

Adverse Effects of Oral Contraceptive Use: Integrative Review

RESUMO

Objetivo: O objetivo deste estudo é realizar uma análise detalhada das evidências científicas disponíveis sobre os potenciais efeitos adversos associados ao uso de anticoncepcionais orais. **Metodologia:** Após uma busca em bases de dados específicas e a aplicação de critérios de inclusão e exclusão, foram analisados oito artigos científicos. **Resultados:** Os principais efeitos adversos encontrados foram: cefaleia, redução da libido, acne, aumento de peso, náusea, vômito, alterações de humor, sonolência diurna excessiva, insônia, spotting (sangramento de escape), além de um aumento do risco de asma e glaucoma. **Conclusão:** Este estudo visa auxiliar os profissionais de saúde na orientação das mulheres sobre os possíveis efeitos adversos dos anticoncepcionais orais, permitindo uma escolha mais informada do método contraceptivo.

DESCRIPTORES: Anticoncepcionais orais; Contraceptivos hormonais; Evento adverso; Saúde materno infantil.

ABSTRACT

Objective: The aim of this study was to carry out a detailed analysis of the available scientific evidence on the potential adverse effects associated with the use of oral contraceptives. **Methodology:** After searching specific databases and applying inclusion and exclusion criteria, eight scientific articles were analyzed. **Results:** The main adverse effects found were: headache, reduced libido, acne, weight gain, nausea, vomiting, mood swings, excessive daytime sleepiness, insomnia, spotting (breakthrough bleeding), as well as an increased risk of asthma and glaucoma. **Conclusion:** This study aims to help health professionals advise women about the possible adverse effects of oral contraceptives, allowing them to make a more informed choice of contraceptive method.

DESCRIPTORS: Contraceptives oral; Contraceptive agents, Hormonal; Drug-related side effects and adverse reactions; Maternal and child health.

RESUMEN

Objetivo: El objetivo de este estudio fue realizar un análisis detallado de la evidencia científica disponible sobre los potenciales efectos adversos asociados al uso de anticonceptivos orales. **Metodología:** Tras la búsqueda en bases de datos específicas y la aplicación de criterios de inclusión y exclusión, se analizaron ocho artículos científicos. **Resultados:** Los principales efectos adversos encontrados fueron: dolor de cabeza, disminución de la libido, acné, aumento de peso, náuseas, vómitos, cambios de humor, somnolencia diurna excesiva, insomnio, manchado (hemorragia intermenstrual), así como un mayor riesgo de asma y glaucoma. **Conclusión:** Este estudio pretende ayudar a los profesionales sanitarios a asesorar a las mujeres sobre los posibles efectos adversos de los anticonceptivos orales, permitiéndoles elegir un método anticonceptivo con mayor conocimiento de causa.

DESCRIPTORES: Anticonceptivos orales; Agentes anticonceptivos hormonales; reacciones adversas y efectos colaterales relacionados con medicamentos; Salud materno-infantil.

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INTRODUCTION

Health needs to be ensured for the entire population, including women, in a comprehensive way, considering various aspects such as anatomical, physiological and social. It is essential to understand that sexuality is intrinsically linked to the totality of the human being, going beyond the simple function of the genitals, and involving biological, psychological, emotional, social, cultural and spiritual elements⁽¹⁾. It is

therefore essential to integrate sexual health with general health, taking into account aspects such as pleasure, emotion, affectivity and communication, and adopting a broad, interdisciplinary approach⁽²⁾.

The Ministry of Health advocates the inclusion of reproductive planning in health actions, with the aim of strengthening sexual and reproductive rights through education, counseling and clinical assistance. This planning must respect sexual and reproductive rights, promote racial, ethnic, gender, generational and sexual orientation equality, and combat discrimination⁽³⁾.

It is believed that Primary Health Care plays an essential role as a facilitator in the exchange of knowledge in health services, promoting awareness of the importance of reproductive planning for improving community conditions. This occurs by ensuring sexual and reproductive rights through empowering and encouraging people⁽¹⁾.

