

Influence of hormonal contraceptives and the occurrence of stroke: integrative review

Influência de anticoncepcionais hormonais e ocorrência de acidente vascular cerebral: revisão integrativa
Influencia de anticonceptivos hormonales y acaecimiento de accidente vascular cerebral: revisión integradora

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How to cite this article:

Lima ACS, Martins LCG, Lopes MVO, Araújo TL, Lima FET, Aquino PS, et al. Influence of hormonal contraceptives and the occurrence of stroke: integrative review. Rev Bras Enferm [Internet]. 2017;70(3):647-55. DOI: <http://dx.doi.org/10.1590/0034-7167-2016-0056>

Submission: 03-12-2016

Approval: 11-02-2016

ABSTRACT

Objective: To identify scientific evidence regarding the influence of hormonal contraceptive use and the occurrence of stroke. **Method:** Integrative review of the literature, through database search using the descriptors “*contraceptive agents*”, “*contraceptive devices*”, “*contraceptives, Oral*” and “*Stroke*”. Original studies in Portuguese, Spanish and English, published in full and available online were included. Studies that did not answer our guiding questions and duplicated studies were excluded. **Results:** Women using combined oral contraceptives have higher risk of stroke, even with a lower hormonal dosage and different types of progestogen, regardless of the duration of use. The use of contraceptives associated with smoking, hypertension, migraine, hypercholesterolemia, obesity and sedentary lifestyle increases the chance of stroke. Contraceptive patch and vaginal ring are associated to increased risk. **Conclusion:** Use of combined hormonal contraceptives, except for the injectable and the transdermal ones, increases the chance of occurrence of the event. Progestogen-only contraceptives were considered safe. **Descriptors:** Stroke; Contraceptives; Contraceptive Devices; Oral Contraceptives; Nursing.

RESUMO

Objetivo: Identificar evidências científicas acerca da influência do uso de anticoncepcionais hormonais na ocorrência do acidente vascular cerebral (AVC). **Método:** Revisão integrativa da literatura, com pesquisa em bases de dados, utilizando os descritores “*contraceptive agents*”, “*contraceptive devices*”, “*contraceptives, Oral*” e “*stroke*”. Foram incluídos artigos originais nos idiomas português, espanhol e inglês, publicados na íntegra e disponíveis eletronicamente. Foram excluídos artigos que não respondiam às questões norteadoras e repetidos. **Resultados:** Usuárias de anticoncepcional oral combinado apresentam risco maior de AVC, mesmo com dosagem hormonal menor e diferentes tipos de progestágeno, independente do tempo de uso. A presença associada de tabagismo, hipertensão arterial, enxaqueca, hipercolesterolemia, obesidade e sedentarismo aumenta a chance desse desfecho. Adesivo anticoncepcional e anel vaginal são relacionados ao aumento desse risco. **Conclusão:** A exposição aos anticoncepcionais hormonais combinados aumenta a chance de ocorrência do evento, exceto o injetável e o transdérmico. Os exclusivos de progestágeno foram considerados seguros. **Descritores:** Acidente Vascular Cerebral; Anticoncepcionais; Dispositivos Anticoncepcionais; Anticoncepcionais Orais; Enfermagem.

RESUMEN

Objetivo: Estudiar las evidencias científicas acerca de la influencia del uso de anticonceptivos hormonales en el acaecimiento de accidentes cerebrales vasculares (ACV). **Método:** Revisión integradora de la literatura, realizada mediante investigación científica en bases de datos, utilizando los descriptores “*anticonceptivos*”, “*dispositivos anticonceptivos*”, “*anticonceptivos orales*” y “*derrame cerebral*”. Se incluyeron artículos originales en los idiomas portugués, español e inglés, publicados en su totalidad y disponibles electrónicamente. Se excluyeron los artículos repetidos y aquéllos que no respondían a las cuestiones orientadoras. **Resultados:** Las usuarias de anticoncepcional oral combinado presentan un riesgo mayor de ACV, inclusive con dosis hormonal menor y diferentes tipos de progestágeno, independientemente del tiempo de utilización. La presencia del tabaquismo, hipertensión arterial, jaqueca, hipercolesterolemia, obesidad y sedentarismo aumenta la probabilidad de ese desenlace. El adhesivo anticonceptivo y el anillo vaginal están relacionados con el aumento de ese riesgo.

