

# Influence of oral hormonal contraceptives on the emergence of deep vein thrombosis

## Influência do anticoncepcional hormonal oral no surgimento da trombose venosa profunda

### Influencia de los anticonceptivos hormonales orales en la aparición de trombosis venosa profunda

Ana Caroline Santos Gondim<sup>1</sup>, Camila Santos Alves de Almeida<sup>2</sup>, Marco Aurélio Ninomia Passos<sup>3</sup>

**How to cite:** Gondim ACS, Almeida CSA, Passos MAN. Influence of oral hormonal contraceptives on the emergence of deep vein thrombosis. REVISA. 2022; 11(2): 120-6. Doi: <https://doi.org/10.36239/revisa.v11.n2.p120a126>

# REVISA

1. Paulista University of Brasília.  
Brasília, Federal District, Brazil.  
<https://orcid.org/0000-0001-7223-500X>

2. Paulista University of Brasília.  
Brasília, Federal District, Brazil.  
<https://orcid.org/0000-0001-9012-1516>

3. Paulista University of Brasília.  
Brasília, Federal District, Brazil.  
<https://orcid.org/0000-0003-4231-8941>

Received: 12/01/2021  
Accepted: 19/03/2021

#### RESUMO

**Objetivo:** Descrever a ação dos anticoncepcionais orais no organismo feminino, relatando os fatores que desencadeiam a trombose venosa profunda. **Método:** Trata-se de uma revisão bibliográfica de caráter qualitativo, onde foram selecionados 11 artigos de maior relevância para compormos a pesquisa. **Resultado:** A análise dos artigos selecionados mostrou que os anticoncepcionais orais possuem ligação com a ocorrência de eventos trombóticos. Os contraceptivos são compostos por um combinado de hormônios que influenciam diretamente no surgimento da trombose venosa profunda. **Conclusão:** Os anticoncepcionais orais exercem influência no surgimento de trombose venosa profunda pois podem causar alterações no equilíbrio hemostático. Para a utilização desses medicamentos, é necessário responsabilidade e acompanhamento de um especialista, em após uma criteriosa avaliação, será selecionado o anticoncepcional mais adequado.

**Descritores:** Trombose Venosa Profunda; Anticoncepcional Hormonal Oral; Contraceptivos.

#### ABSTRACT

**Objective:** To describe the action of oral contraceptives in the female body, reporting the factors that trigger deep vein thrombosis. **Method:** This is a bibliographical review of a qualitative nature, where 11 articles of greatest relevance were selected to compose the research. **Results:** The analysis of the selected articles showed that oral contraceptives are linked to the occurrence of thrombotic events. Contraceptives are composed of a combination of hormones that directly influence the onset of deep vein thrombosis. **Conclusion:** Oral contraceptives influence the development of deep vein thrombosis as they can cause changes in homostatic balance. For the use of these drugs, it is necessary to be responsible and supervised by a specialist, and after a careful evaluation, the most suitable contraceptive will be selected.

**Descriptors:** Deep Venous Thrombosis; Oral Hormonal Contraceptive; Contraceptives.

#### RESUMEN

**Objetivo:** Describir la acción de los anticonceptivos orales en el organismo femenino, informando los factores desencadenantes de la trombosis venosa profunda. **Método:** Se trata de una revisión bibliográfica de carácter cualitativo, donde se seleccionaron 11 artículos de mayor relevancia para componer la investigación. **Resultados:** El análisis de los artículos seleccionados mostró que los anticonceptivos orales están relacionados con la aparición de eventos trombóticos. Los anticonceptivos están compuestos por una combinación de hormonas que influyen directamente en la aparición de trombosis venosa profunda. **Conclusión:** Los anticonceptivos orales influyen en el desarrollo de la trombosis venosa profunda ya que pueden provocar cambios en el equilibrio homeostático. Para el uso de estos medicamentos es necesario ser responsable y supervisado por un especialista, y luego de una cuidadosa evaluación, se seleccionará el anticonceptivo más adecuado.

