

## USE OF ORAL CONTRACEPTIVES AND THEIR EFFECTS RELATED TO THE INTENSITY OF DEPRESSIVE SYMPTOMS IN HEALTHY WOMEN

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**Abstract: Introduction:** Symptoms often found in anxiety and depressive disorders are widely reported by women who use oral contraceptives, however, there are not enough studies in the literature that analyze the correlation between the intensity of anxious and/or depressive symptoms with the onset of use of oral contraceptives by these women. **Goal:** The main objective of this study is to find out if there is a relationship between the use of oral contraceptives and their effects on the intensity of depressive symptoms in healthy women. **Method:** This is a cross-sectional study involving 250 healthy women, between 18 and 39 years old, who live in the city of Salvador - BA. Data were collected through the google forms platform, using the Snowball technique so that we could reach an N of 224. The data were analyzed through the staging given by the Beck Depression Inventory. **Results:** The number of women involved in this research who reported emotional changes was not enough to validate the correlation between the use of oral contraceptives and the intensity of depressive symptoms. **Conclusion:** No relationship was observed between the use of oral contraceptives and the intensity of depressive symptoms in healthy women. **Keywords:** Oral contraceptives; mood disorder; Contraceptive Methods; sex hormones.

## INTRODUCTION

With the advancement of the professional world and the current difficulties of the labor market, a need arose in women to become independent and protagonists of their professional life and, in this new scenario, children have become something increasingly distant from their plans. As a consequence of this change that marks the 21st century, the use of oral hormonal contraceptives has become an active search for many women,

whether teenagers or more mature, since, nowadays, in addition to many choosing not to get pregnant, whether for a period or even throughout their lives, more and more women want to guarantee their autonomy to decide about their future in a practical and safe way.<sup>2</sup>

However, unfortunately, knowledge about the diversity of choice of methods is still limited among users, leading to many questions regarding their long-term adverse effects, one of which will be discussed in this article. Thus, it is necessary to highlight the contraceptive methods most used by society. Currently, they are: male and female condoms (condom), oral pill, mini-pill, monthly and quarterly injectables, intrauterine device (IUD), emergency contraceptive pill, diaphragm and measuring rings. In addition, it is worth mentioning that the improper and indiscriminate use of emergency pupils as a continuous method, by lay users, causes several damages to their health.<sup>5,7</sup>

Among all methods, oral hormonal contraceptives are the most used by women, who seek, in addition to easy access to the medication, independence from their partners. However, symptoms such as depressive mood, feelings of sadness, palpitations and self-devaluation, which are common findings in anxiety and depressive disorders, are frequently cited in the history of patients who use this method for a long time.<sup>1</sup>

Physiological changes in sex hormones occur in all women after menarche, suggesting that the high prevalence of mood disorders may be a result of hormonal changes. The pattern of neuroendocrine changes related to female sex hormones and the reproductive cycle make women more vulnerable to mood swings. It is known that the function of the neuroendocrine axis associated with the female reproductive cycle is labile and exposed to environmental, psychosocial and physiological factors.

Numerous neurotransmitters are involved in mood control, with highlights being glutamate, gamma-aminobutyric acid (GABA), acetylcholine, serotonin, dopamine, noradrenaline and neuropeptides, which together with the fluctuation of gonadal steroid hormones, would be acting directly or indirectly in mood modulation feminine. Thus, the chance of having humoral and behavioral changes influenced by exogenous hormones, such as, for example, hormonal oral contraceptives, is increased, emphasizing the lowering of mood as the main symptom.<sup>3</sup>

That said, based on the premise that female sex hormones act in cognitive and emotional construction, their exogenous use may be related to changes in hormone levels in the body and consequent change in cortical and subcortical stimuli responsible for emotions.<sup>5</sup> This fact gave rise to the motivation for preparing this study and makes it highly relevant for scientific knowledge and for the female community, since this reality affects the well-being and quality of life of these women. In this sense, this work seeks to elucidate the veracity of the interference and the relationship between the use of oral hormonal contraceptives and their effects linked to the intensity of changes in mood, especially depressive mood, in healthy women.<sup>4</sup>

