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Masters Program in Public Health, Universitas Sebelas Maret

Meta Analysis

Meta-Analysis the Effect of Hormonal Contraception on Sexual Disfunction in Injection and Oral Contraceptive Acceptors

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ABSTRACT

Background: One of the factors that cause sexual dysfunction is the use of hormonal contraception. The hormone progesterone in contraceptives functions to thicken cervical mucus. In addition, the hormone progesterone also facilitates the conversion of carbohydrates into fat so that one of the side effects is causing body weight to increase and reducing sexual arousal which causes an effect on sexual desire. This study aimed to analyze the effect of the use of injectable hormonal contraception and pills on the incidence of sexual dysfunction using a meta-analysis study.
Subjects and Method: This study is a systematic review and meta-analysis using the PRISMA flowchart diagram. The process of searching for articles was carried out with a range of 2011-2022 in the Google Scholar, PubMed, Science Direct, Researchgate and Springerlink databases. The keywords used in the article search are "hormonal contraceptive" AND "oral contraception" OR "pills contraceptive" AND "injectable contraceptive" AND "sexual dysfunction" AND "cross-sectional". The inclusion criteria are full text articles with cross-sectional study design, articles using English, multivariate analysis with Adjusted Odds Ratio. Articles that met the requirements were analyzed using the RevMan 5.3 application.
Results: A total of 14 articles with a cross-sectional study design originating from Iran, Indonesia, Malaysia, Ethiopia, Egypt, Washington, Sweden and Polan were meta-analyzed in this study. A meta-analysis of 7 articles showed that there was an effect of using injectable hormonal contraception on the incidence of sexual dysfunction 1.66 times compared to those not using injectable contraception, but this was not statistically significant (aOR= 1.66; 95% CI= 0.65 to 4.26; p= 0.290). Meanwhile, 7 articles showed that women using oral contraceptives had a 1.42 times risk of experiencing sexual dysfunction compared to not using oral contraceptives and this was statistically significant (95% CI= 1.04 to 1.92; aOR= 1.42; p= 0.030).
Conclusion: Injectable hormonal contraceptives show that there is an effect on the incidence of sexual dysfunction, but statistically this relationship is not significant. Hormonal contraceptive pills showed an effect on the incidence of sexual dysfunction and was statistically significant.

Keywords: sexual dysfunction, injectable contraceptives, oral contraceptives, meta-analysis.

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BACKGROUND

Sexual dysfunction in women is still seen as a health problem with low priority because it is not considered a threat to survival. However, the impact of these disorders can affect relationships with partners and wo-

men's quality of life (Hindun and Pastuty, 2011). Sexual dysfunction problems can occur regardless of age and can also have a negative impact on quality of life and health (Ramadhani et al., 2018). Sexual dysfunction is a problem that occurs in the sexual response cycle which can prevent individuals from getting satisfaction in sexual activity. Sexual dysfunction includes various disorders in sexual relations. Disorders can be in the form of a lack of interest, pleasure, failure in the physiological response needed for effective sexual interaction or being unable to control or experience an orgasm (Pratama and Pusparini, 2019).

One of the factors that cause sexual dysfunction is the use of hormonal contraception. Hormonal contraception has a negative impact on a person's quality of life and emotional health. Sexual dysfunction is a common disorder in which women have one type of sexual dysfunction and the most common complaint is low sexual desire or libido (Zettira et al., 2015). The prevalence of sexual dysfunction in Indonesia is quite high, namely 60.8%, which is caused by the use of hormonal contraception (Ramadhani et al., 2018).

Other factors that can increase the risk of sexual dysfunction such as medical conditions such as hypertension, stroke and diabetes. Besides that, other factors that cause sexual dysfunction are the use or consumption of drugs such as anti-depressants, antihypertensives and also hormonal preparations such as ethinyl estradiol which is found in birth control pills and medroxyprogesterone acetate (DMPA) which is found in injectable contraceptives (Hindun and Pastuty, 2011). In terms of health, simple or non-hormonal contraception is much safer for health than hormonal contraception. Long-term use of hormonal contraceptives can disrupt the balance of hormones. However, hormonal contraception is still the top choice among the public. This is because hormonal contraceptives containing estrogen, progesterone or a combination of the two are considered very effective in preventing pregnancy compared to non-hormonal contraceptives (Butt et al., 2019).

