives represented 19.5% of modern method use among women in union (Mwembo *et al*, 2018). Approximately, 2.3% of women who use contraception report that they use the contraceptive injection (KFF, 2020).

A formulation of the injectable depot medroxyprogesterone acetate (DMPA) is one such option for broadening the spectrum of contraceptive choices. The DMPA contraceptive injection is a commonly used reversible contraceptive method among women worldwide. The injectable contraceptive DMPA is a progesterone-only contraceptive method.

The shot works by releasing the hormone DMPA, a progestin, which suppresses ovulation and thickens cervical mucus that also helps keep sperm from fertilizing an egg. DMPA can be provided by an intramuscular shot administered by a clinician or by a subcutaneous shot that can be injected by the patient at home. Both forms need to administer once

every 12 weeks to be effective.

DMPA, like other contraceptive methods, has side effects and complications which may not be acceptable to the women, therefore, leading to discontinuation (Nonye-Enyidah *et al*, 2020). Another research found that progestin-only pills (POPs) are unlikely to have a major impact on sexual desire. POPs with antiandrogenic activity may adversely affect sexual interest and fantasies. The findings of the studies conclude that the effect on sexual function depends on the particular type of progestin and not its dosage (Caruso *et al*, 2022). But the association between female sexual function and DMPA is controversial.

An unsatisfactory number of studies report the influence of the available contraceptives on female sexuality. Although there is currently no recommendation to screen for sexual dysfunction before or during the use of DMPA.

Recently, a prospective cohort study, including data from 1983 women aged 14 to 45 years, found less interest in sex in women using DMPA, compared to nonhormonal contraception (copper intrauterine device (copper IUD)) use (de Castro Coelho and Barros, 2019). DMPA association with a lower sexual function was also supported by users who reported not finding sex pleasurable, compared to copper IUD users and feeling anxious before sex, but this last difference was not statistically significant. In contrast, no association was found between the use of DMPA injection and sexual interest among adolescent users when comparing various hormonal contraceptives (de Castro Coelho and Barros, 2019)

This study aimed to analyze the factors that influence the incidence of sexual dysfunction in women who use DMPA injectable contraception in two private midwifery practices in East Java, Indonesia.

MATERIALS AND METHODS

Study design and population

The design of this study was a cross-sectional study, which included 75 women. Inclusion criteria of this study were women over 18 years of age, sexually active, users of DMPA injection. Exclusion criteria were having a history of sexual dysfunction, body mass index ≥ 30 kg/m², smoking, cognitive limitation or disability, mental illness, chronic metabolic pathologies, antihypertensive use, and those who did not wish to participate. This study was conducted in two private midwifery practices in East Java, Indonesia between 1-30 December 2020. Convenience sampling was performed; all women who met the inclusion criteria and were willing to participate were included as respondents.

Procedure

A professional nurse approached the women who used DMPA injection, invited them to participate, and evaluated the inclusion and exclusion criteria. For those who met the criteria, the objective of the study was explained to them, pointing out the ethical aspects and facilitating the reading of the informed consent. Once signed, in a private area the researcher applied a questionnaire to obtain information on sociodemographic characteristics, as well as the evaluation instrument. Efforts were made to control information bias, facilitating a warm, trusting, and private environment to avoid eventual alterations in memory and/or embarrassment due to questions about their sexual behavior. The Female Sexual Function Index (FSFI) is a questionnaire developed by Rosen *et al* (2000) and made up of 19 items aiming to evaluate six domains: desire (Items 1 and 2), arousal (Items 3 to 6), lubrication (Items 7 to 10), orgasm

(Items 11 to 13), satisfaction (Items 14 to 16), and pain (Items 17 to 19). To score the measure, the sum of each domain score is first multiplied by a domain factor ratio (0.6 for desire; 0.3 for arousal; 0.3 for lubrication; 0.4 for orgasm; 0.4 for satisfaction; and 0.4 for pain) in order to place all domain totals on a more comparable scale, and then subsequently summed to derive a total. Thus, the maximum score applicable is 36. The higher the overall score, the better sexual function, and the lower the score, the greater the risk of sexual dysfunction. It is considered that there is a risk of sexual dysfunction if the total score is <26.55 (Wiegel *et al*, 2005), or if one of the domains is less than 3.6.

Variables

Sociodemographic (age, race, educational level, marital status, occupation, socioeconomic status, origin, sexual and reproductive health variables (age at menarche, age of onset of sexual life, number of sexual partners, parity), and scores of the domains of the FSFI were evaluated.