## METHODS

This is a descriptive, cross-sectional, and quantitative study, carried out between March 2020 and October 2022, with healthy women aged between 18 and 39 years old, residents of the city of Salvador, who are using, both hormonal contraceptive methods and other non-hormonal methods. The data collection instrument consisted of a questionnaire which contained the Beck Depression Inventory (BDI) on the Google Forms platform, and disseminated using the methodological technique *Snowball* (“bola de neve”), in which

selected individuals invite new participants, aiming to reach a greater number of people able to participate in the research.

Data were obtained from the interviewees regarding age, presence of children, type of contraceptive used, time of use, whether there was a diagnosis of depression prior to or after starting contraceptive use, whether there was a lowering of mood after starting use and, whether this demotion interfered with personal life. In addition to these data, a classification on the Inventory depression intensity scale was also obtained, which can range from minimal (0-9 points) and mild (10-16 points) to moderate (17-29 points) and severe (30-63 points).

The variables evaluated were: age, female gender, absence of comorbidity and use of contraceptive methods. Depressive symptoms constituted the dependent variable.

For the elaboration of the database and descriptive analysis, the software *Statistical Package for Social Sciences* (SPSS Inc., Chicago, IL, EUA), version 14.0 *for Windows*. The results were presented through tables. Categorical variables expressed in frequencies and percentages – n (%). Continuous variables with non-normal distribution were expressed as median and interquartile range. The normality of numerical variables was verified using descriptive statistics, graphic analysis and the Shapiro-Wilk test.

For the comparison between the categorical variables with the 2 groups (use and non-use of oral contraceptives) the chi-square test was used. To compare the questionnaire score between the two groups, the Mann-Whitney test was used. For all statistical analyses, a significance level of 5% was considered ( $p < 0.05$ ).

For this research, the Informed Consent Form was used for the questionnaire to gain validity, as well as being submitted and approved by the Research Ethics Committee

(CEP). Furthermore, this study complied with the ethical aspects assumed in Resolution 466/2012 of the National Health Council (CNS) and was approved by the Research Ethics Committee (CEP).

The research presents minimal risks, which are related to the breach of secrecy of the collected data. However, the researchers undertake to maintain confidentiality. Also, participant identification is optional.

The benefits of the study are aimed at establishing the relationship between the use of oral hormonal contraceptives with depressive symptoms and guidance regarding not only changing the contraceptive method to one that is more suitable for each woman.

## RESULT

The sample consisted of 250 women, but of these only 224 answered the questionnaire satisfactorily for the research in question.

Variables	Total (n=224)	Use of oral contraceptives (n=117)	No use of oral contraceptives (n=107)	value of p
<b>Age</b>	n (%)	n (%)	n (%)	0,443*
<18 years	2 (0,9)	1 (0,9)	1 (0,9)	
18-39 years old	215 (96,0)	114 (97,4)	101 (94,4)	
> 39 years old	7 (3,1)	2 (1,7)	5 (4,7)	
<b>Resident Of Salvador</b>	196 (87,5)	104 (88,9)	92 (86,0)	0,511*
<b>Have children</b>	19 (8,5)	5 (4,3)	14 (13,1)	0,029*
<b>How long have you been using the method?</b>				<0,0001*
3 months – 1 year	60 (26,8)	20 (17,1)	40 (37,4)	
1-2 years	49 (21,9)	13 (11,1)	36 (33,6)	
>3 years	115 (51,3)	84 (71,8)	31 (29,0)	
<b>Have you ever been diagnosed with depression?</b>				0,966*
Not	197 (87,9)	103 (88,0)	94 (87,9)	
Yes before using oral contraceptives	0	0	0	
Yes after using oral contraceptives	27 (12,1)	14 (12,0)	13 (12,1)	
<b>Have you observed mood lowering?</b>				0,284*
Yes	51 (22,8)	87 (74,4)	86 (80,4)	
Not	173 (77,2)	30 (25,6)	21 (19,6)	
<b>Does this downgrade interfere with your life? (n=192)</b>				0,553*
Yes	47 (24,5)	26 (26,3)	21 (22,6)	
Not	145 (75,5)	73 (73,7)	72 (77,4)	