According to the BKKBN, active family planning participants among couples of childbearing age (PUS) in 2020 are 67.6%. This figure has increased compared to 2019 of 63.31% based on Indonesian family profile data for 2019. Various types of contraception innovations have emerged, ranging from simple methods to more effective modern methods such as injections, pills, implants, IUDs, vasectomy and tubectomy. The pattern of choosing the type of contraception in 2020 shows that most acceptors choose to use the injection method by 72.9%, followed by the pill by 19.4% (Ministry of Health RI, 2020).

The hormone progesterone in contraceptives functions to thicken cervical mucus and reduce the ability of the uterus to accept fertilized cells. In addition, the hormone progesterone also facilitates the conversion of carbohydrates into fat so that one of the side effects is causing body weight to increase and reducing sexual arousal which causes an effect on sexual desire (Rahmidini, 2020).

Hormonal contraception has contributed to the reduction in the birth rate in Indonesia. But until now there has not been found a contraceptive that is free from side effects. Hormonal contraceptives can cause sexual dysfunction in users. Sexual dysfunction disorders are often associated with the use of hormonal contraceptives. Sexual dysfunction can also have a negative effect on quality of life, health and emotions regardless of age (Arisanti, 2021).

In terms of health, simple or non-hormonal contraception is much safer for health than hormonal contraception. Long-term use of hormonal contraceptives can

disrupt the balance of hormones. However, hormonal contraception is still the top choice among the public. This is because hormonal contraceptives containing estrogen, progesterone or a combination of the two are considered very effective in preventing pregnancy compared to non-hormonal contraceptives (Butt et al., 2019).

Decreased sexual function in women is an important thing in a woman's life. The number of couples of childbearing age (PUS) who use hormonal contraception and experience sexual dysfunction. The sufferer only feels resigned to the situation he is feeling and does not make any effort to find a solution because this is considered taboo and embarrassing to discuss it with doctors or other medical personnel. Even though this attitude of shame can cause women to experience depression. With this, the authors would like to examine the effects of injectable hormonal contraceptives and hormonal contraceptive pills on the incidence of sexual dysfunction in women based on previous research. The aim of this study was to estimate the average effect of the use of injectable hormonal contraception and pills on sexual dysfunction based on the results of previous similar studies.

SUBJECTS AND METHOD

1. Study Design

This study is a systematic review and meta-analysis using the PRISMA flowchart diagram. The process of searching for articles was carried out with a range of 2011-2022 in the Google Scholar, PubMed, Science Direct, Researchgate and Springerlink databases. The keywords used in the article search are “hormonal contraceptive” AND “oral contraception” OR “pills contraceptive” AND “injectable contraceptive” AND “sexual dysfunction” AND “cross-sectional”.

2. Steps of Meta-Analysis

The meta-analysis was carried out in five steps as follows:

1. Formulate research questions in the PICO format (population, intervention, comparison, outcome).
2. Search for primary study articles from various electronic databases including Google Scholar, PubMed, and Science Direct and non-electronics.
3. Conduct screening and critical appraisal (Critical Appraisal) of primary research articles.
4. Perform data extraction and synthesize effect estimates into RevMan 5.3.
5. Interpret and conclude the results.

3. Inclusion Criteria

The inclusion criteria used in this study were full-text articles using a cross-sectional design. The analysis used is multivariate with adjusted odds ratio (aOR). The exclusion criteria in this study were articles published before 2011, articles that did not use English, and previous studies using meta-analysis.

4. Exclusion Criteria

The exclusion criteria in this study were articles published before 2004, articles that did not use English, and previous studies using meta-analysis

5. Operational Definition of Variables

The articles included in this study were adjusted according to the PICO. The article search was carried out by considering the eligibility criteria using the PICO model as follows: Population= women of childbearing age, Intervention= using hormonal contraception, Comparation= not using hormonal contraception, Outcome= sexual dysfunction.

Sexual dysfunction is a sexual response disorder which results in a failure to obtain satisfaction during sexual intercourse. Sexual disorders include interest or desire disorders, lust or arousal disorders, orgasmic disorders and sexual pain disorders.

