The use of contraceptives and its relationship with chronic venous insufficiency

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ABSTRACT

Introduction: Combined oral contraceptives (COC's) are widely used due to their efficacy in contraception, with an efficacy rate of up to 99% when used correctly. However, its use is associated with risks, such as the increased risk of venous thrombosis, a serious concern due to the serious implications it may have for women's health. Objective: This study aims to explore the effects of combined oral contraceptives on women's health, with a special focus on the risks associated with venous thrombosis. In addition, it seeks to highlight the fundamental role of pharmacists in guiding and preventing harm related to the use of these drugs. Materials and methods: A systematic and exploratory literature review was carried out, with a search for articles, theses and dissertations in the SciELO, Bireme, LILACS and Web of Science databases, from 2000 to 2024. Studies that explored the relationship between contraceptives and thrombosis, taking into account the inclusion and exclusion criteria, were included. Results: The results of the study indicate that COCs, especially when they contain estrogen, significantly increase the risk of venous thrombosis, especially in women over 40 years of age. This risk is exacerbated by conditions such as genetic predisposition, hypertension, and diabetes, factors with a higher prevalence in this age group. Third- and fourth-generation progestogens have been identified as associated with a higher thrombotic risk compared to second-generation progestogens. Final thoughts: Despite the benefits in contraception and menstrual control, COCs are not without risks, and a careful assessment of the benefits versus the potential individual harms when prescribing these medications is crucial. The role of pharmacists is vital in educating patients about the risks and carefully selecting the safest contraceptives, taking into account factors such as personal and family medical history, genetic predisposition, and preexisting health conditions. This approach aims to maximize the safety and well-being of women who choose to use combined oral contraceptives.

Keywords: Contraceptive, Chronic venous insufficiency, Thrombosis.

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INTRODUCTION

Combined oral contraceptives (COC's) represent one of the most common and effective forms of contraception, boasting an impressive 99% effectiveness rate when used correctly. With a diversified formulation in terms of dosage and active ingredient, these drugs play an important role both in regulating the menstrual cycle and in preventing pregnancy. However, as with any pharmacological intervention, its use requires a thorough understanding of the associated risks and benefits (Ferreira, D'Avila, and Safatle (2019).

While AOC's offer a number of benefits, it is critical to recognize the potential risks to women's health that can arise from inappropriate or uninformed use of these medications. As observed by Santos, Sato, and Sato (2022), it is common to find cases of inappropriate use of contraceptives, sometimes without medical advice.

One of the risks associated with the use of hormonal contraceptives is the development of venous thrombosis, a condition that is characterized by the formation of blood clots in the vessels. Thrombosis can lead to serious complications, such as partial or total obstruction of the affected vessel, with the potential to cause permanent damage or even death. This concern is reinforced by studies such as those by Alves, Almeida and Balhau (2015) and Ferreira, D'Avila and Safatle (2019), which highlight the relationship between the use of contraceptives and the increased risk of thrombosis, especially in women.

The mechanisms by which hormonal contraceptives favor the risk of thrombosis are complex and involve changes in hemostasis, the system responsible for regulating blood clotting. Estrogen, one of the main components of these medications, plays a significant role in this process, increasing the levels of certain clotting factors while decreasing the levels of anticoagulants (Melo et al., 2006).

However, the increased risk of thrombosis is not exclusively attributed to contraceptives, but is influenced by a complex interaction of factors, such as genetic predisposition, lifestyle, and other medications used (Silva et al., 2018).

In this context, there is a need for a more comprehensive and informed approach to the use of contraceptives, with emphasis on the appropriate guidance of health professionals, particularly pharmacists. This study therefore aims to explore the effects of contraceptive use, highlight scientific evidence related to women's health risks, and discuss the importance of the pharmacist's role in preventing possible harm, with a special focus on Chronic Venous Insufficiency.

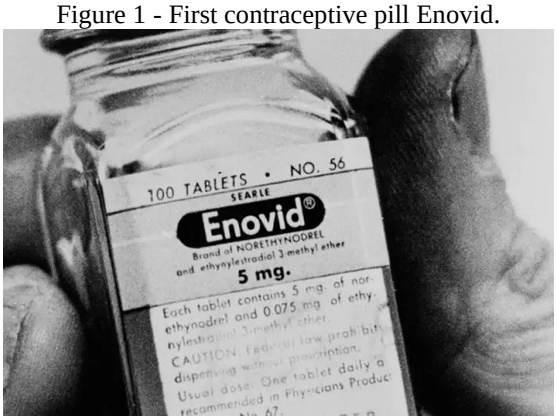
STATE OF THE ART

ORAL CONTRACEPTIVE

The development and commercialization of the first oral contraceptive represented a significant milestone in the history of medicine and society. In 1950, scientists Pincus, Rock, and

Garcia began a quiet revolution that, a decade later, would materialize with the launch of Enovid (figure 1) in the United States. Since then, oral hormonal contraceptives, popularly known as contraceptive pills, have played an important role in women's lives and family dynamics (Almeida; Assis, 2017).