**Descritores:** Trombosis Venosa Profunda; Anticonceptivo hormonal oral; Anticonceptivos.

## Introduction

Oral contraceptives began to be used in Brazil in the 60s. During this period, health services were not accessible to the population, thus resulting in high fertility rates. The pills were inserted in this context, as there was a need for a way to combat the increase in the birth rate.<sup>1</sup>

According to a study carried out at the Johns Hopkins Bloomberg School of Public Health, it is estimated that on average 55% of married women in the world use some type of contraceptive method, and the oral contraceptive is the method that has the most supporters, due to its ease of access and ingestion.<sup>2</sup>

Thus, throughout life, women are exposed to large amounts of contraceptives. These drugs cause changes in the hemostatic balance, thus contributing to the emergence of deep vein thrombosis (DVT) in all users.<sup>3</sup>

DVT is characterized by the formation of thrombi within the dense veins, causing hemostasis in the coagulation system. The prolonged use of hormonal contraceptives composed of the main female sex hormones estrogen and progesterone are factors that can trigger this pathology.<sup>4</sup>

In 1961, the first record of DVT associated with the use of oral contraceptives appeared. A study carried out in 2020 at the Teaching Assistance Unit of Angiology, at the Hospital Universitário Pedro Ernesto and at the State University of Rio de Janeiro (SURJ) confirmed a two to six-fold increase in the risk of thrombosis. It is worth noting that this risk is associated with the amount of hormone that makes up the pill.<sup>5</sup>

As this is the most common and most accessible method among women, oral contraceptives end up being used inappropriately, without any instructions about side effects. This attitude entails greater risk to women's health, as most use the medication erroneously and without professional supervision.<sup>6</sup>

In this context, the question is: what influence does the oral contraceptive exert on the emergence of DVT? Therefore, the aim of this study is to describe the action of oral contraceptives in the female body, report the factors that trigger deep vein thrombosis and suggest prophylactic measures to prevent the onset of DVT associated with oral contraceptives.

## Method

To carry out this research, a literature review was carried out through research of previous studies published in scientific journals, in addition to information available on the website of the Ministry of Health and the World Health Organization.

The selection of articles was made in accordance with the proposed subject and data were collected from March to August 2021 in the following databases: Scientific Electronic Library Online (SciELO), US National Library of Medicine (NLM/Pubmed), Library Health Virtual (VHL), as well as government websites and reports from world conferences.

For the search, the following descriptors were used: Deep Venous Thrombosis; Oral Hormonal Contraceptive and Contraceptives. The Boolean term used associated with the words was AND.

The research was based on the following guiding question: What influence does oral contraceptive have on the emergence of deep vein

thrombosis? Thus, articles published between 2015 and 2021, in Portuguese (Brazil) and foreign language (English) translated into Portuguese were included, where the data were analyzed in detail in order to answer this question.

Preliminarily, the titles and abstracts were read to identify the articles that explained the subject. The objective, method, results and conclusions of each study were evaluated through analysis, where the year of publication and the journal of publication were taken into account. Subsequently, after a rigorous analysis, the studies that discussed the subject in full were identified and selected to compose the research.

## **Results and Discussion**

The present work sought to describe the action of contraceptives associating their use with the emergence of deep vein thrombosis. After the selection of articles related to the topic, 11 articles from the last 7 years were included to compose the discussion. Data were analyzed and interpreted in order to answer the guiding question that guides the research. It is noted that most articles indicate that the emergence of DVT is linked to changes that these drugs cause in the hemostatic balance, in addition to factors such as the continued use of oral contraceptives composed of estrogen, age, weight and in women with a predisposition to the development of hereditary thromboembolic phenomena.