Hormonal contraception is a type of contraception that contains a combination of synthetic estrogen and progesterone or only progestin.

6. Instrument

The quality and design of the research analyzed in the meta-analysis is very important because it will affect the results. Assessment of research quality uses a critical appraisal checklist for cross-sectional studies from the specialist unit for reviewing evidence. The following are 12 questions used in the assessment checklist (SURE, 2018):

a. Does the study address a clearly focused question or problem?
b. Are the research methods (study design) appropriate to answer the research questions?
c. Was the subject selection method clearly described?
d. Does the sampling method lead to selection bias?
e. Is the subject sample representative of the study population?
f. Is the sample size based on pre-study considerations of statistical power?
g. Was the response satisfaction level reached?
h. Is the measurement (questionnaire) likely to be valid and reliable?
i. Was statistical significance assessed?
j. Are there confidence intervals for the main results?
k. Could there be confounding factors that haven't been taken into account?
l. Can the results of the research be applied to your organization?

***7.* Data Analysis**

The collected articles are processed using the Review Manager application (RevMan 5.3). Data processing is done by calculating effect sizes and heterogeneity values to determine the model of combining research and form the final meta-analysis results which are presented in the form of forest plots and funnel plots.

RESULTS

The article review process was carried out using a database based on the PRISMA flowchart diagram which can be seen in Figure 1. The total number of articles obtained was 14 articles spread across 4 continents, namely Asia, Africa, America and Europe. 7 articles in Asia, 2 articles in Africa, 2 articles in America, and 2 articles in Europe, can be seen in Figure 2.

The total number of primary studies included in the meta-analysis synthesis regarding the use of injectable hormonal contraceptives and pills for sexual dysfunction consists of several primary studies spread over 4 continents, namely Asia, Africa, America and Europe. The primary research included in the synthesis of this meta-analysis totaled 14 articles originating from Washington, Sweden, Iran, Poland, Iran, Peru, Egypt, Ethiopia, Indonesia.

The forest plot in Figure 3 shows that there is an effect of the use of injectable hormonal contraception on the incidence of sexual dysfunction. Women who use injectable contraception are 1.66 times more likely to experience sexual dysfunction than those who do not use injectable hormonal contraception, but this relationship is not statistically significant (aOR= 1.66; 95% CI= 0.65 to 4.26; p= 0.290). The forest plots show high heterogeneity of effect estimates between primary studies (I^2= 91%; p <0.001). Thus, the average effect estimation is carried out using the Random Effect Model (REM).

The funnel plot in Figure 4 shows that the distribution of effect estimates in small sample primary studies is not symmetrical between the right and left of the vertical line. The estimated effect is located to the right more than to the left of the vertical line.

Thus, indicating the presence of publication bias. Because the average estimate on the forest plot is also on the right, the publication bias is overestimating the true effect.