Conclusión: La utilización de anticonceptivos hormonales combinados aumenta la probabilidad del acaecimiento del evento, excepto con el inyectable y el transdérmico. Los exclusivos de progestágeno se consideran seguros.

Descriptores: Accidente Cerebral Vascular; Anticonceptivos; Dispositivos Anticonceptivos; Anticonceptivos Orales; Enfermería.

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INTRODUCTION

Estrogen, specifically ethinyl estradiol, the hormone contained in the combined hormonal contraceptives, induces significant changes in the coagulation system, causing an increase in thrombin activity and in clotting factors, as well as a reduction of natural coagulation inhibitors⁽¹⁾. In addition, this hormone acts directly on the vascular wall, altering factors that stimulate endothelial dysfunction⁽²⁾. These transformations may lead to the development of thromboembolic events, such as stroke⁽³⁾.

This condition causes neurological deficits that compromise patients' quality of life⁽⁴⁾. The chance of having a stroke is higher when the woman has other clinical conditions, such as Systemic Lupus Erythematosus (SLE), smoking, hypertension, medical history of previous stroke and migraine⁽⁵⁾. Therefore, the presence of these risk factors must be considered in the choice and/or indication of contraceptive method.

Over the last few decades, different hormonal contraceptive methods (HCMs) have been developed, including combined and progestogen-only oral contraceptives, combined and progestogen-only injectables, subdermal implants, transdermal patch, and vaginal tablets and rings. Thus, after the introduction of the first HCMs, thromboembolic events were recorded among the users.

With the progress of the pharmaceutical industry, new formulas were developed, with lower and progestogen-only dosages, in addition to other contraceptive methods containing natural estrogen⁽⁵⁻⁶⁾. However, the occurrence of strokes is still being reported⁽⁷⁾.

Considering that the new contraceptive formulations still lead to a high risk of stroke, it is relevant to investigate the impact of their use and stroke. Considering the above, this study assesses the need to know the scientific evidence regarding the association between the use of hormonal contraceptives and occurrence of stroke, seeking to identify if the hormone

dosage and duration of use of hormonal contraceptives may influence the severity of this event.

Previous literature review assessing the risk of stroke in users of combined oral contraceptives has already been conducted⁽⁸⁻⁹⁾. However, other HCMs have not been addressed in these reviews.

Aiming to guide this analysis, a question was raised: what is the influence of the use of hormonal contraceptives on the occurrence of stroke?

While answering this question, a reflection regarding the safe use of these contraceptives will be promoted, considering that there are other non-hormonal methods that can be indicated by the multipurpose team acting on birth control planning.

The objective of this study was to identify scientific evidence regarding the influence of the use of hormonal contraceptives in the occurrence of stroke.

METHOD

An integrative review that gathered results of completed studies was carried out, based on the following stages: 1) formulation of the problem; 2) data collection and literature search; 3) data evaluation; 4) data analysis; and 5) presentation and interpretation of results⁽¹⁰⁾.

The problem identified (stage 1) corresponded to the need to gather the available knowledge regarding the association between the use of hormonal contraceptives and stroke.

Data collection and literature search (stage 2) was conducted in May 2015, by two researchers simultaneously. Searches were made in the following databases: Scopus, Cumulative Index to Nursing and Allied Health Literature (Cinahl), Medline, Latin American and Caribbean Center on Health Sciences Information (Lilacs), Spanish Bibliographic Index on Health Sciences (Ibecs), PubMed and Cochrane Library (Table 1). These databases were accessed through the Virtual Health Library (BVS) and CAPES Journal Portal.