\* Chi-square test; n=number of practitioners;

Table 1- Comparison of sociodemographic and clinical characteristics between groups of women who use and do not use oral contraceptives.

<b>Intensity of depressive symptoms</b>	n=224
Minimum	128 (57,1)
Light	67 (29,9)
Moderate	27 (12,1)
Severe	2 (0,9)

N= number of participants;

Table 2- Description of the prevalence of the intensity of depressive symptoms in the studied sample.

<b>Variables</b>	<b>Use of oral contraceptives (n=117)</b>	<b>No use of oral contraceptives (n=107)</b>	<b>Value of p</b>
<b>Intensity of depressive symptoms</b>	n (%)	n (%)	0,553*
Minimum	66 (56,4)	62 (57,9)	
Light	36 (30,8)	31 (29,0)	
Moderate	13 (11,1)	14 (13,1)	
Severe	2 (1,7)	0	
<b>BECK M(IIQ) inventory score</b>	8(3-14)	8(3-15)	0,755**

\* Chi-square test; Mann-whitney test; M=median; IIQ- Interquartile Range.

Table 3. Association between the use of oral contraceptives and the intensity of depressive symptoms

<b>Variables</b>	<b>3 months – 1 year</b>	<b>1-2 years</b>	<b>&gt; 3 years</b>	<b>Value of p</b>
<b>Oral Contraceptives (n=117)</b>				
Intensity of depressive Symptoms	n (%)	n (%)	n (%)	0,708
Minimum	13 (65,0)	7 (53,8)	46 (54,8)	
Light	6 (30,0)	3 (23,1)	27 (32,1)	
Moderate	1 (5,0)	3 (23,1)	9 (10,7)	
Severe	0	0	2 (2,4)	
<b>Intensity of depressive symptoms No oral contraceptives (n=107)</b>				0,340
Minimum	23 (57,5)	23 (63,9)	16 (51,6)	
Light	9 (22,5)	11 (30,6)	11 (35,5)	
Moderate	8 (20,0)	2 (5,6)	4 (12,9)	
Severe	0	0	0	

\* Chi-square test

Table 4- Association between the time of contraceptive use with the intensity of depressive symptoms within each group.

## DISCUSSION

From the data collected, it was observed that there was no relationship between women who use oral contraceptives and the intensity of depressive symptoms in healthy women. Since, although there are reports of these symptoms in women who use the method in question, when compared to those who do not use hormonal oral contraception, we obtained similar numbers, without statistically significant differences that would change the course of the research.

We can observe that the users of oral contraceptives covered by this study are between the age group of 18 to 39 years, this interval, which courses with important hormonal oscillations that provide emotional and cognitive instability. Observational studies also indicate that estrogen improves mood and has antidepressant action. Progesterone and its derivatives have shown effects opposite to those of estrogens<sup>11</sup>. A cohort study carried out in Denmark obtained results consistent with the theory of the involvement of progesterone in the etiology of depression, associating the use of hormonal contraceptives with the subsequent use of antidepressants and the diagnosis of depression<sup>12</sup>. Thus, it is possible to highlight the difficult role that sexual steroids assume in our evaluation, in order to interfere in the real impact of contraceptive pills on women's mood, since it is not possible to evaluate these participants isolating them from the physiological hormonal effects of the organism.