In this context, there is a continuous increase in unplanned pregnancies, whose socioeconomic, demographic and behavioral characteristics reflect inequalities and have a significant impact on the lives of women and their partners. An additional concern is the situation of vulnerability faced by puerperal women, especially young women, who live in precarious households and have large families, and are particularly affected by unplanned pregnancies⁽⁴⁾.

The low demand for contraceptives, their inappropriate use and method failures contribute to high rates of unplanned pregnancies. On the other hand, the most effective methods, such as Long-Acting Reversible Contraception (LARCs), are preferred by women who have already experienced an unplanned pregnancy⁽⁵⁾. However, there is a high prevalence of women using oral hormonal contraceptive methods. In this context,

there is concern about knowledge about this method, which may not be adequate enough, thus impacting on its correct use and effectiveness⁽⁶⁾.

Given this scenario, it is essential that health professionals adopt a comprehensive approach during consultations, discussing reproductive counseling, pregnancy plans, individual characteristics, health conditions, as well as providing detailed information on contraceptive methods, including their risks, benefits, side effects, duration of use, impact on menstruation and fertility⁽⁷⁾.

It is essential that women have a clear understanding of the purposes and effects of hormonal oral contraceptives in the short, medium and long term before they start using them. Contraception without professional supervision can be practiced indiscriminately, putting health at risk due to the possible adverse effects associated with the method⁽⁸⁾. Contraceptives are generally considered safe, although they do have some risks, the occurrence rates of which are low and sometimes related to other factors. Some adverse events can be experienced by women, which can affect adherence to contraceptive methods⁽⁹⁾.

It is important to carry out research aimed at identifying the scientific evidence on the use of oral hormonal contraceptives and their possible effects.

adverse events. The knowledge obtained from these studies can be used as a basis for health care and education practices and strategies developed by health professionals with the aim of preventing unwanted pregnancies⁽¹⁰⁾.

OBJECTIVE

The aim of this study is to carry out a detailed analysis of the available scientific evidence on the potential ad-

verse effects associated with the use of oral contraceptives.

METHODOLOGY

This is an integrative literature review. This type of study synthesizes the results of research already carried out, highlighting the conclusions of the body of literature on a particular phenomenon related to the guiding question that guides the search for literature. From this, the summarized and compared data enables general conclusions to be drawn about the research problem⁽¹¹⁾.

Because it follows a process of systematic and summarized analysis of the literature, the integrative review, in addition to contributing to evidence-based practice, makes it possible to identify gaps in knowledge in relation to the phenomenon studied, identify the need for future research, reveal central issues in the area of health and nursing, identify conceptual or theoretical frameworks and show the state of the art of scientific production resulting from research on a given topic⁽¹¹⁾.

To develop this integrative review, the following steps were followed: (1) identification of the topic and research question; (2) establishment of criteria for inclusion and exclusion of studies (sampling) and definition of databases; (3) definition of the information to be extracted from the selected studies (categorization of studies); (4) evaluation (critical analysis) of the studies included in the integrative review; (5) interpretation of the results and (6) presentation of the review/synthesis of knowledge⁽¹²⁾.

Initially, the PICO strategy was used to identify the problem and draw up the research question. PICO stands for Population, Intervention or area of interest, Context and Outcomes⁽¹³⁾.

P - women; I - use of oral contraceptives; C - context of use; O - ad-

verse effects. Thus, the following research question was outlined: what is the scientific evidence about adverse effects resulting from the use of oral contraceptives by women?

Three databases were used to select the articles: Latin American and Caribbean Health Sciences Literature (LILACS), Scientific Electronic Library Online (SCIELO) and National Library of Medicine (MEDLINE) via the Virtual Health Library (VHL).

To choose the Medical Subject Headings (MeSH) and Health Sciences Descriptors (DECs), in order to expand the retrieval of research in the databases, a search was carried out to find out which descriptors and keywords were present in articles published in scientific journals about the use of oral contraceptives and their adverse effects.