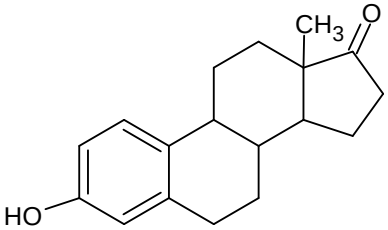
Figure 1 - First contraceptive pill Enovid.



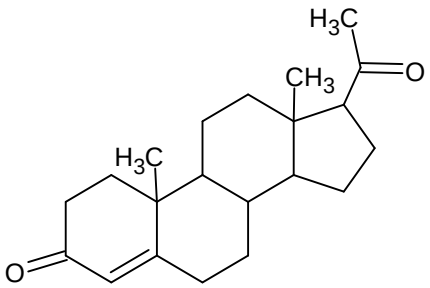
Source: DW (2015).

The Ministry of Health defines oral hormonal contraceptives as steroids that aim to prevent conception through the combined action of hormones, mainly estrogen and progesterone (figure 2). These hormones, when interacting with the menstrual cycle, inhibit the maturation of the egg and consequently ovulation, making pregnancy less likely (Correa et al. 2011).

Figure 2 - Chemical structure of estrogen and progesterone.



Estrogênio



Progesterona
Source: ACD/ChemSketch

It is important to note that the use of oral contraceptives can cause adverse effects. These effects can range from mild and reversible changes, such as hyperpigmentation and weight variations, to more severe clinical manifestations, such as thromboembolic events, which can occur. Therefore, it is essential that the use of these drugs is monitored by health professionals, who can advise on individual risks and benefits, in addition to monitoring possible side effects (Silva et al., 2018).

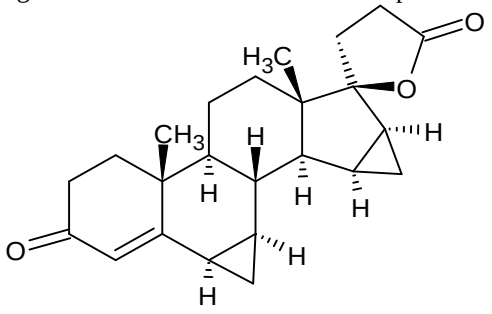
Despite the challenges and controversies, oral contraceptives remain one of the most popular and effective fertility control options. Its impact on modern society is undeniable, providing women with the power to decide on their own reproduction and contributing to a future in which family planning is a reality accessible to all (Souza and Alvares, 2018).

Oral hormonal contraceptives (CHO) represent one of the most popular and effective options for female fertility control. These contraceptives can be categorized based on their hormonal composition, dosage, and type of hormone used (Silva et al., 2018).

Initially, as for hormonal composition, oral contraceptives can be divided into two main types: the combined method, which contains both an estrogen and a progesterone, and the isolated method, which contains only progesterone, known as a mini-pill. This distinction is important, as each type can have different efficacy and side effects, and it is necessary to choose the most appropriate one for each specific case (Grossman, 2011).

In addition, oral contraceptives are classified into different generations, which refer to the evolution of formulations over time. We have the first, second and third generations, corresponding to single-phase, two-phase and three-phase formulations, respectively. There are also studies that propose an additional classification, considering contraceptives containing drospirenone (Figure 3) as fourth-generation, although this classification still lacks a clear definition (Correa et al., 2011).

Figure 3 - Chemical structure of Drospirenone.



Drospirenona
Source: ACD/ChemSketch.

The benefits brought by effective control of contraception are undeniable. The increase in women's rights and their participation in the labor market was greatly facilitated, as the ability to plan the family provided by contraceptives allowed a better match between the number of children and the economic conditions of the families. In addition, there was a significant change in mentality and

customs, promoting greater sexual liberality and contributing to the advancement of gender equality (Almeida; Assis, 2017).

Although they are highly effective in preventing pregnancy, it is important for women to consult their doctors before starting use in order to assess which option is best for their individual health and needs. In addition, regular medical follow-up is essential to monitor possible side effects and ensure safe and effective contraception.