Statistical analysis

The qualitative variables are described with absolute and relative frequencies, and the quantitative ones through measures of central tendency and dispersion according to their distribution. To analyze the data, descriptive statistics were calculated, and Chi-square and Fisher's exact tests were used to compare the qualitative variables. Multiple logistic regression ($\alpha=5\%$) was used to predict a single binary variable using one or more other variables. Statistical Package for the Social Sciences (SPSS) version 16 (SPSS Inc, Chicago, IL) was utilized. A p -value of 0.05 is considered statistically significance.

Ethical consideration

The study was approved by the Research Ethics Committee of STIKES Katolik St Vincentius a Paulo Surabaya (Approval No. 659/Stikes. Vinc/KEPK/II/2020).

RESULTS

This study was conducted on 75 women, whose demographic characteristics and FSFI scores are presented in Table 1. More than half ($n = 43, 57.3\%$) of the women who participated in the study had sexual dysfunction.

The average age of the women who participated in the study was 33.1 ± 6.04 years. Based on the occupation, most respondents in both groups (group with sexual dysfunction and group with normal sexual function) were employees. Most of the respondents in both groups are multipara with the average parity is 2.08 ± 0.8 and the last delivery was >2 years. Based on traumatic sexual experience, most of the respondents in the two groups did not have a traumatic sexual experience. In terms of length of DMPA use, 50% of the normal sexual function respondents had been using DMPA injection for >2 years while 55% of those who had sexual dysfunction used DMPA injection for >2 years. As for psychological stress, 75% of respondents in normal sexual function group didn't have psychological stress, but 58.1% of respondents in the dysfunctional sexual group had psychological stress. In univariate analysis, there was no significant relationship between sexual function and age ($p=0.441$), occupation ($p=0.308$), parity ($p=0.708$), and traumatic sexual experiences ($p=0.502$) but significant relationship was found

Table 1
Multiple logistic regression showing the relationship between respondents' characteristics and female sexual function index (FSFI) scores

Characteristic	Female sexual function index (FSFI) score		OR (95% CI)	p-value*
	FSFI≥26.55 (N = 32)	FSFI<26.55 Mean ± SD (N = 43)		
Age, n (%)		33.1 ± 6.4		0.441
18-27 years	8 (25.0)	6 (14.0)	Reference	
28-36 years	11 (34.4)	15 (34.9)	0.692 (0.140-3.419)	
37-45 years	13 (40.6)	22 (51.2)	0.638 (0.098-4.148)	
Occupation, n (%)				0.308
Housewives	15 (46.9)	14 (32.6)	Reference	
Employees	17(53.1)	29 (67.4)	0.529 (0.182-1.531)	
Parity, n (%)		2.08 ± 0.8		0.708
Parity 1	7 (21.9)	8 (18.6)	Reference	
Parity 2	20 (62.5)	25 (58.1)	0.176 (0.048-0.647)	
Parity >2	5 (15.6)	10(23.3)	0.264 (0.049-1.425)	
Last delivery n (%)				0.041
0 to 6 months	5 (15.6)	1 (2.3)	Reference	
>6 months to 2 years	4 (12.5)	12 (27.9)	0.000 (0.000-0.000)	
>2 years	23 (71.9)	30(69.8)	0.000 (0.000-0.000)	

Table 1 (cont)

Characteristic	Female sexual function index (FSFI) score		OR (95% CI)	p-value*
	FSFI≥26.55 (N = 32)	FSFI<26.55 (N = 43)		
Length of DMPA use, n (%)		Mean ± SD		<0.001
1 month - 1 year	12 (37.5)	1 (2.3)	Reference	
>1 year to 2 years	4 (12.5)	18 (41.9)	4.17 (2.221-56.625)	
>2 years	16 (50.0)	24 (55.8)	1.72 (1.002-11.116)	
Traumatic sexual experience, n (%)				0.502
Have	3 (9.4)	7 (16.3)	2.604 (0.404-16.795)	
Do not have	29 (90.6)	36 (83.7)	Reference	
Psychological stress, n (%)				0.009
Yes	8 (25.0)	25 (58.1)	3.24 (1.089-10.752)	
No	24 (75.0)	18 (41.9)	Reference	

Note: A total FSFI score of 26.55 is optimum for discriminating between women with and without sexual dysfunction. Sexual dysfunction is considered with FSFI score <26.55.

*Significantly different when p-value<0.05)

CI: confidence interval; DMPA: depot medroxyprogesterone acetate; FSFI: female sexual function index; SD: standard deviation

between sexual dysfunction and last delivery ($p=0.041$), length of DMPA use ($p<0.001$) and psychological stress ($p=0.009$) (Table 1).