Table 1 - Results of the search for associated descriptors in the databases

Databases/descriptors	Articles found	Title-based selection	Abstract-based selection	Full text based selection	Excluded due to repetition	Artigos selected
Cinahl					2	11
<i>Stroke and contraceptive agents</i>	21		2	2		
<i>Stroke and contraceptives, Oral</i>	91		15	13		
<i>Stroke and contraceptive devices</i>	4		0	0		
Medline					3	13
<i>Stroke and contraceptive agents</i>	61	13	8	5		
<i>Stroke and contraceptives, Oral</i>	315	39	17	11		
<i>Stroke and contraceptive devices</i>	7	0	0	0		

To be continued

Table 1 (concluded)

Databases/descriptors	Articles found	Title-based selection	Abstract-based selection	Full text based selection	Excluded due to repetition	Artigos selected
Pubmed					8	11
<i>Stroke and contraceptive agents</i>	114	21	10	9		
<i>Stroke and contraceptives, Oral</i>	483	29	12	10		
<i>Stroke and contraceptive devices</i>	3	0	0	0		
Lilacs					-	0
<i>Stroke and contraceptive agents</i>	0	0	0	0		
<i>Stroke and contraceptives, Oral</i>	0	0	0	0		
<i>Stroke + contraceptive devices</i>	0	0	0	0		
lbecs					-	0
<i>Stroke and contraceptive agents</i>	1	0	0	0		
<i>Stroke and contraceptives, Oral</i>	3	0	0	0		
<i>Stroke and contraceptive devices</i>	1	0	0	0		
Scopus					24	16
<i>Stroke and contraceptive agentes</i>	700	43	25	20		
<i>Stroke and contraceptives, Oral</i>	701	41	21	20		
<i>Stroke and contraceptive devices</i>	64	1	1	1		
Cochrane					0	0
<i>Stroke and contraceptive agents</i>	0	0	0	0		
<i>Stroke and contraceptives, Oral</i>	7	3	2	0		
<i>Stroke and contraceptive devices</i>	0	0	0	0		
Total						52
Duplicated studies excluded						34
Total (sample)						18

The DeCS/MeSH descriptors “*contraceptive agents*”, “*contraceptive devices*”, “*contraceptives, Oral*” were applied separately and associated with “*stroke*” integrated by the connector *and*, in all indexes, according to the associations *Stroke and contraceptive agents*, *Stroke and contraceptives, Oral*, *Stroke and contraceptive devices*.

The following inclusion criteria were considered for selection of the studies: original studies in Portuguese, Spanish or English, published in full and available online. There was no time criterion for the selection of the studies, which allowed an analysis of the evolution of the research on the subject. Studies that did not answer the guiding question and duplicated studies were excluded, meaning that studies that appeared in more than one database were counted only once. The final sample consisted of 18 studies.

In the data collection stage, the studies that met the inclusion criteria were read in full. Data were extracted using an instrument constructed by the authors, containing information related to the study, such as the title, journal, year of publication, setting, objective, method and main results that addressed the influence of hormonal contraceptives on the occurrence of stroke. The results were synthesized and the key reports of each article were pointed out. The studies received a numerical sequence code to facilitate the identification and presentation of the results (Study 1 (S1), S2, S3 ...), and were classified according to evidence level.

Seven levels of evidence were considered: level 1, evidence from a systematic review or meta-analysis of randomized controlled trials or clinical guidelines based on systematic reviews of

randomized controlled trials; Level 2, evidence from randomized controlled trials; Level 3, evidence from controlled trials without randomization; Level 4, evidence from case-control and cohort studies; Level 5, evidence from systematic reviews of descriptive and qualitative studies; Level 6, evidence from single descriptive or qualitative studies; Level 7, evidence from the opinion of authorities and/or reports of expert committees⁽¹¹⁾.

Data was analyzed through reading the studies in full, summarizing them and filling in the instrument mentioned above, enabling the identification of different aspects that influenced the occurrence of stroke. These aspects were analyzed in detail and grouped in order to simplify the integration of the findings. Six categories emerged from this analysis: types of hormonal contraceptives and stroke; use of Combined Oral Contraceptives (COCs) and types of stroke; use of COCs and risk of stroke according to ethinyl estradiol dosage and progestogen type; duration of use of COC; other risk factors associated with stroke; use of COC and stroke severity.

In the presentation and interpretation stage, the results were presented in a tabular form, showing the characteristics of the studies, and then arranged according to the categories mentioned above, pointing out the convergences and divergences between the findings, as well as the limitations.

RESULTS

Chart 1 summarizes the characteristics of the studies included in the review. The publication years of the studies

ranged from 1986 to 2014, one published in 1986, ten in the 1990s, five between 2000 and 2010 and two in the last five years. As for the methodological design, 13 were case-control and five were cohort studies, classifying the entire sample with level of evidence 4.

