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Dolna 17, Warsaw,
Poland 00-773
+48 226 0 227 03
editorial_office@rsglobal.pl

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THE EFFECT OF ORAL CONTRACEPTIVES USE ON DEVELOPMENT OF MENTAL DISORDERS SUCH AS DEPRESSION – A REVIEW ARTICLE

Małgorzata Krzyżanowska
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0003-6287-5777

Natalia Pacocha
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0001-3370-9521

Jakub Jędrychowski
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0002-8496-292X

Justyna Popczyńska
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0008-7654-932X

Natalia Karpowicz
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0000-6636-9546

Marta Zgierska
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0009-0007-4472-0631

Julia Kaszucka
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0000-0002-9017-3604

Agnieszka Raczyńska
Faculty of Medicine, Medical University of Warsaw, Poland
ORCID ID: 0000-0002-0423-3325

Kinga Kosiec
Faculty of Medicine, Medical University of Gdańsk, Poland
ORCID ID: 0009-0008-8756-3012

Oliwia Krzemień
Faculty of Medicine, Medical University of Gdańsk, Poland
ORCID ID: 0009-0003-1863-3025

ABSTRACT

Introduction
Oral hormonal contraception is considered to be one of the most effective methods used to prevent unwanted pregnancy. The ease of use and wide availability make woman reach for it even more willingly. However, the treatment is associated with a number of adverse effects. The oral contraceptive pills not only interfere with the physical well-being, but also markedly affect mental health and may predispose to the development of mood disorders. The aim of this study is to conduct a comprehensive review of the effect of oral contraceptives use on development of mental disorders, in particular depression.
Materials and Methods
A comprehensive review of literature available in the PubMed database was performed. This process involved a thorough search of articles written in English containing the following key terms: "hormonal contraception", "oral contraceptives", "oestrogen", "progesterone", "mood disorders", "depression". The gathered data was then scrupulously examined and analyzed.
Results
Studies show that the use of hormonal contraception is associated with a higher risk of subsequent use of antidepressants and diagnosis of depression. This correlation is particularly prominent in adolescents. Trends show that women taking OCPs with a higher amount of progesterone compound were more likely to develop symptoms of depression.
Conclusions
The evidence suggests a deep correlation between the use of an oral hormonal contraception with the risk of developing mood disorders, such as depression. Further research must be performed in order to determine why some women are more susceptible to such changes of an emotional state during hormone contraceptive treatment, while other present resistance to it.

KEYWORDS:
Hormonal Contraception, Oral Contraceptives, Oestrogen, Progesterone, Mood Disorders, Depression

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Introduction.

Hormonal contraception is considered to be one of the most effective methods used to prevent unwanted pregnancy. It includes birth control pills, intrauterine devices, contraceptive patches and contraceptive injections. This method of contraception involves delivering artificial hormones, oestrogen and/or progestogen, to the body, which inhibit ovulation and change the consistency of the cervical mucus, making it thick in order to prevent the sperm from passing to the uterus. (Mu & Kulkarni, 2022) Oral contraceptives (OCPs) are the most common method of hormonal anticonception used by woman of reproductive age in Poland. (Zgliczynska et al., 2019) There are different forms of oral contraception available for women - combined estrogen-progesterone pills and progesterone-only pills, also called „the minipill". The first one, the combined hormonal pill with estrogen and progesterone, is the most commonly prescribed form of OCPs. (Cooper & Patel, 2024) The combined hormonal pill we can further classify into monophasic and multiphasic pills depending on the dosage of hormones provided during a menstruation cycle. The monophasic pills deliver the same dose of both components, estrogen and progestogen. The multiphasic pills vary in the weekly doses of both or either component. The most commonly used progestogens in hormonal contraceptives include levonorgestrel, drospirenone and norethindrone, while the most commonly used estrogen component constitutes of ethinylestradiol. Ethinylestradiol inhibits the secretion of FSH, preventing the maturation of Graafian follicles and thus of egg cells, while progestogens inhibit ovulation, or the release of the egg cells. Moreover, they affect the composition of the cervical mucus, making it thicker, thus harder for sperm to pass through female reproductive tract. Furthermore, progestogens cause endometrial morphological changes, which may impede embryo implantation. (Cooper & Patel, 2024; Song & Fraser, 1995)

Despite high efficacy of oral contraceptive pills and many additional benefits which they may offer, they aren't left with no side effects. Adverse effects of the OCPs vary significantly. The most common physical side effects include breakthrough bleedings, nausea, headaches, abdominal cramps, breast tenderness, increased vaginal discharge and weight gain. Long term therapy may also pose an increased risk of developing cancers, in particular the endometrial cancer. (Dawson, 1979) It has been observed that the oral contraceptive pills not only interfere with our physical well-being, but also markedly affect our mental health and may predispose to the development of mood disorders. (Johansson et al., 2023; Mu & Kulkarni, 2022) The aim of this study is to conduct a comprehensive review of the effect of oral contraceptives use on development of mental disorders, particularly depression.

Materials and Methods.