CONTRAINDICATIONS OF ORAL CONTRACEPTION

The use of oral contraceptives, commonly referred to as birth control pills, is widely adopted by women around the world. However, as noted by Souza and Alvares (2018), it is essential to take into account the contraindications associated with this contraceptive method.

One of the main points highlighted by Wannmacher (2003) is the significant, albeit small, increase in systolic and diastolic pressures associated with the prolonged use of these drugs. This increase in blood pressure can be especially worrisome in hypertensive women, as even a small increase in blood pressure can trigger serious complications, such as stroke or acute myocardial infarction (AMI) (Grossman, 2011).

In addition to high blood pressure, several other risk factors and medical conditions contraindicate the use of oral contraceptives. Among these conditions are diabetes mellitus with vascular disease, female smokers over 35 years of age, cardiovascular diseases, thromboembolism, and migraine with aura (Correa et al., 2011).

Another critical point to be considered is the predisposition to the development of breast cancer associated with the use of oral contraceptives. The Ministry of Health identifies several well-established risk factors for breast cancer linked to women's reproductive life, including early menarche, nulliparity, first pregnancy after the age of 30, late menopause, hormone replacement therapy, and use of oral contraceptives (Souza and Alvares, 2018).

In light of these contraindications, it is essential for women considering oral contraceptive use to consult with their doctors for a thorough evaluation of their health and medical history. Choosing the appropriate type of contraceptive method should not only take into account its effectiveness in preventing pregnancy, but also the potential risks and benefits associated with each available option. For many women with specific medical conditions or risk factors, non-hormonal contraception is often more appropriate and safer.

COMPLICATIONS DUE TO THE USE OF ORAL CONTRACEPTIVES

As indicated by Souza and Alvares (2018), the prolonged use of oral contraceptives can trigger significant changes in the hemostatic system of the human body, leading to the development

of clots in the veins. Deep vein thrombosis (DVT) is one of the most serious complications associated with the use of oral contraceptives, leading to acute thrombi formation in the superficial or deep venous system.

Thrombi formed during DVT can cause partial or total occlusion of the vein, posing a serious threat to health. In addition, parts of these thrombi can detach and trigger a pulmonary embolism (PE), a potentially lethal complication. As highlighted by Santos, Magalhães and Morato (2017), PE is often underdiagnosed due to its nonspecific clinical presentation, which makes its treatment and management even more challenging.

The consequences of DVT and PE go beyond the immediate risks to the patient's life. In its chronic phase, DVT can result in significant physical disability and enormous socioeconomic costs, contributing to the development of postthrombotic syndrome. In addition, venous thromboembolism is described as one of the main causes of preventable hospital death, highlighting the importance of preventive measures and effective interventions (Correa et al., 2011).

Symptoms of DVT can range from edema and pain in the affected limb to venous distention, although many patients may be asymptomatic. In view of this diversity of clinical presentations, a detailed anamnesis and a careful physical examination become essential for the early diagnosis and appropriate management of DVT. It is important to note that some risk factors, such as a history of previous surgery, prolonged immobilization, and the use of estrogen-containing oral contraceptives, can increase susceptibility to DVT. Therefore, the individualized evaluation of each patient, considering their medical history and risk factors, is essential for the prevention and effective treatment of this condition (Barros, Pereira and Pinto, 2012).

Deep vein thrombosis (DVT) affects millions of people worldwide, with significant health and mortality consequences. According to Rollo et al. (2005), the estimated incidence of this disease in Brazil is calculated at 0.6 cases per 1,000 inhabitants per year. In addition, DVT, along with its serious complication, pulmonary embolism (PE), represents a serious public health problem, especially among the elderly.

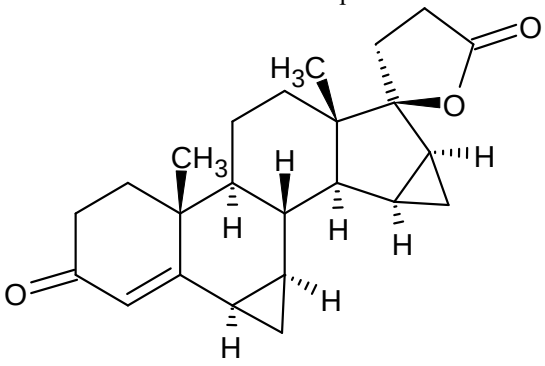
Several risk factors are associated with the development of deep vein thrombosis, as defined by the Ministry of Health (2019). These include the use of oral contraceptives, immobility due to prolonged hospital stays, economy class syndrome (associated with immobility during long journeys), varicose veins, surgeries, smoking, and hormone replacement therapy. Currently, recommendations and relevant information are widely disseminated on the Ministry of Health website in order to prevent DVT prophylactically (Ministry of Health, 2019).