Considering the study setting, eight studies were conducted in European countries, and two of them were multicenter;

four studies were conducted in North America, specifically in the United States of America; two were conducted in Asia, both in China; one was conducted in Oceania; and three were multicenter and occurred in countries in Africa, Asia, Latin America and Europe. Studies conducted in Brazil were not found in this review, and those that reported research in Latin American countries were published in the 1990s.

Chart 1 - Characteristics of selected studies in chronological order (Study 1-S1, Study 2-S2...)

Authors/Year	Local	Type of study/Method
E1. Chang KK, 1986 ⁽¹²⁾ .	China	Case-control. Case: 323 women hospitalized with stroke Hospital control: 250 women without stroke, hospitalized in the same hospital as the cases Neighborhood control: 646 women without stroke
E2. Hannaford, Croft, Kay, 1994 ⁽¹³⁾ .	United Kingdom	Case-control Case: 253 women with stroke Control: 759 women without stroke
E3. Who, 1996 ⁽¹⁴⁾ .	Africa, Asia, Europe and Latin America	Case-control Case: 697 with stroke Control: 1,962 without stroke
E4. Who, 1996 ⁽¹⁵⁾ .	Africa, Asia, Europe and Latin America	Case-control Case: 1068 with stroke Control: 2910 without stroke
E5. Petitti et al., 1996 ⁽¹⁶⁾ .	California	Case-control Case: 295 women with stroke Control: 3 times the number of cases
E6. Heinemann, et al., 1997 ⁽¹⁷⁾ .	United Kingdom, Germany, France, Switzerland and Austria	Case-control Case: 220 women with stroke Control: 775 women without stroke
E7. Heinemann et al., 1998 ⁽¹⁸⁾ .	United Kingdom, Germany, France, Switzerland and Austria	Case-control Case: 220 women with ischemic stroke Control: 775 women
E8. Mant; Painter; Vessey, 1998 ⁽¹⁹⁾ .	United Kingdom	Cohort 17,032 married women between 25 and 39 years old Group that never used COCs: 5,881 women Group that used COCs for eight years or more: 3,520 women Remaining group: 5,891 women
E9. Lidegaard, O, 1998 ⁽²⁰⁾ .	Denmark	Case-control Case: 219 with stroke Control: 1041
E10. WHO, 1998 ⁽²¹⁾ .	Africa, Asia, Europe and Latin America	Case-control Case: 3,697 with cerebrovascular disease and 2,196 with stroke Control: 9,997 without stroke
E11. Schwartz et al., 1998 ⁽²²⁾ .	USA	Case-control Case: 175 women with ischemic stroke, 198 women with hemorrhagic stroke Control: 1,191 women without stroke
E12. Kemmeren et al., 2002 ⁽²³⁾ .	Netherlands	Case-control Case: 203 women with stroke Control: 925 women without stroke
E13. Siritho et al., 2003 ⁽²⁴⁾ .	Melbourne, Austrália	Case-control Case: 234 women with stroke Control: 234 women without stroke
E14. Li et al., 2006 ⁽²⁵⁾ .	China	Cohort Case: 44 408 users of hormonal contraceptive (HA) Control: 75,230 intrauterine device users (IUDs)
E15. Cole et al., 2007 ⁽²⁶⁾ .	USA	Cohort Transdermal users: 98,790 women COC users: 256,981 women

To be continued

Chart 1 (concluded)

Authors/Year	Local	Type of study/Method
E16. Yang et al., 2009 ⁽²⁷⁾ .	Sweden	Cohort 45,729 women between 30 and 49 years old
E17. Lidegaard et al., 2012 ⁽⁷⁾ .	Denmark	Cohort 1,626,158 women: 3,311 had a stroke, with 1,051 CM users and 2,260 non-users between 15 and 49 years old
E18. Ryan et al., 2014 ⁽²⁸⁾ .	Baltimore, Maryland, USA	Case-control 572 women between 15 and 49 years old Case: 224 with stroke Control: 348 without stroke

Note: COC: combined oral contraceptive; IUD: intrauterine device; CM: contraceptive method.