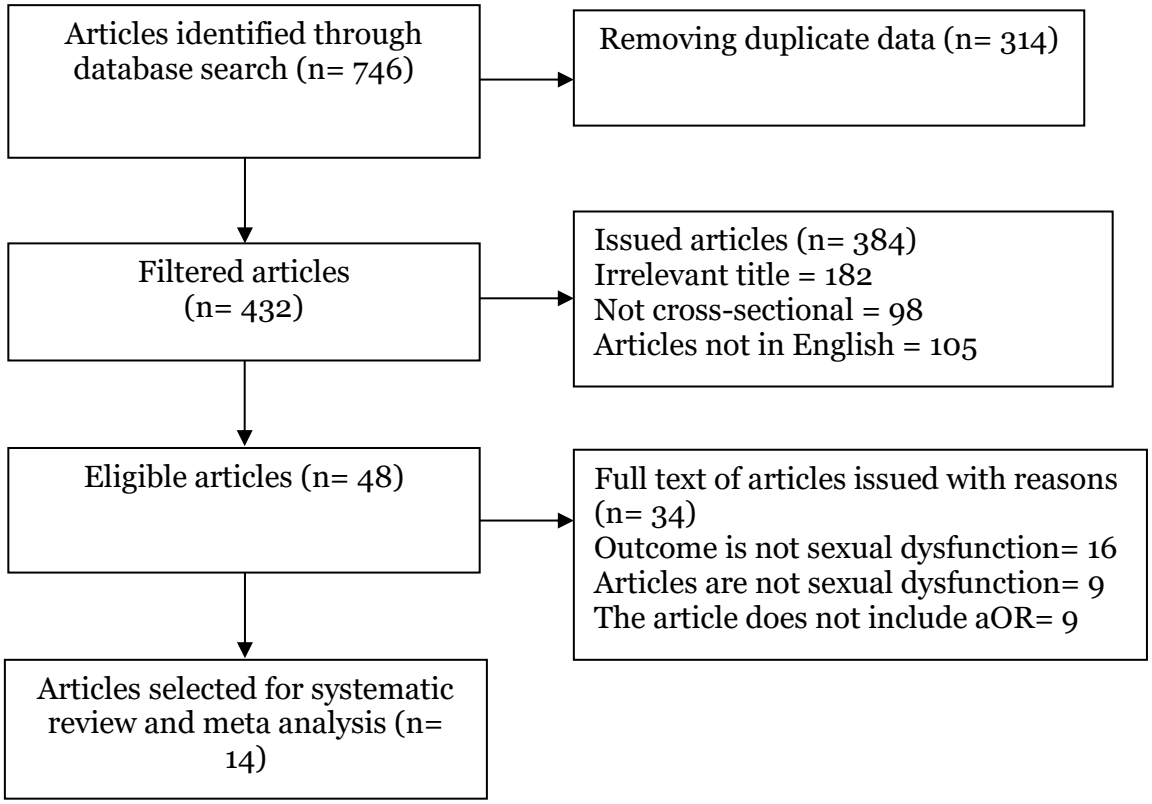

Figure 1. PRISMA flowchart diagram

Figure 2. Map of Research Area

1. Summary of Articles

a. The Effect of Injecting Contraceptive Use on Sexual Dysfunction

Table 1. Description of the primary injectable hormonal contraceptive studies included in the meta-analysis

Author (year)	Country	Study Design	Sample Size	P (Population)	I (Intervention)	C (Comparation)	O (Outcome)	aOR (95% CI)
Yosin et al. (2016)	Indonesia	Cross-sectional	99	Women of reproductive age who are injectable birth control acceptors	Injectable hormonal contraceptives	Non-hormonal contraceptives	sexual dysfunction	20.17 (6.62-61.42)
Boozalis et al. (2016)	Washington	Cross-sectional	110	Women of childbearing age are injectable birth control acceptors, UIDs and implants	Injectable hormonal contraceptives, IUDs and implants	IUD contraception and implants	sexual dysfunction	2.61 (1.47-4.61)
Gebrezgabhier et al. (2019)	Ethiopia	Cross-sectional	146	Kb implant acceptors, injections, pills	Injectable hormonal contraceptives	Non-hormonal contraceptives	sexual dysfunction	0.38 (0.11-1.33)
Batlajery et al. (2015)	Indonesia	Cross-sectional	104	KB acceptor injection 3 months	Injectable hormonal contraceptives	Non-hormonal kb acceptor	sexual dysfunction	0.694 (0.513-2.72)
Alimohammadi et al. (2018)	Iran	Cross-sectional	198	Injecting kb acceptors, condoms, pills	Injectable hormonal contraceptives	condom contraception	sexual dysfunction	4.3 (0.3-8.3)
Ningsi et al. (2012)	Indonesia	Cross-sectional	220	Injectable contraceptive acceptor	Injectable hormonal contraceptives	Non-hormonal contraceptives	sexual dysfunction	3.353 (1.923-5.846)
Priyanti et al. (2018)	Indonesia	Cross-sectional	73	Old and new injecting contraceptive acceptors	Injectable hormonal contraceptives	Non-hormonal contraceptives	sexual dysfunction	0.275 (0.100-0.756)

b. The Effect of Using Contraceptive Pills on Sexual Dysfunction

Table 2. Description of the Primary Pill Contraceptive Studies Included in the Meta-Analysis