Risk factors for DVT can be categorized into general factors (such as age and gender), clinical factors (such as obesity and infections), medications (including oral contraceptives and hormone therapy), and surgical factors (such as the type of surgery performed and the time of procedure). It is

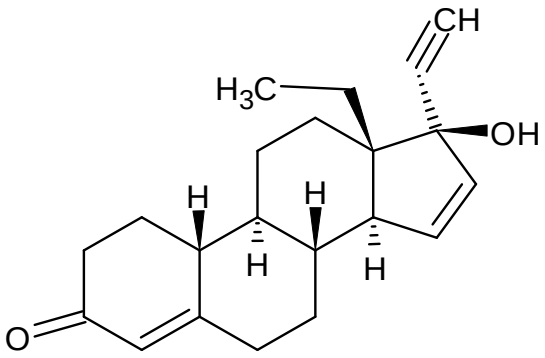
important to emphasize that the use of oral contraceptives leads the list of risk drugs that can trigger DVT (Garcia et al., 2002).

As highlighted by Sousa and Alvarez (2018), the hormones present in oral contraceptives, such as estrogen and progesterone, can trigger significant changes in the body's hemostatic system, increasing the risk of clots forming in the veins. Women who use contraceptives containing drospirenone, gestodene or desogestrel (Figure 4) have an increased risk of developing venous thromboembolism compared to those who do not use combined hormonal contraceptives (Brazil, 2016).

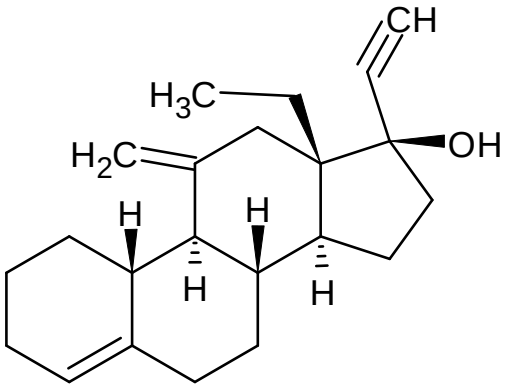
Figure 4: Chemical structures of combined oral contraceptives that cause venous thromboembolism.



Drospirenona



Gestodeno

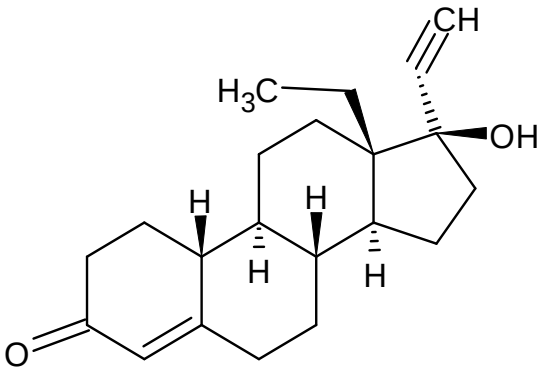


Desogestrel

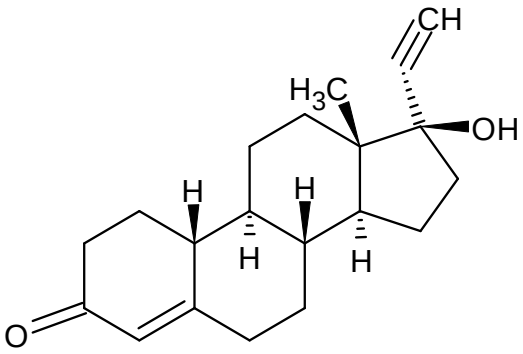
Source: ACD/ChemSketch.

In addition, Júnior and Baracat (2010) point out that third-generation progestogens, such as gestodene and desogestrel, present an even higher risk compared to second-generation first-generation progestogens. Thus, the use of progestogens alone, such as levonorgestrel and norethisterone (Figure 5), does not seem to significantly increase the risk of DVT.

Figure 5: Chemical structures of hormones of the second generation of progestogens.



Levonorgestrel



Noretisterona

Source: ACD/ChemSketch.

Given this scenario, it is essential that health professionals know the risk factors associated with deep vein thrombosis, especially associated with the use of oral contraceptives. An individualized approach and careful assessment of benefits and risks are essential when prescribing these medications, thereby ensuring the safety and well-being of patients. In addition, public awareness and education about preventive measures play an important role in reducing the incidence of this serious health condition.