Category 1 – Types of hormonal contraceptives and stroke

A total of 16 studies analyzed investigated the association between COCs and stroke. Other hormonal contraceptives were addressed in three studies (S10, S15, S17). The patch and the vaginal ring were investigated together in one study (S17). The use of progestogen-only methods of progestin, both oral and injectable, was addressed in two studies (S10, S17), and in one of those (S10) the combined injectable contraceptive was addressed.

The high risk of stroke among COC users was demonstrated in 14 studies. On the other hand, three studies indicated no association between those (S5, S11, S16). Regarding the COCs, some variables associated with risk arose, such as type of stroke, hormone dosage, type of progestogen, duration of use, other associated risk factors, and severity of the stroke. Therefore, specific categories to present these results are presented below.

The only study that investigated transdermal system (TS) users (S15) did not report cases of stroke between 2002 and 2004⁽²⁶⁾. In Denmark, a cohort study (S17) followed 1,626,158 women between 1995 and 2009 and reported cases of stroke, showing a risk of 3.15 among users of contraceptive patch and 2.49 among those who used the vaginal ring⁽⁷⁾.

Studies assessing the risk of stroke among users of progestogen-only methods, whether oral or injectable (S10, S17), and the combined injectable (S11) showed that all are safe and do not increase the chance of presenting this event.

Category 2 - Use of combined oral contraceptives and types of stroke

There was no comparison between the other methods and the type of stroke. A total of 15 studies addressed only ischemic stroke and one addressed only hemorrhagic stroke. The comparison between COC use and both types of stroke was addressed in four studies.

Out of the four, one cohort study showed a higher risk for hemorrhagic stroke for users of COCs (S14), and three showed that the use of the method did not influence the occurrence of any of the two events (S5, S11, S16).

Category 3 - Use of combined oral contraceptives and risk of stroke according to ethinyl estradiol dosage and progestogen type

Low-dose COCs contain 30 micrograms (0.03 μg) or less of ethinyl estradiol and medium-dose COCs contain 50 microgram (0.05 μg) of ethinyl estradiol. First generation pills have

high doses of estrogen (75 a 150 μg), second generation pills have 50 μg and third generation pills have 30 μg , associated with the use of progestogen⁽⁶⁾.

Regarding the analysis of the composition and dosage of ethinyl estradiol in the COCs, 11 studies (S1, S3, S5, S6, S8, S3, S11, S13, S14, S15, S16) did not assess the risk of stroke by comparing the different doses of ethinyl lestradiol in the COCs compositions, and five (S2, S4, S9, S12, S17) addressed this relation. Out of these, three confirmed that the use of higher dosage formulations puts the individual at higher risk (S2, S4, S17). In contrast, two publications indicated that the risk is similar, independent of the estrogen dosage (S2, S12) (S2, S12).

Regarding the type of progestogen in the COC formulas, six studies addressed this relation (S2, S3, S7, S9, S12, S17); five reported that the individual may be at greater risk according to the progestogen component; three studies reported that third generation COCs (gestodene/desogestrel) put individuals at greater risk of stroke than second generation (levonorgestrel) (S2, S7, S17); and one study stated the opposite (S9).

Category 4 - Duration of use

The association between duration of use of COC and risk of stroke was identified in three studies of the final sample. In S17, the analysis of duration of use was divided in less than 1 year, between 1 and 4 years and longer than 4 years of use, according to hormonal type, and it showed no greater risk according to duration of use⁽⁷⁾.

Similarly, S11 grouped two case-control studies to identify the relation between low-dose COCs and the occurrence of ischemic and hemorrhagic stroke, pointing out that the occurrence of these was not related to the duration of use of the hormones, whether current or past use⁽²²⁾. S14 showed that women who use COCs currently are at higher risk of having stroke compared to those who used COC and stopped in the last five years or before, with RR: 3.60; RR: 3.0 and RR: 1.18, respectively⁽²⁵⁾.

Category 5 - Risk factors associated with stroke

A total of 11 studies were identified in this category, representing 61.1% of the final sample. Those addressed, in addition to the use of COC, some risk factors associated with the occurrence of stroke. The main factors assessed were smoking and history of arterial hypertension, but social class, alcohol use, migraine, hypercholesterolemia, obesity and sedentary lifestyle were also addressed.