After logistic regression, it was found that length of use and psychological stress affect the occurrence of sexual dysfunction ($p=0.008$ and 0.043 , respectively). DMPA injection users for 1-2 years have a risk of experiencing sexual dysfunction 4.17 times greater than those who used DMPA <1 year; users of DMPA for >2 years have a risk of experiencing sexual dysfunction 1.7 times greater than that of users of DMPA <1 year and people who experience stress is at risk of experiencing sexual dysfunction by 3.24 times greater than people who do not experience stress (Table 1).

Table 2 shows that of the 6 domains of sexual function, the lubrication and pain domains have the lowest values compared to the other domains (3.94 ± 0.82 and 3.96 ± 1.00).

Table 2
Respondents' FSFI scores of domain sexual function

Domain	FSFI score (Mean \pm SD)
Desire	4.28 \pm 1.13
Arousal	4.29 \pm 0.73
Lubrication	3.94 \pm 0.82
Orgasm	4.44 \pm 0.93
Satisfaction	4.33 \pm 0.82
Pain	3.96 \pm 1.00

FSFI: female sexual function index, SD: Standard deviation

DISCUSSION

Sexuality is an inseparable part of the human life. A healthy sexual life is one of the most important parameters of the health and quality of life. Contraceptive is a concept which affects couples in having a baby. Fear of pregnancy or the desire of pregnancy could affect the sexual desire and performance and also that the contraceptive methods used in order to prevent pregnancy have an effect on sexual life.

The result showed that the average FSFI score was 24.8 with a standard deviation of 4.46. Notably, 57.3% had a low score (below 26.55), while 42.7% had a higher score (26.55 or above). DMPA is administered intramuscularly at three-month intervals (12-13 weeks) (Saptatangtrakul *et al*, 2016). DMPA works primarily by inhibiting the secretion of pituitary gonadotropins, thereby suppressing ovulation (Teal and Edelman, 2021). Women enter a hypoestrogenic state and their progesterone is low due to anovulation. DMPA also increases the viscosity of cervical mucus and induces endometrial atrophy (Casado-Espada *et al*, 2019). In long-term DMPA use, atrophic change of endometrium and vagina mucosa are demonstrated in several studies (Moreira *et al*, 2020). The atrophic vaginal mucosa and vaginal dryness may cause sexual pain or dyspareunia (Walker and Badawy, 2013).

Among other side effects of DMPA, half of the users will experience sexual dysfunction (de Castro Coelho and Barros, 2019). Hormonal contraceptives can cause vaginal dryness, resulting in pain (dyspareunia) during sexual intercourse (Andryani *et al*, 2021). It was evidenced that progesterone has central sedative effects and progestins can induce depression and also have inhibitory effects on sexual behavior (Shahin *et al*, 2021). Progesterone in DMPA has an effect on vaginal epithelium; estradiol level was tangibly low, and may even cause suppression of

estrogen (Walker and Badawy, 2013). On the other hand, many women using DMPA had amenorrhea which may have affected their sexual desire or sexual enjoyment, through unexpected bleeding.

Shahin *et al* (2021) concluded that progestin-only contraceptives were associated with impairment of FSF; the injectable was worse than the POP while neither IUDs users nor participants on COP suffered from impaired sexual function. It also in line with the study by Saptatangtrakul *et al* (2016) who showed that women using DMPA had sexual pain or dyspareunia more than those using another contraception (IUD).

This study also showed that less than 50% respondents had FSFI Score ≥ 26.55 . It meant they had normal sexual function. This showed that sexual function is not only affected by hormonal alone. A person's perception of sexual difficulties is influenced by her opinion about normal or abnormal sexual function, which is related to self-perception which is ultimately related to culture. Other factors that influence sexual response are the duration and quality of a relationship and personal-psychological factors. Sexual response occurs through complex interactions of psychological, social, environmental, and biological factors (hormonal, vascular, muscular and nerve (Moreira *et al*, 2020) Respondents who had normal sexual function may have adapted with the imbalance condition.

The result of this study showed that there was a significant correlation between length of DMPA use and sexual dysfunction ($p < 0.001$). This study in line with Andriyani *et al* (2021) who showed there was a significant relationship between the length of time using DMPA injections to sexual dysfunction in family planning acceptors at the Bara Baraya Makassar Health Center in 2016.