Clinical studies carried out in other countries ratified the results obtained in this research<sup>11</sup>, however, we must emphasize that, as the surveys were applied outside Brazil, they have limitations such as; the use of oral contraceptives for a period of 3 months, restricting long-term results, and not least, genetic factors linked to different nationalities.

Thus, it is possible to consider variations in results due to different locations.

It is worth mentioning that, despite the congruent findings, anxious traits were observed in women who used OAC for 3 months<sup>11</sup>, this being a predisposing factor for mood disorders, since progesterone and most of its metabolites used in contraception have the potential to induce psychochromimetic effects mediated by gamma-aminobutyric acid (GABA) receptors, one of the main inhibitory neurotransmitters of the nervous system central<sup>14</sup>. Furthermore, the use of these drugs was related to a first diagnosis of depression and an association with greater risks of developing depressive disorders in adolescents who use the aforementioned method<sup>12</sup>.

A study carried out with non-human primates showed that females that used ACO showed an increase in activity levels, basal cortisol and sensitivity to the adrenocorticotrophic hormone (ACTH) response compared to the control group, in addition to a decrease in central serotonergic activity<sup>13</sup>. Such hormonal alterations may explain the mood swings reported by women who start using the mentioned treatment, in addition to suggesting that the use of these drugs has a certain degree of interference in their social behavior.

According to the data collected, we can verify that there is a predominance of use for more than three years by women who opt for oral contraception and correlating with the intensity of depressive symptoms, we note that most of them have the mildest form. However, no scientific evidence was found to support this correlation. Despite this, the exclusion of these data is not optional, since they can serve as a research tool for further studies on the topic addressed.

However, a double-blind, randomized study carried out in Sweden, which defends

the relationship between the use of OACs and the appearance of depressive symptoms, concluded that 88.2% of women reported them as the most common side effect<sup>9</sup>. We must point out that this research cited contains an N of 34 women, which is restricted and may thus distance itself from real results. The same defends the hypothesis that the use of contraceptives based on levonorgestrel delays the activity of the amygdala, resulting in deterioration of mood, unlike our study that covers the oral contraceptives, not only the isolated progesterone base, also having estrogen in its composition<sup>10</sup>, acting as a protective factor against cognitive and emotional deficits. Due to the indications made previously, our study is supported, therefore, more consistent in its claims.

Despite the outcome obtained, the importance of conversation with users, to inform and raise awareness about emotional changes subsequent to the use of oral contraceptives, is not ruled out. Thus, it is important to clarify the presence of mental disorders, such as depression and anxiety, in consultations with the accompanying professional, and, based on this, decide on the appropriate conduct for each patient, making the treatment more individualized and holistic.

Given the findings of this study, it is assumed that the population sample described here has limitations, such as the age range, restriction of collection to the city of Salvador-BA, women without previous comorbidities, which prevents a greater range of contexts, realities and audiences of women linked to the use of oral hormonal contraceptives. Controlled studies, carried out with more participants, greater control of the variables involved and more contraceptive methods analyzed must be carried out in order to observe whether the

results obtained in these new studies will be different from those obtained in this work.

We believe that our work can serve as a stimulus for the development of other works on this still little explored theme. Leading to a considerable improvement in the work of professors with regard to the understanding and practical approach to patients, both in the choice of contraceptive methods within the offices and in the dissemination of knowledge on the subject, thus being able to broaden the discussions on the subject in question, solving possible doubts about biopsychic alterations. This way, our work becomes a tool for possible new studies and discoveries that will bring benefits to women who aim to avoid pregnancy, primarily linking their quality of life.

## **CONCLUSION**

No relationship was observed between the use of oral contraceptives and the intensity of depressive symptoms in healthy women. The multivariate analysis showed that the time of use also did not present this correlation. New studies that include not only oral hormonal methods, but also other contraceptives that contain hormones in their composition are needed to clarify the existence of this association more clearly.

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