In all the studies included in the sample, these factors represented a significant increase in the chance of stroke, specifically regarding women using COCs and presenting these factors. S7 identified that those who smoke more than 10 cigarettes a day and use a COC have 8.57 more chances of having a stroke, while those who do not smoke have only 3.1⁽¹⁸⁾. The same relation was assessed by the study S8, that identified that women currently using a COC and smoking more than 15 cigarettes a day have a higher risk of having a stroke, compared to those who never used a COC, with RR: 4.9 and RR: 4.2, respectively⁽¹⁹⁾.

In the study S12, besides use of cigarettes, history of hypertension, hypercholesterolemia and diabetes were also addressed. This study identified that all these factors lead to a higher chance of having a stroke in women currently using a COC, compared to those who do not use it⁽²³⁾.

Category 6 - Use of combined oral contraceptives and stroke severity

The only study that presented an association between COC and stroke severity (S10) aimed to quantify the clinical impacts of venous and arterial thrombotic diseases among young non-pregnant women and to assess the influence of COCs on these measures. A 2.4 risk of stroke (CI: 1.4-4.2) was identified in users of second generation COCs, compared to those who do not use a COC. Regarding severity, comparing second generation COC users to third generation users, the study identified an increase of 30% in the morbidity rate, 260% in the mortality rate and 220% in the disability rate⁽²⁰⁾.

DISCUSSION

The scarcity of studies addressing other hormonal methods may be explained by their recent introduction in the market when compared to COCs, in addition to the lack of specific health descriptors for them. The World Health Organization reinforces that the other methods are relatively new and that information on the safety of these methods for women with specific clinical conditions is scarce⁽⁵⁾, which was confirmed in this review.

It was possible to perceive that COCs, vaginal ring and contraceptive patch are related to the risk of stroke. Epidemiological studies show an association of these with other thromboembolic events⁽²⁹⁻³⁰⁾. The use of combined injectables showed no increased risk; however, the only study that addressed this method was conducted more than a decade ago. It is worth mentioning that use of injectable contraceptives has increased in recent years, becoming the hormonal method most used by women in some countries⁽³¹⁻³²⁾. Likewise, the use of vaginal ring and contraceptive patch has increased as they became more easily available and users became more aware of them⁽³³⁾.

In the study that addressed the transdermal system, the follow-up period was of only two years, which might explain the lack of identification of stroke⁽²⁶⁾. A recent study comparing users of the transdermal system to users of combined oral contraceptives confirms that the average daily exposure to ethinyl estradiol and the daily concentration-time curve is similar⁽³⁴⁾. Consequently, the exposure to the risk of complications related to this component is equal.

Considering the above, it is possible to perceive the necessity of the development of research investigating the association between the use of these contraceptive methods and stroke.

Regarding the use of COCs and types of stroke, two cohort studies showed divergent results, even with a high sample^(25,27). In the study conducted in China, 44,408 COC users were followed between 1997-2000, with a relative risk of hemorrhagic stroke of 3.6; regarding ischemic stroke, there was no difference. Selection of participants was strict, since the assessed cities had high prevalence of this method and data was collected face to face⁽²⁵⁾. Regarding the study developed in Sweden, 45,729 women were followed between 1991-2004, showing that COC users were not exposed to the risk of stroke, considering a Relative Risk <1. Follow-up occurred through telephone calls through national health registries⁽²⁷⁾. Even though the investigation was conducted during a smaller period, the first study showed a higher risk when compared to the second.

Estrogen, a component of COCs, is responsible for thrombogenic changes and alteration of coagulation factors, which favors the formation of thrombi and, consequently, the possibility of triggering a stroke⁽²⁾. In addition to this, this method causes endothelial alterations, vasospasm and atypical vascular proliferation, which may lead to appearance of atherosclerosis and arterial hypertension. It can also cause vascular lesions, leading to ischemic and hemorrhagic strokes⁽³⁾.

During the last decades, COCs with lower estrogen dosage, as well as in association with progestogens, have been developed, in an attempt to reduce the incidence of thromboembolic events⁽⁵⁻⁶⁾. In the studies included in this review, it was observed that the most recent associations continue to record the onset of stroke regardless of the dosage, and that third generation pills seem to present a higher risk when compared to second generation.