In the LILACS databases, the search strategy was based on the words: ("ANTICONCEPTIONALS") or "ORAL ANTICONCEPTIONALS") or "HORMONAL CONTRACEPTIVES") or "FEMALE ANTICONCEPTIONALS") or "HORMONAL CONTRACEPTION" [Words] and ("ADVERSE EVENTS") or "ADVERSE EFFECTS") or "MEDICATION INTERACTIONS" [Words] and ("SPANISH") or "ENGLISH") or "PORTUGUESE" [Language].

The following strategy was used in the SCIELO database: ((ANTICONCEPTIONALS) OR (ORAL ANTICONCEPTIONALS) OR (HORMONAL CONTRACEPTIVES) OR (FEMALE ANTICONCEPTIONALS) OR (HORMONAL CONTRACEPTIVES) AND (ADVERSE EVENTS) OR (ADVERSE EFFECTS)) AND (Spanish) OR (English) OR (Portuguese).

The following search strategy was used in the MEDLINE database: contraceptive agents) OR (contraceptives, oral) OR (contraceptive agents, female hormonal) AND (adverse event) OR (drug-related side effects AND adverse reactions). Associated with the follow-

ing filters: AND mj:("Oral Hormonal Contraceptives" OR "Oral Contraceptives") AND type_of_study:("risk_factors_studies" OR "etiology_studies" OR "observational_studies" OR "prognostic_studies" OR "clinical_trials" OR "diagnostic_studies" OR "incidence_studies" OR "prevalence_studies" OR "qualitative_research" OR "evaluation_studies") AND la:("en" OR "pt" OR "es") AND type:("article").

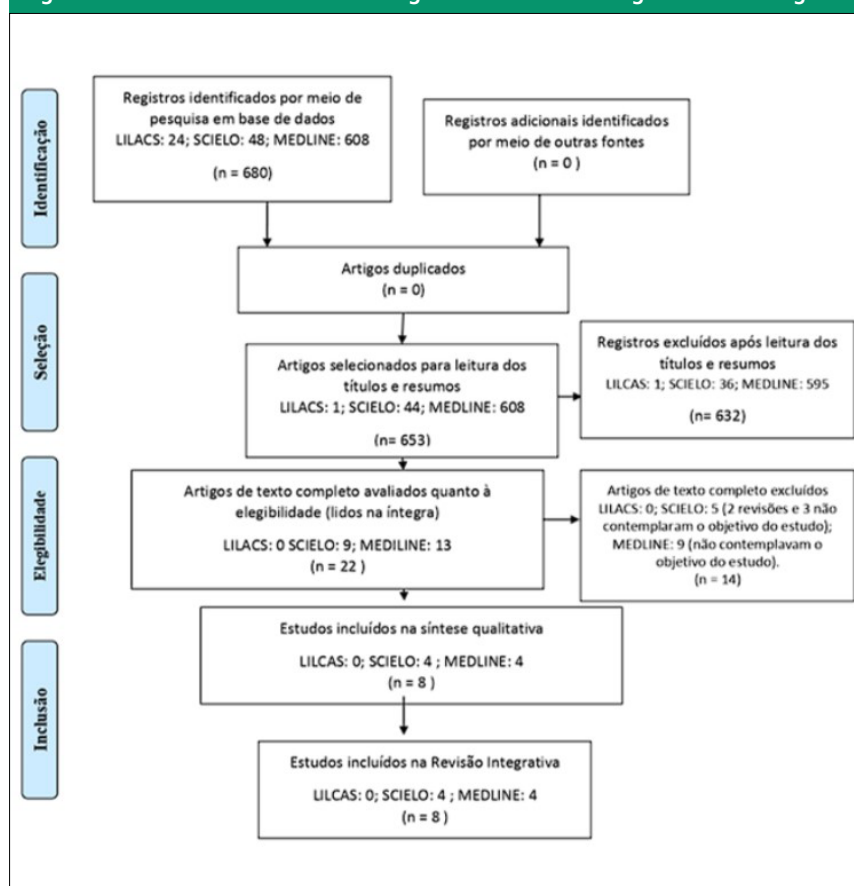
The inclusion criteria for the studies were: primary studies, available in full online and free of charge, in Portuguese, Spanish or English, and which addressed adverse effects or drug interactions resulting from the use of oral contraceptives.