Author (year)	Country	Study Design	Sample Size	P (Population)	I (Intervention)	C (Comparation)	O (Outcome)	aOR (95% CI)
Ghanbarzadeh et al. (2012)	Iran	Cross-sectional	223	Acceptor of birth control pills, condoms, IUDs	Birth control pills.	Non-hormonal contraceptives	sexual dysfunction	1.74 (1.06-2.86)
Malmborg et al. (2015)	Swedia	Cross-sectional	159	hormonal contraceptive acceptors	Hormonal contraceptive pills	Non-hormonal contraceptives	sexual dysfunction	2.39 (1.66-3.43)
Boozalis et al. (2016)	Washington	Cross-sectional	133	Hormonal contraception acceptor	Hormonal contraceptive pills	Non-hormonal contraceptives	sexual dysfunction	1.41 (0.79-2.52)
Gebrezgabhier et al. (2019)	Ethiopia	Cross-sectional	51	Woman of childbearing age Hormonal birth control acceptor	Hormonal contraceptive pills.	Non-hormonal contraceptives	sexual dysfunction	0.24 (0.06-0.95)
Ali et al. (2020)	Egypt	Cross-sectional	222	Acceptor of birth control pills, depo, implants	Hormonal contraceptive pills, depo	Non-hormonal contraceptives	sexual dysfunction	1.21 (1.019-1.457)
Vargas et al. (2011)	Peru	Cross-sectional	385	Condar acceptor	Emergency pills, premature ejaculation	Non-hormonal contraceptives	sexual dysfunction	1.87 (1.04-3.38)
Zgliczynska et al. (2019)	Poland	Cross-sectional	56	Acceptor for birth control pills, IUDs, implants	Hormonal contraceptive pills, IUDs, implants	Non-hormonal contraceptives	sexual dysfunction	0.91 (0.66-1.28)

1. Research Quality Assessment

a. Assessment of the quality of the cross-sectional study of the effect of injecting contraceptive use on sexual dysfunction

Primary Study	Criteria												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Yosin et al. (2016)	2	2	2	2	2	2	2	2	2	2	2	2	24
Boozalis et al. (2016)	2	2	2	2	2	2	2	2	2	2	2	2	24
Gebrezgabhie et al. (2019)	2	2	2	2	2	2	2	2	2	2	2	2	24
Batlajery et al. (2015)	2	2	2	2	2	2	2	2	2	2	2	2	24
Ningsi et al. (2021)	2	2	2	2	2	2	2	2	2	2	2	2	24
Alimohammadi et al. (2018)	2	2	2	2	2	2	2	2	2	2	2	2	24
Priyanti et al. (2018)	2	2	2	2	2	2	2	2	2	2	2	2	24

Note: 2: Yes; 1: Can't Tell; 0: No

b. Quality assessment of cross-sectional study of contraceptive pill use on sexual dysfunction

Primary Study	Criteria												Total
	1	2	3	4	5	6	7	8	9	10	11	12	
Ghanbarzadeh et al., (2012)	2	2	2	2	2	2	2	2	2	2	2	2	24
Malmborg et al., (2015)	2	2	2	2	2	2	2	2	2	2	2	2	24
Boozalis et al., (2016)	2	2	2	2	2	2	2	2	2	2	2	2	24
Gebrezgabhie et al., (2019)	2	2	2	2	2	2	2	2	2	2	2	2	24
Vargas et al., (2011)	2	2	2	2	2	2	2	2	2	2	2	2	24
Ali et al., (2020)	2	2	2	2	2	2	2	2	2	2	2	2	24
zgliczynska et al., (2019)	2	2	2	2	2	2	2	2	2	2	2	2	24