In 1994, the International Conference on Population and Development (ICPD) was held in Cairo. The conference resulted in an action plan aimed at improving people's lives and supporting family planning as well as sexual and reproductive health. The concept of reproductive health was defined as a state of complete physical, mental and social well-being. Within this concept, it was implicit that the person can have a safe sex life and have the autonomy to reproduce and decide how many times they want to do it. This decision is guaranteed by the right to have access to contraceptive methods of their choice.<sup>7</sup>

According to data collected in the national survey on demography and health of children and women, women are starting sexual activities at an earlier age. These data showed that by the age of 15, almost half of the women interviewed had already started their sexual life. Due to this beginning, it is necessary to choose a contraceptive method as well as the beginning of family planning.<sup>8</sup>

### **The action of contraceptives**

The oral contraceptive is a revolutionary method discovered in 1961 with the main purpose of preventing a pregnancy. Over the years, these drugs have caused discussions, where science affronts society because of prejudices and taboos surrounding these drugs. These discussions drag on until today, without consensus. 50 years ago, Enovid, the first oral contraceptive, was approved. For some, a practical and affordable solution, but for others, a hormone pump with many side effects.<sup>9</sup>

According to data from the United Nations (UN), in Brazil, the contraceptive pill is the most adopted method by women due to the variety of combinations in different dosages of the hormones estrogen and progesterone.

These drugs are available in the Unified Health System (UHS) and in the pharmaceutical market.<sup>10</sup>

As the most used contraceptive method, these drugs are considered reliable and reversible. This confidence makes it more popular and easily accessible.<sup>11</sup>

The main objective of oral contraceptives is to inhibit ovulation through anovulatory reproductive cycles, thus resulting in the regular development of the proliferative endometrium without the production of the corpus luteum. Staying in this phase until the onset of menstruation.<sup>12</sup>

Contraceptives are made up of the synthetic hormones estrogen and progesterone that act in excess of ovulation-stimulating hormones. They help maintain hormone levels by inhibiting the secretion of FSH and LH through negative feedback resulting in preventing ovulation..<sup>13</sup>

### **Linkage of oral contraceptives with deep vein thrombosis**

Venous thrombosis is a condition caused by the obstruction of a blood vessel due to excess structures composed of fibrin and platelets. This obstruction can occur throughout the body, and in 90% of cases the lower limbs are the most affected. DVT is caused in the deep veins, and it can be triggered by a number of factors. In Brazil, in 2015, 113,817 hospitalizations for thrombosis were recorded, where the data evaluated showed that the highest incidence of cases remained in females between 20 and 40 years of age, where the use of contraceptives is more frequent.<sup>14</sup>

DVT risk factors are classified as hereditary or idiopathic and acquired or induced. Hereditary factors present risks as resistance to protein C, hyperhomocysteinemia, increased fibrinogen, among others. Examples of acquired factors are obesity, myeloproliferative diseases, trauma and estrogen therapy.<sup>15</sup>

Thus, the risk of DVT associated with the use of oral contraceptives is linked to changes in hemostasis. Physiologically, estrogen increases the concentration of clotting factors and reduces protein S and antithrombin, which are anticoagulant factors. The risk of DVT associated with continuous use of oral contraceptives increases with the dose of estrogen, age, weight and in women with a predisposition to develop hereditary thromboembolic phenomena.<sup>16</sup>

The signs and symptoms present in DVT are: pain, edema, erythema, cyanosis, dilation of the superficial venous system, temperature increase, muscle swelling and pain on palpation. Studies recommend anamnesis and physical examination of the patient associated with laboratory and imaging tests. The Wells score is the most used clinical prediction system. This model consists of analyzing the clinical probability of developing DVT through a table where factors such as active cancer, paralysis, swollen whole leg, among others, are evaluated. Each clinical characteristic has a specific score and, at the end, the sum is made and, according to the resulting values, the risk is classified into low, moderate and high probability. The exams that complement the diagnosis are the D-dimer (DD), Color Doppler Echo (EDC), Venography/Flebography, Computed Tomography (CT) and Magnetic Resonance (MRI) tests.<sup>15</sup>