Duplicate studies that did not respond to the objective of the study, lit-

erature reviews, projects, conferences, dossiers, ministerial manuals, editorials, reviews, protocols, rapid communication, theoretical reflections, dissertations, theses, monographs and abstracts published in event proceedings were excluded. No time frame was pre-established in order to cover a greater number of studies.

The search was carried out according to the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA), and took place in March 2023, as described in the Flowchart Selection of studies in the integrative review according to the PRISMA guide (Flowchart 1).

Figure 1 - Selection of studies in the integrative review according to the PRISMA guide



Source: Prepared by the author, 2023.

The LILACS database identified 24 studies. Of these, none addressed the adverse effects of oral contraceptives, only injectable contraceptives.

A total of 48 studies were identified from the SCIELO database, of which 40 were excluded after reading the titles and abstracts (four duplicates; eight review articles; two rapid communications; one abstract; one editorial; 24 did not meet the study's objective). Nine studies were selected to be read in full. After reading, five studies were excluded (two literature reviews and three for not meeting the research objective). Four studies were selected for the sample.

A total of 608 studies were identified in the MEDLINE database. Of these, 595 were excluded after reading the titles and abstracts (15 review studies; 580 did not meet the study objective). Thirteen studies were selected to be read in full. After reading, nine were excluded as they did not meet the study's objective. Four articles were selected for the sample.

A total of eight studies were selected to form the corpus of analysis. During selection, the title and abstract were read, while eligibility was determined by reading the full text, checking the pre-established criteria. Articles indexed in more than one database were included once to avoid repetition. The articles were placed in a Microsoft Word table for selection, reading, organization and categorization.

Data was extracted from each article included in the review using a tool designed by the author to identify the studies, which contained the following items: code, title, database, year of publication, country of publication, journal, objective, method, results and level of evidence (LE).

To determine the level of evidence of the studies, the following classification was adopted: level I - meta-analyses and randomized

controlled studies; level II - experimental studies; level III - quasi-experimental studies; level IV - descriptive, non-experimental or qualitative studies; level V - experience reports; and level VI - consensus and expert opinions⁽¹³⁾.

Data analysis was carried out jointly by the main researcher and the supervisor. Based on questions such as: "Was the research question answered? Was the objective achieved? Is the methodology described appropriate?" it was possible to analyze convergent and divergent issues, confronting them.

After careful reading, the findings were summarized and interpreted in a descriptive and detailed manner, linking them to the relevant literature and identifying gaps and similarities.

In order to present an integrative review that provides the reader with a critical reflection on the use of oral contraceptives and their adverse effects, the presentation of the review/synthesis of knowledge was carried out initially in a descriptive table, then through the interpretation and discussion of the content of the studies.

As this is a review study, based on published articles available in the literature, it can be carried out without having to be submitted to the Research Ethics Committee. It should be noted that ethical aspects were respected, in accordance with Copyright Law no. 9,610 of February 19, 1998.

RESULTS

Eight studies were examined, four published in the SCIELO database and four in MEDLINE. Of these, four were conducted in Brazil, one in the United States, one in Germany, one in Italy and one was carried out simultaneously in Denmark, Estonia, Iceland, Norway and Sweden. In

terms of publication years, one article was found for each of the years 2018, 2021 and 2022, two in 2009 and three in 2020.

The studies were published in various journals, including two in the Brazilian Journal of Gynecology and Obstetrics, one in the journal *Ciência & Saúde Coletiva*, one in the Journal of the Brazilian Medical Association, one in the British Journal of Clinical Pharmacology, one in the Journal of Sleep Research, one in the journal *Gynecological Endocrinology* and one in the Journal of Allergy and Clinical Immunology.