MATERIALS AND METHODS

This research is a systematic bibliographic review with an exploratory, descriptive and explanatory character, based on an electronic bibliographic survey carried out in several databases. The sources used to search for studies include Google Scholar and the SciELO database, Bireme, LILACS and Web of Science, among others, which have numerous indexed works. It should be noted

that this review covers the literature composed of articles, theses, and dissertations published between the years 2000 and 2024, as well as books from any period.

STUDY VARIABLES

The survey of research data was carried out in the aforementioned databases, where articles, dissertations, and theses published between 2000 and 2024 were selected, which contained data and information on the use of contraceptives and their relationship with chronic venous insufficiency.

DATA COLLECTION

The following terms were used: "contraceptive"; "thrombosis" and "venous insufficiency". The searches were carried out in the following databases: SciELO, Bireme, LILACS and Web of Science.

TIME LIMIT AND LANGUAGE

This study includes only articles published in Portuguese and English, as found in the available databases. Publications of articles, theses, and dissertations in the period from 2000 to 2024 were considered.

INCLUSION CRITERIA

Scientific articles that presented in their title, objectives and conclusions with the words mentioned in the previous topic, addressing the subject in question and published in the research databases, were included.

EXCLUSION CRITERIA

Articles that did not present a theme related to the theme proposed in the title, objective and/or conclusion, that did not fit the time interval stipulated in this review, or that had already been screened in other databases, resulting in duplicates, were excluded. In addition, materials without a scientific character, that is, without ISSN or DOI, were also excluded.

DATA ANALYSIS

A research was carried out through a critical reading, with the purpose of organizing the information contained in the selected studies that complemented the objectives proposed in this review. Articles that met these criteria were cited in the study.

ETHICAL ASPECTS

The ethical aspects of this study were based on the reliability of the data obtained in the reviewed studies, the correct citation of the authors, and the accuracy of the data description. It was not necessary to obtain an opinion from the research ethics committee or consent from the authors of the studies published in the databases, following the guidelines of the Brazilian Association of Technical Standards (ABNT) for academic papers.

RESULTS AND DISCUSSION

The articles analyzed in this review were found in the following databases: SciELO (5 articles), Bireme (3 articles), LILACS (4 articles) and Web of Science (2 articles).

After the eligibility process, 14 articles were selected that met the inclusion and exclusion criteria, in addition to aligning with the main objectives for the development of this review. These articles were analyzed in detail, considering the established selection criteria, which allowed us to answer the questions proposed by the review.

According to the inclusion criteria, Tables 1, and Tables 2, 3 and 4 in the annex, list the articles selected for the discussion of this theme. In this review, the synthesis of the publications included, based on the searched databases, presents the author(s), the year of publication, the title, the considerations/objectives and the results of interest

Table 1: Main information of the articles selected for study in SciElo.

AUTHOR/ YEAR	TITLE	OBJECTIVE	RESULTS
Padovan and Freitas (2015)	Oral Contraceptive That Is Associated With The Risk Of Deep Vein Thrombosis	To highlight and critically discuss the use of different classes of oral contraceptives, investigating their correlation with cases of venous thrombosis.	The result found was that thrombosis is considered a serious diagnosis and occurs in more than 80% of cases, mainly due to the use of oral contraceptives.
Santos and Barbosa (2018)	Use of oral contraceptives associated with the risk of deep vein thrombosis	To demonstrate the association between the use of oral hormonal contraceptives and deep vein thrombosis.	The use of oral contraceptives increases the probability of deep vein thrombosis (DVT) due to the action of the hormones contained in these drugs on the cardiovascular system.
Ferreira and Passion (2021)	The relationship between the use of the anticon ceptional pill and the deve-lopment of deep venous throm-bosis in Brazil	To demonstrate the adverse reactions, especially Deep Vein Thrombosis (DVT), associated with the chronic use of oral contraceptives.	To minimize adverse reactions, it is essential that a gynecologist conducts a detailed anamnesis, considering the physiological history of each patient, to select the contraceptive method most appropriate to their individual needs.