In a systematic review intending to assess the risk of venous thromboembolism, stroke or myocardial infarction(MI) associated with the use of oral contraceptives, as well as to describe how these risks vary according to the dosage or formulation, seven studies were found. The study found that the highest dose of ethinyl estradiol increases in 2.7 times the chance of having a stroke. However, data were insufficient to estimate the risk of stroke associated to progestogen⁽⁹⁾.

Regarding duration of use of COCs, the results point to current use of COC as more related to the risk of stroke, regardless of how long it was used. It was also noted that women who have never used COCs are less likely to have a stroke compared to those who have used COCs. The Brazilian Ministry of Health and the World Health Organization conclude in documents used in primary health care that the use of COCs has as stroke as a complication, corroborating these results⁽⁵⁻⁶⁾.

Regarding the risk factors associated with occurrence of stroke, several clinical conditions related to an increase in the chance of a woman having a stroke were identified in the present study. These clinical conditions, when associated with the use of COC, increase the vulnerability. Probably, women who had any of these diagnoses pre-stroke and who used COC were not informed about the risks of using it and the possible complications during birth control planning visits.

The World Health Organization directs the use of COCs and points out that the presence of headache, diabetes, arterial hypertension, family history of thrombotic diseases contraindicate the use of COCs, since this association increases the chance of stroke among users of these methods⁽⁵⁾.

The severity of the stroke associated with the use of COC was only reported in one study, in which the measurement of this severity was not through scales, but through clinical outcome (morbidity, mortality, and disability). There are specific scales for stroke assessment that consider the degree of neurological impairment and are used to verify new treatments, to monitor clinical evolution and to make therapeutic decisions. These scales have already been tested in Brazil, presenting adequate reliability. Therefore it is possible to use them to evaluate patients who had a stroke and used a COC, which would bring more specific results related to the severity of stroke associated with use of COCs⁽³⁵⁾.

Contributions to the area of nursing, health or public policy

It is possible to ensure that the results presented in this review will bring a comprehensive knowledge about a complication (stroke) arising from the use of hormonal methods, which expose young women to a neurological impairment that may lead to limitations on her daily living activities⁽³⁶⁾. Therefore, the present review provides information that may contribute to professional clinical practice, by orienting the care of women using hormonal methods, emphasizing the need for regular follow-up and constant search for clinical conditions that may increase the risk of stroke, such as migraine, blood pressure, dyslipidemia and smoking⁽⁵⁾.

The nurse, a professional who works in primary health care and is part of the multipurpose team, plays a fundamental role in birth control planning by conducting nursing consultations on contraception. This involves health education regarding contraceptive methods, detailed guidance about correct use, complications, indications and contraindications, as well as prescription of the method and monitoring of clinical conditions that expose women to health risks.

Therefore, the contribution of the study to healthcare science in the area of women's health is prominent. It highlights

the need to instruct professionals to safely prescribe contraceptives and to perform proper follow-up and guidance about risk factors, adverse reactions and contraindications⁽³⁷⁾.

Study limitations

As limitation of this study the non-inclusion of literature review studies stands out, since one of the inclusion criterion was original studies. This way, the results from other studies that could be available in other less usual databases were not addressed. Although the concern to explore different databases is evident, the choice of these may have directed the results obtained.

CONCLUSION

The studies included showed controversial results regarding the risk of COC use and stroke over the last few decades, although most show that this association exists, even in more recent studies. Although other combined hormonal methods were not sufficiently investigated, the contraceptive patch and vaginal ring showed increased the risk, whereas the transdermal patch and combined injectables were not associated with the incidence of this condition. Regarding progestogen-only hormonal methods, studies have shown that they are safe and do not increase the chance of presenting this outcome.

Regarding the dosage of ethinyl estradiol in COCs, studies have shown that the risk is evident in any hormonal dosage, but higher dosages lead to greater risk of stroke. Association with progestogens such as gestodene and desogestrel is more related to the triggering of this clinical condition. The findings regarding the duration of use of this method leads to the assertion that the incidence of comorbidity is not related the number of years of use.

The need for new investigations aiming to identify the influence of the use of other contraceptive methods in the outcome of stroke, addressing the vaginal ring, combined injectables, transdermal patch and adhesive, is prominent. Also, given the scarcity of studies assessing the severity of stroke associated with use of COCs, it is recommended that further research is developed, in order to investigate the neurological impairment of COC users who had stroke.

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