As for the method used, one study applied online questionnaires, one carried out qualitative research, one was a case-control observational study, two were cross-sectional studies, one was a retrospective cohort study with case-control analysis and one was a population-based study. The level of evidence was predominantly level IV.

The main adverse effects associated with oral hormonal contraceptives have been identified as headaches, reduced libido, acne, significant weight gain, nausea, vomiting, mood swings, increased likelihood of developing cervical lesions induced by the human papillomavirus (HPV), increased excessive daytime sleepiness and insomnia, spotting (breakthrough bleeding) and increased risk of asthma and glaucoma, as detailed in the Table of general characteristics of the included studies (Table 1).

Table 1 - General characteristics of the included studies (n= 8).

Code/ Authors	Database	Year	Journal	Objective	Results
A1/PANNAIN, G.D. et al.	SCIELO	2022	Revista Brasileira de Ginecologia e Obstetrícia	Understanding patients' perceptions of the adverse effects of contraceptive methods in order to improve medical care and women's adherence to treatment.	Of the 536 women surveyed, 110 reported headaches when using hormonal contraceptives, while 72 reported spotting. There was a relative risk indicating that the use of these pills increases the risk of these adverse effects, in addition to edema. It was also identified that the use of combined oral hormonal contraceptives is a risk factor for reduced libido. On the other hand, the use of hormonal contraceptives was shown to be protective against acne.
A2/BRAN- DÃO, E.R.	SCIELO	2009	Ciência & Saúde Coletiva	From a socio-anthropological perspective, it addresses the challenges faced by young people in managing their affective-sexual lives, in terms of preventing unforeseen pregnancies. It discusses some of the difficulties they encounter in managing contraception during their affective-sexual lives, identifying situations that lead to non-use of contraceptive methods (CAM).	Side effects of hormonal methods: the centrality of the body for the younger generations makes the interviewees ponder the continued use of the contraceptive pill, due to significant weight gain, an increase in pimples, nausea, headaches, changes in mood. These side effects contribute to discontinuing use or abandoning the method.
A3/VOLPATO, L.K.	SCIELO	2018	Revista Brasileira de Ginecologia e Obstetrícia	To evaluate the association between hormonal contraception and the presence of lesions induced by the human papilloma virus (HPV) in the uterine cervix of patients at the gynecology and obstetrics service of the medical specialty outpatient clinic of the University of Southern Santa Catarina - AME/UNISUL.	When comparing the occurrence of HPV lesions in users of combined oral contraceptives (COCs) with non-users, there was an association with doses of 0.03 mg or higher of ethinylestradiol (EE), in which they were 1.9 times more likely to develop HPV-induced cervical lesions; when separating these cases by the grade of the lesion, the likelihood of these patients presenting a low-grade cervical lesion was 2.1 times higher, but with no impact on high-grade cervical lesions and the occurrence of invasive cancer.
A4/MONTEI- RO, D.L.M. et al.	SCIELO	2020	Revista da Associação Médica Brasileira	To analyze the level of knowledge of Brazilian adolescents in relation to emergency contraception (EC), such as correct administration, frequency of use, efficacy, mechanism of action, adverse effects and complications.	As for side effects, 58.8% of 10-14 year olds and 17.6% of ≥15 year olds couldn't answer, but 60.5% of 15-19 year olds mentioned nausea and vomiting. A significant proportion (17.6-41.2%) believe that EC causes abortion, cancer, infertility and fetal malformations. More than 80% agree that it can cause menstrual irregularity.
A5/HOGDEN et al.	MEDLINE	2021	British Journal of Clinical Pharmacology	To investigate the association between the use of hormonal contraceptives (HC) and the incidence of glaucoma in women of reproductive age, focusing on the duration and type of HC used.	Regular users of hormonal contraceptives had an increased risk of glaucoma compared to non-users. Regular use of HCs was associated with an increased risk of glaucoma.
A6/BEZERRA, A.G. et al	MEDLINE	2020	Journal of Sleep Research	To evaluate the impact of hormonal contraceptive use on subjective self-reports of sleep through a web-based cross-sectional survey.	Contraceptive users reported more frequent sleep complaints and had higher scores, which means increased excessive daytime sleepiness and more insomnia symptoms. Women using progestogen-only therapies reported shorter total sleep duration compared to combined therapy. Users of third-generation contraceptives had shorter total sleep time.