A comprehensive review of literature available in the PubMed database was performed. This process involved a thorough search of articles written in English containing the following key terms: "hormonal contraception", "oral contraceptives", "oestrogen", "progesterone", "mood disorders", "depression". The gathered data was then scrupulously examined and analyzed.

Results.

A large Danish study, consisting of 1 061 997 female participants, compared OCPs nonusers to OCPs users and their first use of antidepressants and first diagnosis of depression. The results have shown that the use of hormonal contraception was associated with subsequent use of antidepressants and a first diagnosis of depression. This correlation was especially prominent in adolescents. In addition, the rate ratio of first use of antidepressants by contraceptive type was higher in the group that used progestin-only contraceptives in comparison to the group that used combined estrogen-progesterone contraceptive pills. (Skovlund et al., 2016)

An English cohort study, which included data from 264,557 women from the UK Biobank, not only showed that the OCPs intake is related with a higher risk of depression but also examined the timeline of its development. It was observed that the first 2 years of OCPs use were associated with a higher rate of depression. (Johansson et al., 2023) This could be caused by the hormonal fluctuations, which occur at the beginning of the OCPs treatment.

A study performed on woman taking OCPs was evaluated clinically using Hamilton Rating Scale and it was found that women undergoing the contraceptive treatment were more likely to be depressed than a random control group. Additionally, participants' previous history of depression were evaluated. The participants with previous episodes of depression were significantly more depressed, thus scored higher on the Hamilton Rating Scale, in comparison to participants with no history of depression. Another trend that was observed during the study was that women taking OCPs with greater amount of progesterone compound were more likely to score higher on the Hamilton Rating Scale, or present depressive symptoms. (Lewis & Hoghughi, 1969)

An extensive overview of literature performed by the Department of Psychology in Lakehead University, Canada revealed that out of 13 examined by them controlled prospective studies, all except one study found differences in affect between the oral contraceptives users and non-users. (Oinonen & Mazmanian, 2002)

Discussion.

The studies show that oestrogen and progesterone contained in the oral contraceptive pills may affect neurotransmission and thus influence brain function, which may lead to development of mood disorders, such as depression, in patients undergoing contraceptive treatment. (Mu & Kulkarni, 2022) This is one of the main reasons why patients discontinue or withdraw of their treatment. (Sanders et al., 2001)

Oestrogen receptors (ER) are highly expressed in amygdala, hypothalamus, hippocampus, and brainstem, while progesterone receptors (PR) are mainly found in amygdala, cerebellum, hypothalamus and in the substantia nigra of human brain. (Toffoletto et al., 2014) Clinical evidence suggests that estrogen exposure might have a neuroprotective effect protecting the brain from neurodegenerative disorders, such as the Alzheimer's disease. It might also delay the onset or slow down the progression of schizophrenia or enhance recovery from traumatic brain injuries such as stroke. (Garcia-Segura et al., 2001) Postulated mechanisms that may be responsible for oestrogen's neuroprotective phenomenon include the known anti-oxidant activities of estrogen. (Behl & Manthey, 2000) Another argument supporting this thesis is based on the fact that the nuclear estrogen receptor, through which estrogen alters expression of estrogen responsive genes, plays a role in apoptosis and axonal regeneration. (Garcia-Segura et al., 2001)

Contradictory to oestrogen, progesterone isn't found to be neuroprotective. In fact, it can be responsible for the deterioration of the psychological symptoms. (Mu & Kulkarni, 2022) This could be explained by the correlation of progesterone with high concentrations of monoamine oxidase, which decomposes serotonin thus causing low levels of serotonin concentrations. (Klaiber et al., 1996; Oinonen & Mazmanian, 2002)

Conclusions.

The evidence suggests that the use of oral hormonal contraception correlates with the risk of developing mood disorders, such as depression. This fact must be taken into consideration when choosing a contraceptive method. Particular vigilance needs to be preserved when dealing with women who have a personal or family history of depression. Further research must be performed in order to determine why some women are more susceptible to changes of mood and emotional state during hormone contraceptive treatment, while other preserve resistant to it and do not experience any psychological symptoms or mental health issues. Such future findings would enable us to take on a more individual approach concerning women patients seeking contraceptive advice, simultaneously ensuring their comfort and safety.

Author's contribution

Research concept and design: Małgorzata Krzyżanowska, Natalia Pacocha, Jakub Jędrychowski, Julia Kaszucka.

Data collection and/or compilation: Małgorzata Krzyżanowska, Justyna Popczyńska, Oliwia Krzemień, Kinga Kosiec, Marta Zgierska.

Data analysis and interpretation: Małgorzata Krzyżanowska, Agnieszka Raczyńska, Oliwia Krzemień, Kinga Kosiec, Natalia Karpowicz.

Writing: Małgorzata Krzyżanowska, Natalia Pacocha, Justyna Popczyńska, Natalia Karpowicz, Marta Zgierska.

Critical review of the article: Małgorzata Krzyżanowska, Natalia Pacocha, Agnieszka Raczyńska, Jakub Jędrychowski, Julia Kaszucka.

Supervision, project administration: Małgorzata Krzyżanowska.

All authors have read and agreed with the published version of the manuscript.

Conflict of Interest Statement

The authors declare that they have no conflict of interest.

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