DMPA users for 1-2 years have a risk of experiencing sexual dysfunction 4.1724 times greater than those who have been using DMPA

for <1 year. This means that the use of DMPA injection for a long-term resulted a sexual dysfunction. The use of hormonal contraceptives, one of which is DMPA, triggers a feedback mechanism that regulates the levels of estrogen and progesterone. Giving the body extra hormones such as estrogen and progesterone will increase the levels of these two hormones in the blood. These increasing levels will be detected by the anterior pituitary and cause negative feedback by reducing the secretion of follicle-stimulating hormone (FSH) and Luteinizing hormone (LH) then blocked ovarian function and reduction in androgen and estrogen production (Moreira *et al*, 2020)

Within 1 year of DMPA use, the user's body is still able to compensate for the hormonal imbalance that occurs, thus preventing sexual dysfunction. Based on study by Veri *et al* (2021), the longer the exposure to DMPA, the thinner the thickness of the vaginal epithelium. Long-term use of progesterone contraceptives can change the vascular structure of the vagina and the morphology of vaginal tissue, along with the occurrence of oxidative stress and apoptosis due to a deficiency in the endogenous hormone estrogen. The decrease in estradiol occurs with prolonged use of DMPA contraceptives and results in vaginal dryness and dyspareunia (Walker and Badawy, 2013).

Aspects of sexual function include a woman's desire or desire to engage in sexual activity, a person's ability to start and maintain stimulation, experience lubrication, orgasm, enjoy a real sensation of sexual activity and minimize sexual pain and discomfort. Vaginal dryness and dyspareunia cause discomfort during sexual intercourse thereby reducing sexual functions. DMPA differs from other progesterone-only contraceptives in that it does not suppress follicle stimulation hormone as strongly as LH. The remaining DMPA users will have lower estradiol levels. However, chronic suppression of FSH leads to diminished estradiol

and progesterone production such that symptoms occur. Hypoestrogenic condition is a significant factor in causing dyspareunia as shown in this case. This is due to atrophy of vaginal epithelium and lack of secretions (Walker and Badawy, 2013).

However, the results of this study also showed that women using DMPA for >2 years had a lower risk of experiencing sexual dysfunction when compared to those who used DMPA for 1-2 years, although it still had a higher risk compared to the duration of use of less than 1 year. Using DMPA injections over two years poses a big risk of the impact of low serum estradiol levels, which can include bone mass loss, prolonged amenorrhea and sexual dysfunction such as low sexual desire that affects a person's sexual life (Andryani *et al*, 2021). However, this study shows that the risk of sexual dysfunction in DMPA users >2 years is lower than the users of 1 to less than 2 years. It is possible that there are other factors that also affect women's sexual function, such as self-acceptance and partners towards changes in female organs due to hormonal changes as a result of using DMPA.

Stress is one of the psychological factors that affect the sexual function. The findings of this study indicated a significant association between psychological stress and sexual function ($p=0.009$). Respondents who had stress psychological had 3.24 times greater risk to sexual dysfunction. Sexual function was associated with individual's mental status. There were significant associations between stress and domains of function except pain and sexual desire; between depression and all domains except sexual pain; and between anxiety and all domains of sexual function. Stress, anxiety and depression have a significant inverse relationship with the total score of sexual function. The strongest and weakest relationships of these domains with these three psychological factors were observed in satisfaction and sexual pain, respectively

(Yazdanpanahi *et al*, 2016; Galanakis *et al*, 2015). Several previous studies have shown that progestin-only hormonal contraceptives including DMPA injection cause depressive symptoms (Keyes *et al*, 2013; Singata-Madliki *et al*, 2021; Skovlund *et al*, 2018).

Progesterone causes vitamin B6 deficiency. It causes the body feels weak, lethargic, and feel depressed. Progesterone participates in controlling opioidergic, serotonergic and cholinergic systems. The mechanism of contraception affects emotions due to the suppressive effect of several neuroactive steroids that affect the expression and activity of gamma-aminobutyric acid receptors and decrease the concentration of free testosterone. This indicates that there is a possibility that the stress experienced by respondents is a side effect of using DMPA injection. However, this cannot be ascertained, because the stress on the respondents was not carried out further research related to its causes.

The limitations of this study were that an in-depth analysis was not carried out for each domain of sexual function and there was no comparison group either with other users of hormonal contraceptives or with non-users of hormonal contraceptives.

In conclusion, this study's main findings showed length of use of DMPA injection as birth control ($p=0.008$) and stress ($p=0.043$) affect the occurrence of sexual dysfunction. DMPA injection users for 1-2 years have a risk of experiencing sexual dysfunction 4.17 times greater than DMPA injection users <1 year. DMPA injection users for >2 years are at risk of experiencing sexual dysfunction by 1.72 times greater than those who use birth control <1 year. Respondents who experience stress are at risk of experiencing sexual dysfunction by 3.242 times greater than people who are not experiencing stress. For this reason, it is important for health service providers to provide sexuality-related counseling for DMPA injection users, especially those who have used it for

more than 1 year. Finally, further research is needed to develop other factors, increase the sample, and readjust the inclusion and exclusion criteria that may relate to female sexual function.

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CONFLICT OF INTEREST DISCLOSURE

The authors declare no conflict of interest.

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