A7/GUIDA, M.	MEDLINE	2020	Gynecological Endocrinology	To evaluate possible associations in sleep alterations induced by estrogen-progestagens in contraceptives in 108 women aged between 20 and 50.	The longest average nocturnal sleep time, compared to the control (450 min), occurred in women who used progestogen-only oral contraception (510 min).
A8/MACSA-LI, F.	MEDLINE	2009	Journal of Allergy and Clinical Immunology	To investigate the association between the use of oral contraceptive pills (OCPs) and asthma in a Nordic-Baltic population-based study, taking into account the possible interaction with body mass index (BMI).	Oral contraceptive pills have been associated with an increased risk of asthma, asthma with hay fever, wheezing with shortness of breath, hay fever and 3 asthma symptoms.

Source: Prepared by the author, 2023.

DISCUSSION

Contraceptives are widely adopted by women, representing a significant achievement in terms of reproductive and sexual rights. However, there are still challenges to be overcome, including access to contraceptive methods, especially for women in situations of social vulnerability, as well as access to health services and complete and reliable information. Lack of adequate guidance can hinder family planning, making it difficult to transform information into effective health protection and promotion practices. It is estimated that around 18% of married or partnered women in developed countries use oral contraceptives, compared to 75% in developing countries⁽¹⁰⁾.

It is well known that, like any medication, hormonal contraceptives can trigger adverse effects in different systems of the human body. These include alterations in immune, metabolic, nutritional, psychiatric, vascular, ocular, gastrointestinal, hepatobiliary, skin-subcutaneous, renal/urinary, auditory, Central Nervous System (CNS) and Reproductive System disorders⁽¹⁴⁾.

A study revealed that, among 536 women analyzed, 110 of them (20.5%) reported experiencing headaches while using oral hormonal contraceptives. In addition, 72 wom-

en (13.4%) reported spotting. It was also observed that the use of combined oral hormonal contraceptives was associated with an increased risk of reduced libido (A1).

In young people, the side effects of contraceptives can negatively affect continuity of use, leading to abandonment of the method due to significant weight gain, increased acne, nausea, headaches and mood swings (A2).

Use of oral contraceptives can lead to symptoms such as weight gain due to an excessive increase in appetite, depression, fatigue, decreased libido, acne, increased breast size, increased low-density lipoprotein (LDL) cholesterol, decreased high-density lipoprotein (HDL) cholesterol and itching. These adverse effects are associated with the use of progestogens. The combination of progestogens and estrogens can result in breast tenderness, headaches, increased blood pressure and the risk of acute myocardial infarction⁽¹⁰⁾.

Another study revealed that with regard to side effects, 58.8% of women aged between 10 and 14 and 17.6% of those aged 15 and over could not provide a clear answer. However, 60.5% of women aged between 15 and 19 mentioned experiencing nausea and vomiting. A significant proportion (between 17.6% and 41.2%) believe that the Emergency Contraceptive can cause

abortion, cancer, infertility and fetal malformations. In addition, more than 80% agreed that the method can cause menstrual irregularities (A4).

In today's society, body image plays an important role in the construction of personal identity, influenced by various factors. Many people try to conform to a standard of beauty considered ideal, which often results in body dissatisfaction. Young people and adolescents, in particular, are more susceptible to these dissatisfactions due to the social pressures imposed by family, friends and the media, among others⁽¹⁵⁾. Therefore, it is crucial to offer contraceptive methods that do not compromise women's health, taking these concerns into account.