Blood stasis, hypercoagulability, endothelial damage and increased thrombin formation are factors that increase the chance of clotting and decrease inhibitors, causing a pro-coagulant effect resulting in DVT. Protein C is an anticoagulant that depends on vitamin K for inhibit blood clotting. The absence of an anticoagulant results in hypercoagulability, increasing the risk of venous thromboembolism. In general, the chance of developing DVT is in the first year that a woman uses the contraceptive. It is recommended that whenever there is a change of contraceptive, an anamnesis is carried out in the patient, in order to investigate and identify possible factors that trigger thrombosis.<sup>13</sup>

A survey conducted at the University of Brasília interviewed 100 women aged 18 to 40 years and identified that of these, 84 used oral contraceptives and 13 reported cases of thrombosis. Prevalence data indicated that the majority of cases prevailed among women aged 18 to 25 years. In this same study, it was observed that many women use contraceptives inappropriately and often without professional guidance. This action reflects the risks offered by these drugs, if they were used for long years.<sup>17</sup>

In this context, the use of oral contraceptives can increase the risk of deep vein thrombosis. Initially, the risk of thrombosis was related to the effects of estrogen on hemostatic factors, however, the risk of deep vein thrombosis (DVT) varies between contraceptives composed of progesterone. Due to the popularity and wide adherence to oral contraceptives, the increased risk of DVT is of concern and must be treated with great importance.<sup>18</sup>

### **Prophylactic measures**

Several factors can increase the risk of thromboembolism, therefore, the choice of contraceptive must be made under the guidance of a health professional, as a family investigation is necessary to verify whether there is a family history of hereditary thrombosis. Therefore, the choice of method should be based on all data collected, which should consider the risk factors and benefits of the method.<sup>19</sup>

There is no consensus on the best contraceptive, however it is known that second-generation contraceptives (levonorgestrel and norethisterone) should be the first choice for most women, as they are safer than third- and fourth-generation ones.<sup>16</sup>

Therefore, it is concluded that these drugs increase the risk of blood clotting, which may be for hereditary or acquired reasons, thus causing DVT. It is recommended that each patient have individual medical monitoring in order to prevent future harm to women's health.<sup>20</sup>

### **Conclusion**

Contraceptives emerged with the aim of giving women freedom, giving them the possibility to choose the right moment of pregnancy. Given the above, it is clear that contraceptives are drugs of first choice for most women, due to their accessibility. In general, these drugs are used inappropriately by most users, as in Brazil these drugs are sold without a medical prescription. This is a worrying factor, because like most drugs, contraceptives have side effects, especially since they are a combination of hormones.

With the elaboration of this work, we concluded that the prolonged use of these drugs can increase the risk of deep vein thrombosis, therefore, the user should seek medical advice, where her history and individual characteristics will be evaluated, resulting in the choice of the most appropriate contraceptive that meet your needs.

## Acknowledgment

This research did not receive funding for its use..