Cruz, Bottega and Paiva (2021)	Oral contra-ceptive: side effects and its relationship with venous thrombosis	To review the correlations between the use of oral hormonal contraceptives and deep vein thrombosis, analyzing the pharmacological effects of these contraceptives on hemostasis and the coagulation cascade.	It was concluded that oral hormonal contraceptives may increase the risk of venous thrombosis as an adverse effect. This is due to the hormones present in these contraceptives, which alter the coagulation cascade and inhibit factors that help prevent hypercoagulability in the body.
Soares et al. (2022)	Venous thromboembolism associated with the use of oral contraceptives: an integrative review	To analyze the association between venous thromboembolism and the use of oral contraceptives	An elevated risk of deep vein thrombosis (DVT) has been identified among patients using combined oral contraceptives.

Source: Prepared by the authors (2024

The discussion of the risks associated with the use of oral hormonal contraceptives (OC) in women over 40 years of age reveals a complex interaction between hormonal, physiological, and health factors that increase vulnerability to severe thrombotic events, such as deep vein thrombosis (DVT).

First, it is important to note that OCTs contain synthetic estrogen and progesterone, hormones that mimic those involved in the female reproductive cycle. These compounds are effective in preventing pregnancy, but they also introduce significant health risks, especially as women age. Studies such as those by Silva et al. (2021) and Morais, Santos, and Carvalho (2019) indicate that women over 40 years of age have an increase in cardiovascular risk associated with the use of these medications. This is due to the natural physiological changes that occur with aging, such as changes in body composition and the functioning of the cardiovascular system.

In addition to natural physical changes, such as a decrease in endogenous production of sex hormones and an increased prevalence of conditions such as hypertension and diabetes, women in this age group tend to have a greater predisposition to thrombotic events. The review by Silva, Duarte, and Cardoso (2021) and Correa, Barroso, and Araújo (2021) highlights that the prolonged use of OCCs can accentuate this predisposition, since these contraceptives can influence the coagulation cascade, increasing procoagulant factors and decreasing natural anticoagulants.

Deep vein thrombosis is of particular concern due to the ability of synthetic hormones, especially estrogen, to increase the production of thrombin and other clotting factors, while decreasing the activity of natural anticoagulants such as protein S and antithrombin III (Ferreira and Paixão, 2021). This condition is aggravated by advanced age, which naturally increases blood coagulability and decreases the efficiency of anticoagulant mechanisms (Padovan and Freitas, 2015).

In addition, predisposing genetic conditions, such as the presence of mutations in factor V Leiden, can further intensify the risk of thrombosis in women after the age of 40 who use OCOs (Santos and Lima, 2020). Therefore, the choice of contraceptive method for women in this age group

should consider not only the contraceptive benefits, but also the associated individual risks, including personal and family history of thrombosis, pre-existing health conditions, and lifestyle.

An important aspect highlighted by Santos and Barbosa (2018) is the increase in female independence and autonomy in family planning, which has resulted in a significant increase in the use of ACOs since their introduction. However, as mentioned by Silva, Duarte, and Cardoso (2021), women over 40 years of age face an increased risk of thrombotic events associated with long-term use of these contraceptives. This is due not only to physiological changes related to aging, but also to the higher prevalence of health conditions such as hypertension, obesity, and diabetes, which are additional risk factors for cardiovascular complications.

The interaction between estrogen and progestogen in OCAs is a critical point, as discussed by Ferreira and Paixão (2021), who highlight how these hormones can increase blood coagulability by altering viscosity and vascular wall. Women over 40 years of age, especially those with a genetic predisposition to thrombosis, as mentioned by Correa, Barroso, and Araújo (2021), face a high risk of thrombotic events due to the combination of exogenous hormonal factors and physiological changes resulting from aging.

In addition, as pointed out by Morais, Oliveira and Trevisan (2015), the risk profile varies significantly with the age of women. While younger women generally have a lower risk of thrombotic complications, this likelihood increases considerably after age 40 due to changes in hemostasis and cardiovascular function associated with aging.

According to Silvério et al. (2022), COCs, composed of synthetic estrogen and progestogen, mimic the natural hormones of the female reproductive cycle. This hormonal composition can significantly influence women's cardiovascular system, increasing thrombin production and, consequently, the risk of deep vein thrombosis (DVT). The absolute risk of DVT tends to increase with age, as indicated by Moraes, Oliveira and Trevisan (2015), due to the physiological changes that occur in aging, such as a greater predisposition to hypercoagulability.

Magalhães and Morato (2018) corroborate this view, highlighting that women over 40 years of age have a higher incidence of chronic diseases, such as diabetes and hypertension, which are additional risk factors for cardiovascular complications. Long-term use of COCs in this age group, combined with these health conditions, intensifies the risks of serious adverse events such as stroke and DVT.