When it comes to prescribing a contraceptive method, it is essential that the health professional takes into account the profile of the woman for whom the method is intended. This involves understanding her health needs, social context, access to reliable information and personal concerns, such as weight gain and acne. It is crucial to be aware of each woman's individual characteristics, personal history and specific concerns, ensuring that the method chosen is suited to her unique needs and circumstances⁽¹⁶⁾.

Other adverse effects associated with the use of oral contraceptives, as shown in studies, include sleep prob-

lems, increased risk of HPV lesions, risk of glaucoma and asthma. With regard to the risk of HPV lesions, it was not mentioned whether the study addressed condom use. With regard to sleep, one study found that contraceptive use is associated with more frequent sleep complaints, resulting in increased excessive daytime sleepiness and more symptoms of insomnia (A6). These findings highlight that the use of contraceptive methods can have a negative impact on women's quality of life, potentially leading to abandonment of these methods and, consequently, an unplanned pregnancy.

Two studies showed contrasting results when comparing the type of hormone used in contraceptives. According to study A6, women using progestogen-only therapies reported a shorter total sleep duration compared to those using combined therapy. However, in study A7, it was observed that the average nightly sleep time was longer in women using oral contraceptives containing only progestogen compared to the control group (450 min), reaching 510 minutes. No additional evidence was found to corroborate or contradict these results.

With regard to HPV, glaucoma and asthma, it has been observed that the use of ethinylestradiol increases the likelihood of developing HPV-induced cervical lesions (A3). According to Gomes et al. (2022) ((17))there is no definitive consensus on this issue. The authors point out that the mechanisms underlying the persistence and incidence of HPV lesions are still not fully understood, indicating the need for further research to determine the best approaches in relation to the type of contraceptive, route of administration and hormonal doses that are not associated with HPV-induced lesions⁽¹⁷⁾. Furthermore, it is suggest-

ed that research into the possible association between HPV-induced lesions and frequent condom use be expanded.

In addition, an increased risk of asthma associated with the use of oral contraceptive pills has been observed (A8). However, the relationship between the use of these contraceptives and asthma is still not clearly defined. The authors suggest that fluctuations in estrogen levels may be responsible for asthma exacerbations in women⁽¹⁸⁾.

Study limitations

The limitation of this review is the limited number of publications available that deal with the subject under investigation, as well as the methodology adopted, since it involves only a few databases.

Contributions to Nursing, Health or Public Policy

By identifying and detailing the adverse effects of using oral contraceptives, the study helps to promote women's sexual and reproductive health, enabling more informed and safer contraceptive choices. This can contribute to reducing complications associated with inadequate use of the methods and to improving women's quality of life.

The study reinforces the importance of including reproductive planning in public health actions, as recommended by the Ministry of Health, promoting the strengthening of sexual and reproductive rights. The integrative review also contributes to evidence-based practice, allowing nurses to identify gaps in knowledge and improve reproductive counseling during consultations.

CONCLUSION

It is essential to emphasize that access to information not only em-

powers women to make informed decisions about their reproductive health, but also strengthens the relationship between patients and health professionals, promoting a collaborative approach to health care. Nurses play a crucial role in this context, as they are often at the forefront of providing care to women on issues related to sexual and reproductive health.

By understanding the adverse effects of oral contraceptives and being aware of women's individual needs and social contexts, nurses can offer more personalized and comprehensive care. This includes providing guidance on alternative contraceptive options, promoting adherence to treatment and identifying possible complications or side effects early on.

Furthermore, by recognizing the importance of a holistic approach to maternal and child health, nurses can make a significant contribution to promoting a healthy and planned pregnancy, thus reducing the health risks for both mother and baby.

Therefore, this study not only provides valuable information on the adverse effects of oral contraceptives, but also highlights the relevance of the role of nurses in promoting women's reproductive health and building a more inclusive and patient-centered health system.

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