Note: 2: Yes; 1: Can't Tell; 0: No

2. The Effect of Using Injectable Hormonal Contraceptives on the Incidence of Sexual Dysfunction

a. Forest Plot

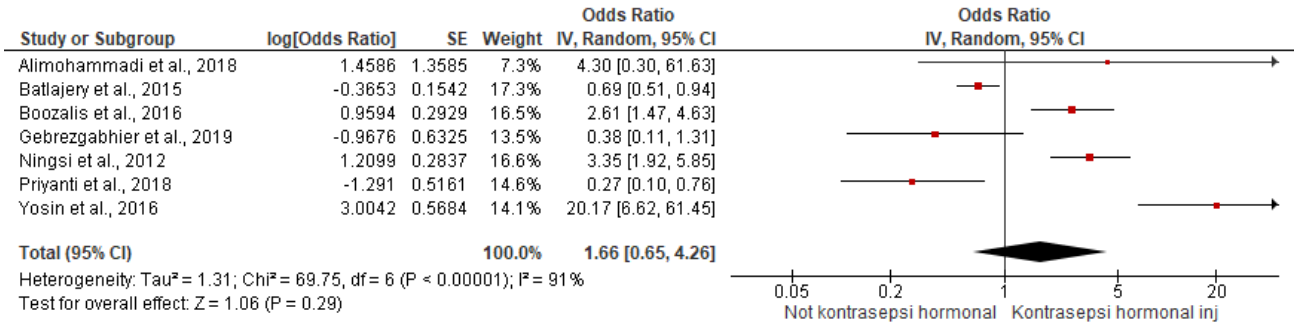

Figure 3. Forest plot of the use of injectable hormonal contraception on the incidence of sexual dysfunction

b. Funnel Plot

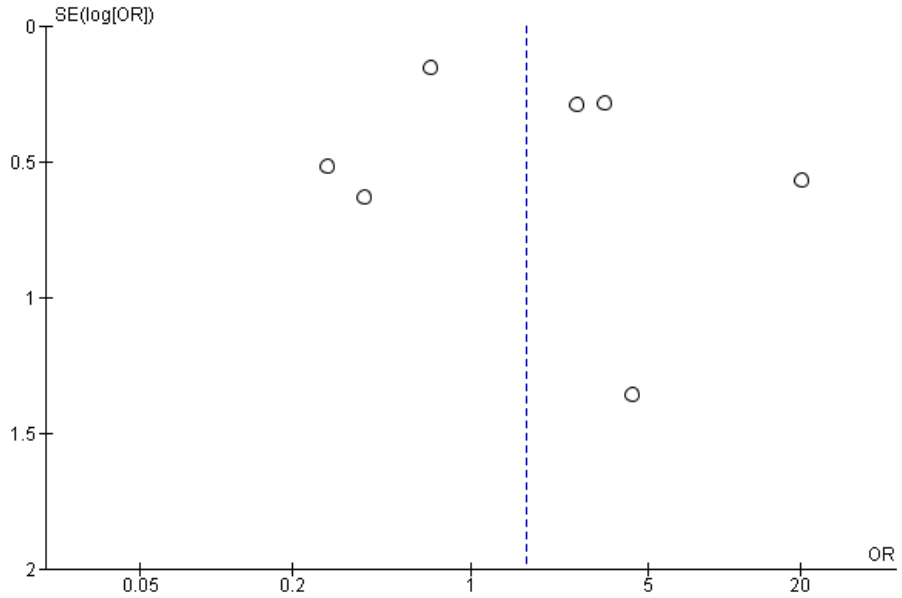

Figure 4. Funnel plot of hormonal contraceptive use injections against incidents of sexual dysfunction