In addition, Lago et al. (2022) emphasize that different progestogens present in COCs can influence the risk of DVT in different ways. Progestogens such as drospirenone, gestodene, cyproterone, and desogestrel are associated with a higher risk of DVT compared with norgestimate, levonorgestrel, and norethisterone. Women over the age of 40, who already have an increased

predisposition to blood clotting due to aging, may be particularly vulnerable to the thrombotic effects of these riskier progestins.

Cruz, Bottega, and Paiva (2021) add that, after the age of 40, the risk of thrombotic events related to the use of COCs becomes even more prominent due to the complex interaction between synthetic hormones (figures 3, 4, and 5) and the physiological changes associated with age. The ability of estrogens to decrease natural anticoagulation factors, such as protein S and antithrombin, contributes to a state of hypercoagulability in this age group.

One of the main points of concern is the increased risk of venous thromboembolic events (VTE), such as deep vein thrombosis (DVT) and pulmonary embolism (PE). Synthetic estrogens, such as ethinylestradiol, are associated with increased blood clotting, through increased levels of clotting factors and decreased natural clotting inhibitors, such as protein C and S (Silva et al., 2021; Magalhães and Morato, 2018). This creates a prothrombotic state in the body, increasing the propensity for clot formation (Morais et al., 2019).

In addition, the progestogens used in OCCs also play an important role. Third- and fourth-generation progestogens, such as desogestrel, gestodene, and drospirenone, have been associated with a higher risk of VTE compared to second-generation progestins, such as levonorgestrel (Santos and Barbosa, 2018; Ferreira and Paixão, 2021). These modern progestins, despite having lower androgenic activity, increase the overall estrogenic effect, which can reduce sensitivity to activated protein C, further increasing thrombotic risk (Santos and Lima, 2020; Santos and Barbosa, 2018).

Another concerning aspect is the impact of OCOs on blood pressure and liver function. Estrogen can cause water and sodium retention, resulting in increased blood pressure, which can be especially dangerous for women with pre-existing hypertension (Silvério et al., 2022). In addition, long-term use of OCOs has been associated with a higher risk of hepatic adenomas, possibly due to hormonal effects on the liver (Silverio et al., 2022).

While OCPs offer clear benefits in preventing pregnancy, controlling menstrual care, and reducing risks such as ectopic pregnancies, uterine fibroids, and ovarian cancer, these benefits need to be weighed against the potential risks mentioned (Silvério et al., 2022; Silva et al., 2021).

The choice of the specific type of OCP is also important, as different generations of progestogens have varying risk profiles for VTE (Padovan and Freitas, 2015; Ferreira and Paixão, 2021). The decision must be individualized, considering factors such as age, personal and family medical history, as well as the presence of genetic predisposition to thrombophilias (Santos and Barbosa, 2018; Moraes, Oliveira and Trevisan, 2015).

In summary, while oral hormonal contraceptives are widely used and effective, it is essential for doctors and patients to be aware of the potential risks associated with them. The decision to

initiate or continue with ACOs should be based on a careful assessment of the expected benefits in relation to each patient's individual risks, thereby ensuring an informed and safe choice.

FINAL CONSIDERATIONS

In view of the results addressed in this study on the risks associated with the use of oral hormonal contraceptives (OC) in women over 40 years of age, the complexity of the interactions between chemical and physical compound, hormonal, physiological, and health factors that influence vulnerability to severe thrombotic events, such as deep vein thrombosis (DVT), becomes evident.

OCOs, containing synthetic estrogen and progesterone, are effective in preventing pregnancy, but they also pose substantial health risks, especially as women age. Recent studies highlight that women over the age of 40 face an increase in cardiovascular risk with the prolonged use of these medications. This increased risk is amplified by the natural physiological changes associated with aging, such as reduced endogenous production of sex hormones and increased predisposition to conditions such as hypertension and diabetes.

The complex interaction between the synthetic hormones of OCCs and the body's clotting mechanisms contributes significantly to the increased risk of deep vein thrombosis. The studies reviewed here underline how estrogens, in particular, can increase blood clotting by decreasing levels of natural blood thinners and elevating pro-clotting factors.

In addition to the hormonal changes induced by OCAs, the choice of the specific type of progestogen also plays an important role. Third- and fourth-generation progestogens were associated with a higher risk of thrombotic events compared with second-generation progestogens, further complicating the therapeutic decision.

It needs to be recognized that while OCPs offer significant benefits in contraceptive and menstrual control, as well as in reducing risks such as ectopic pregnancies and ovarian cancer, these benefits must be weighed against the potential risks, especially in older women with preexisting health conditions.