## References

1. Dias T M, Bonan C, Nakano AR, Maksud I, Teixeira L A. Estará nas pílulas anticoncepcionais a solução? Debate na mídia entre 1960-1970. *Rev Estud Feministas*.2018; 26(3): 1-19
2. Spanhol KT, Panis C. Contraceptivos orais e eventos trombóticos. *Infarmacia-Ciências Farmacêuticas*.2013; 21(3/4): 7-13.
3. Gialeraki A. et al. Oral contraceptives and HRT risk of thrombosis. *Clinical and Applied Thrombosis/Hemostasis*.2018; 24(2): 217-225.
4. Morais LX, Pereira LS, Carvalho IFFR. Tromboembolismo venoso relacionado ao uso frequente de anticoncepcionais orais combinados. *RECHST*.2019;8 (1):91-125.
5. Oliveira ALML, Paschôa AF, Marques MA. Tromboembolismo venoso na mulher: novos desafios para uma velha doença. *J Vasc Bra*. 2020;19 (20) 190148.
6. Araujo MMF, Bandeira ICJ. Associação entre o uso contínuo de anticoncepcionais orais e o desenvolvimento de trombose venosa profunda. *Encontro de Extensão, Docência e Iniciação Científica*. 2019; 6(1) 1-4.
7. Nações Unidas. Relatório da Conferência Internacional sobre População e Desenvolvimento. Cairo; 1994.
8. Brasil. Saúde sexual e saúde reprodutiva. Ministério da Saúde: Cadernos de Atenção Básica; 2013.
9. Freitas FS, Giotto AC. Conhecimento sobre as consequências do uso de anticoncepcional hormonal. *Rev Inic Cient Ext*.2018; 1(2): 91-5.
10. Ferreira LF, D'Avila AMFC, Safatle GCB. O uso da pílula anticoncepcional e as alterações das principais vias metabólicas. *Femina*.2019; 47(7):426-432
11. Santos RL dos, Barbosa A de L de O, Santana AL, Farias JVC, Macêdo PR de, Farias ICC. The risks of prolonged use of hormonal contraceptives. *RSD*. 2020;9(11):e69791110394. Doi: <https://doi.org/10.33448/rsd-v9i11.10394>
12. Almeida APF, Assis MM. Efeitos colaterais e alterações fisiológicas relacionadas ao uso contínuo de anticoncepcionais. *Rev Eletrônica Atualiza Saúde*.2017;5 (5): 85-93.
13. Freitas EM, Ceron R, Nowacki L. Uso de anticoncepcionais orais e dispositivo intrauterino hormonal (Mirena) relacionado ao risco de trombose venosa profunda (TVP). *Revista Eletrônica Biociências, Biotecnologia e Saúde*. 2019; 12(24): 30-7.
14. Sousa ICA, Alvares ACM. A trombose venosa profunda como reação adversa do uso contínuo de anticoncepcionais orais. *REVISA*. 2018; 7(1): 54-65.
15. SBACV. Projeto Diretrizes. Trombose venosa profunda. Diagnostico e tratamento. Novembro; 2015.

16. Oliveira ALML, Paschôa AF, Marques MA. Tromboembolismo venoso na mulher: novos desafios para uma velha doença. J. Vasc. Bras. 2020; (19): e20190148. Doi: <https://doi.org/10.1590/1677-5449.190148>
17. Silva CS, Sá R, Toledo J. Métodos Contraceptivos e Prevalência de Mulheres Adultas e Jovens com risco de Trombose, no Campus Centro Universitário do Distrito Federal-UDF. REVISIA. 2019; 8(2):190-7.
18. Dragoman MV, et al. A systematic review and meta-analysis of venous thrombosis risk among users of combined oral contraception. Int J Gynaecol Obstet. 2018; 141(3): 287-94.
19. Couto PLSV, Alba BA, Gomes AMT, Ferreira LC, Neves MLP, Pereira SS, et al. Evidências dos efeitos adversos no uso de anticoncepcionais hormonais orais em mulheres: uma revisão integrativa. Enfermagem em foco (Brasília). 2020;11(4): 79-86
20. Araujo MMF, Bandeira ICJ. Associação entre o uso contínuo de anticoncepcionais orais e o desenvolvimento de trombose venosa profunda. Encontro de Extensão, Docência e Iniciação Científica. 2019 6(1) 1-4.

**Correspondent Author**

Ana Caroline Santos Gondim  
Universidade Paulista de Brasília  
SGAS 913 CJ B. ZIP: 70390-130. Asa Sul. Brasília,  
Federal District, Brazil.  
[carolgondim23@gmail.com](mailto:carolgondim23@gmail.com)