4. The Effect of Using Hormonal Contraceptive Pills on Sexual Dysfunction
a. Forest Plot

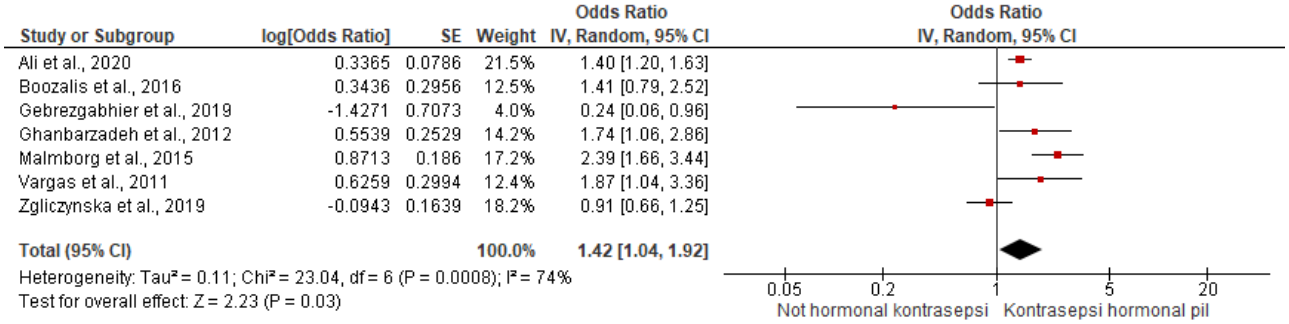

Figure 5. Forest plot of hormonal contraceptive use for sexual dysfunction

The forest plot in Figure 5 shows that there is an effect of hormonal contraceptive pills on the incidence of sexual dysfunction. Women who use oral contraceptives have a risk of experiencing sexual dysfunction 1.42 times compared to not using hormonal contraception. The effect is statistically significant (aOR= 1.42; 95% CI= 1.04 to 1.92; p= 0.030). The forest plots show high heterogeneity of effect estimates between primary studies. (I^2 = 74%; p <0.001) Thus the average effect estimate is calculated using the Random Effect Model (REM).

The funnel plot in Figure 6 shows that the distribution of effect estimates in small sample primary studies is not symmetrical between the plots to the right and left of the vertical line. Estimates of the effect are more located on the right than on the left of the vertical line. Thus, indicating the presence of publication bias. Because the average estimate on the forest plot is also on the right, the publication bias is overestimating the true effect.

b. Funnel Plot

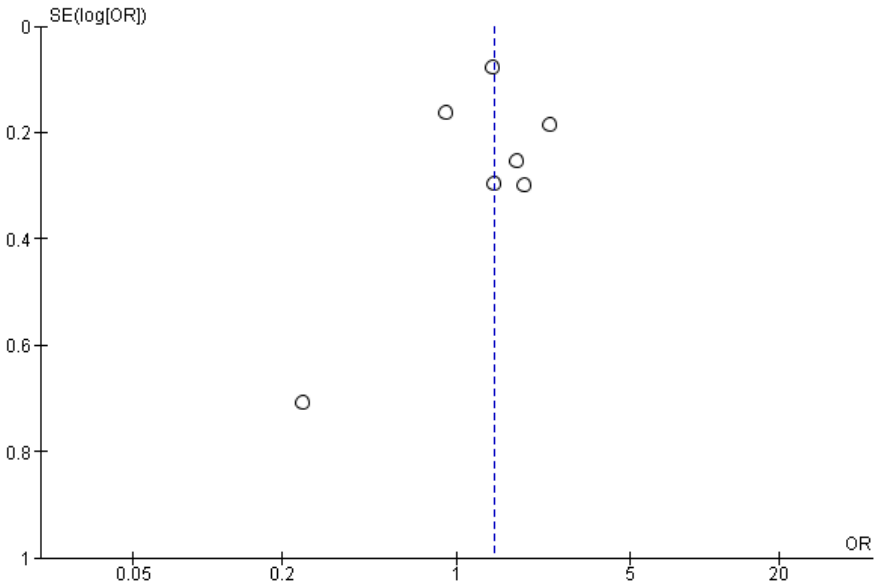

Figure 6. Funnel plot of hormonal contraceptive use for sexual dysfunction

DISCUSSION

This systematic review and meta-analysis research discusses the effect of using injectable hormonal contraceptives and pills on sexual dysfunction. The independent variable used in this study was hormonal contraceptive acceptors. While the dependent variable used is the incidence of sexual dysfunction.

This study uses the results of aOR statistics from multivariate analysis, which aims to control for confounding factors. Confounding factors can cause research results to be invalid because confounding factors also affect relationships or affect the population studied.

The Effect of Injecting Contraceptive Use on Sexual Dysfunction

There were 7 primary studies with a cross-sectional study design that carried out systematic review and meta-analysis showing heterogeneity between studies (I^2= 91%; p <0.001) so that the analysis used the Random Effect Model (REM). This heterogeneity is based on the asymmetrical distribution between the left and right plots in the funnel plot. Publication bias in cross-sectional studies due to variation or diversity between populations as seen from the different number of samples indicated by the primary study articles is due to the relatively small number of samples (n= 51). It also makes the CI range wide. However, the administration of injectable hormonal contraceptive intervention was able to increase the incidence of sexual dysfunction by 1.66 times compared to not using hormonal contraception. However, it was not statistically significant (aOR= 1.66; 95% CI= 0.65 to 4.26; p= 0.290).