Therefore, the decision to prescribe or continue ACOs should be individualized and based on a careful assessment of the specific risks and benefits for each patient. This includes considering personal and family medical history, the presence of genetic predisposition to thrombophilias, as well as the choice of the most appropriate type and specific generation of OC to minimize thrombotic risks.

Ultimately, it is essential that physicians and patients are fully informed about the potential risks associated with ACOs, ensuring that any decision is made with knowledge of the facts and in pursuit of maximum patient safety and well-being.

ACKNOWLEDGMENT

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ATTACHMENT

Table 2: Main information on the articles selected for study at Bireme.

AUTHOR/ YEAR	TITLE	OBJECTIVE	RESULTS
Moraes, Oliveira and Trevisan (2015)	Relationship between oral contraception and the risk of deep vein thrombosis in women in the productive period	To correlate the use of oral contraceptives in women of reproductive age with the risk of deep vein thrombosis (DVT).	It was concluded that the use of oral contraceptives increases the probability of deep vein thrombosis (DVT) due to the action of the hormones contained in these drugs on the cardiovascular system.
Santos and Lima (2020)	Vascular Effects of Contraceptive Use: A Literature Review	To review the vascular effects of contraceptive use, with a focus on venous thrombosis as one of the main side effects, and to discuss its clinical implications.	Individuals with a genetic predisposition to thrombosis should avoid the use of contraceptives. For those without known risk, it is recommended not to self-medicate and use contraceptives with medical or specialized guidance.
Silvério et al. (2022)	Influence of hormonal oral contraceptives on women's health	Describe the risks to women's health arising from the prolonged use of hormonal oral contraceptives.	Several risks have been identified, including breast cancer, high blood pressure, and deep vein thrombosis (DVT), all of which are associated with long-term use of hormonal oral contraceptives.

Source: Prepared by the authors (2024).

Table 3: Main information on the articles selected for study in LILACS.

AUTHOR/ YEAR	TITLE	OBJECTIVE	RESULTS
Magalhães and Morato (2018)	Evaluation of the Use of Combined Oral Contraception as a Risk Factor for the Development of Thrombosis in Young Women in the City of Patos	To evaluate and compare coagulation tests and risk factors associated with the development of thrombosis in young women using combined oral contraceptives.	Risk factors should be identified and clarified for hormonal contraceptive users in order to guide the choice of the most appropriate contraceptive method based on individual analysis. It is essential that treatment is accompanied by health professionals to minimize risks.
Silva, et al. (2021)	Risk of Venous Thrombosis Associated with the Use of Oral Contraceptives: Literature Review	To associate homeostatic alterations resulting from the continuous use of oral contraceptives with the development of thrombosis.	Combined oral contraceptives (OCOs) are widely used by women, but it is crucial that there is medical guidance and follow-up to prescribe the method that presents the lowest risk of thrombosis according to the biological profile of each patient.
Correa, Barroso and Araújo (2021)	The use of combined oral contraceptives and the risk of venous thromboembolism: a systematic review	To assess the risk of deep venous thromboembolism (VTE) among users of oral hormonal contraceptives.	The main risk factors associated with VTE include hereditary thrombophilia, use of third-generation combined oral contraceptives (COCs), pregnancy, previous history of venous or arterial thrombosis,

			postpartum period, and use of combined oral contraceptives (COCs).
Silva, Duarte and Cardoso (2021)	The occurrence of thrombotic events in users of Combined Oral Contraceptives	To analyze the occurrence of thrombotic events in users of Combined Oral Contraceptives (COCs) and to investigate the mechanisms that influence their occurrence.	Studies have indicated that there is a high probability of developing deep vein thrombosis associated with the use of combined oral contraceptives, especially in women who have some risk factor for thrombus formation.

Source: Prepared by the authors (2024).

Table 4: Main information of the articles selected for study in the Web of Science.

AUTHOR/ YEAR	**TITLE**	**OBJECTIVE**	**RESULTS**
Morais, Santos and Carvalho (2019)	Venous thromboembolism related to frequent use of combined oral contraceptives	To relate the formation of venous thromboembolism to the use of combined oral contraceptives.	Several circumstances favor the formation of arterial and venous thrombi. One of the significant risk factors for the development of these pathologies is the use of combined oral contraceptives.
Lago, et al. (2022)	Risk of venous thrombosis related to the use of oral contraceptives	To highlight the relationships between the use of oral contraceptives and the occurrence of venous thrombosis.	A relationship between the use of oral contraceptives and the occurrence of venous thrombosis was confirmed.

Source: Prepared by the authors (2024).