The results of a study conducted by Schaffir et al. (2010) stated that Depo Medroxyprogesterone Acetate (DMPA) contraception is another form of hormonal contraception that does not contain estrogen so it is considered not to make a major contribution in increasing the concentration of sex hormone binding globulin (SHBG) so that does not reduce the concentration of the hormone testosterone. Although a prospective analysis of women with DMPA showed no difference in sexual function from baseline to 4 months after use, another survey

revealed that DMPA use can reduce libido by up to 15%.

Research conducted by Batlajery et al., (2015) stated that the largest presentation of DMPA acceptors with incidence of sexual dysfunction in women reached 32.7%. However, there is no significant relationship between the use of the 3-month injection contraceptive method and sexual dysfunction. Decreased libido occurs due to the effects of progesterone, especially those containing 19-progesterone, causing vaginal dryness. However, psychological factors can also have an effect on this. One of the primary studies conducted by Boozalis et al. (2016) stated that 20% of DMPA contraceptive users reported not finding pleasure in sex and feeling anxious before sexual intercourse. The lack of interest in sex was strongly related to the duration of contraceptive use in the first 6 months of use (aOR= 4.22; 95% CI= 2.77 to 6.43) and was multivariable (aOR= 3.98; 95% CI= 2.58 to 6.14).

Research conducted by Alimohammadi et al. (2018) in 300 participants in Iran stated that the highest prevalence of sexual dysfunction was sexual arousal (33.0%) and the lowest was orgasm (16.3%). The frequency of dysfunction in other components of sexual function was 28.0% for desire, 18.3% for lubrication.

The Effect of Using Contraceptive Pills on Sexual Dysfunction

There are 7 research articles with a cross-sectional study design which are sources of meta-analysis of the use of hormonal contraceptive pills on sexual dysfunction. The results of the forest plot show heterogeneity between studies (I^2= 74%; p <0.001) so that the analysis uses the Random Effect Model (REM). Research articles show that using hormonal contraceptive pills has a 1.42 times risk of experiencing sexual dysfunction compared to using non-hormonal contraceptives and is statistically significant (aOR= 1.42; 95% CI= 1.42 to 1.92; p= 0.030).

These results are in line with research conducted by Malmborg et al. (2015) in Sweden stated that the only variable found to be correlated with decreased sexual desire was the use of hormonal contraceptive methods (aOR= 2.39; 95% CI= 1.66 to 3.43;). Another study conducted by Ghanbarzadeh et al. (2012) stated that unsatisfactory sexual activity was positively related to the use of contraceptive pills (OR = 1.74; 95% CI= 1.06 to 2.86).

Although there is conflicting evidence regarding the relationship between progestin and decreased libido. However, there is some evidence to suggest that estrogen plays an important role in female sexuality. Previous research has found that decreased sexual function in women is most closely related to decreased estrogen levels. Systemic progestin use may be associated with loss of sexual desire as a result of suppression of ovarian function and endogenous estrogen production (Boozalis et al., 2016).

Most studies mention the contraceptive pill, vaginal ring, and implants have a higher prevalence of causing sexual dysfunction than other forms of contraception. However, it is important to remember that the antiandrogenic effect of hormonal contraceptives is not universal and depends on the susceptibility of the woman. Some women may not feel and report any mood or sexual side effects even though their testosterone level is clinically low (Graham et al., 2011).

The limitation of this study is that there is a research bias because it only uses 5 databases, namely Google Scholar, PubMed, Science Direct, Research gate and Springer-Link, thus ignoring research from other databases. In this study there is also a language bias because only the selected articles are published in English, thus ignoring articles published in other languages.

AUTHOR CONTRIBUTION

Sumiyati is the main researcher who selects topics, searches for and collects study data. Uki Retno Budihastuti and Bhisma Murti played a role in analyzing the data reviewing study documents.

FUNDING AND SPONSORSHIP

This study is self-funded.

CONFLICT OF INTERESTS

There is no conflict of interest in this study.

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