



# The prolonged effect of using hormonal contraception in female patients with ischemic stroke in developing countries

Virna Puspaningtyas <sup>1</sup>, Baksono Winardi <sup>2\*</sup>, Sulistyowati <sup>2</sup>

<sup>1</sup> Department of Midwifery, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo Regional Public Hospital, Surabaya 60131, INDONESIA

<sup>2</sup> Department of Obgyn, Faculty of Medicine, Universitas Airlangga - Dr. Soetomo Regional Public Hospital, Surabaya 60131, INDONESIA

\*Corresponding author: [Bakso\\_dr@yahoo.com](mailto:Bakso_dr@yahoo.com)

## Abstract

**Background:** Hormonal contraception is a common method used by the FP receiver in Indonesia. Usually, hormonal contraception contains progestins and/or in combination with estrogens. Estrogens known has a potential of complication such as the development of thromboembolism thereby increasing the risk of developing ischemic stroke. While in other studies, the impact of progesterone contraception on cardiovascular disease cannot yet be explained.

**Objective:** This study aims to determine the characteristics of hormonal contraceptive users in ischemic stroke patients.

**Method:** This study used a descriptive observational study with a successive sampling of all stroke ischemic patients with a history of hormonal contraceptive users. Research variables include age, occupation, medical records, type and duration of hormonal contraceptive use, also the time that a stroke has struck after stopping contraception. Univariate or descriptive analysis is applied to the frequency distribution of this variable

**Results:** The highest age group was obtained from the 'Middle Age Begins' Patients (46-55 years) (40%) as many as 42% of respondents worked as housewives. About 40% of respondents have suffered from hypertension and also 50% have a history of hereditary hypertension. 54% of respondents used hormonal contraception for more than 5 years with the most frequent type of hormonal contraception being injection only progestin (42%) 68. stroke episodes that appear at the age of fewer than 12 years after the termination of hormonal contraception.

**Conclusion:** the characteristics of hormonal contraceptive users in ischemic stroke patients as follows: the majority of the age group is 'Middle Age Begins' (46-55 years) with most of them working as housewives, with a history of hypertension, most sufferers of hereditary disease, the highest proportion used hormonal contraception more than 5 years with most types of use injected with progesterone only, and the average respondent stopped using hormonal contraception at a low of 12 years before the occurrence of ischemic stroke.

**Keywords:** the combination of hormonal contraception, progestin contraception, ischemic stroke, thromboembolism

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## INTRODUCTION

Today, some parts of the world are experiencing a population explosion. One solution to overcome this population problem is to use contraception, both for women and men (Lestari, et al. 2019). Hormonal contraception is a type of family planning method used by many women in developing countries (Roach, et al. 2015). However, hormonal contraception also has a risk of causing other diseases. Dewata et al found that hormonal contraception significantly increased the risk of meningioma (Dewata, et al. 2017). Also, a meta-

analysis report in 2000 showed that hormonal contraception correlates with ischemic stroke (Faubion, Casey, & Shuster, 2012).

Hormonal contraception usually contains estrogen and/or progesterone. Based on the cohort and several RCTs there is a risk of arterial thromboembolism about 1,6 times compared to non-hormonal users( Roach, et al. 2015; Ea, et al, 2015). Especially ethinylestradiol,

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**Table 1. Age**

Category	Age (year)	Number (n=50)	Percentage (100%)
Young Adult Begins	26 - 35	2	4%
Youth Adult Ends	36 - 45	9	18%
Middle Age Begins	46 - 55	20	40%
Middle Age Ends	56 - 65	16	32%
Old Age Begins	66 - more	3	6%

**Table 2. Occupations**

No.	Occupations	Number (n=50)	Percentage (100%)
1.	Housewife	21	42%
2.	Civil Servant	4	8%
3.	Private Employee	7	14%
4.	Others	18	36%

**Table 3. Medical Records**

No.	Medical Records	Number (n=104)	Percentage (100%)
1.	Hypertension	42	40%
2.	Heart disease	15	15%
3.	Diabetes mellitus	16	15%
4.	Hypercholesterolemia	31	30%

General estrogen ConteNT in combined oral / injection contraception to induce significant coagulation systems, thrombin-enhancing activity, and coagulation factors as well. On the other hand, this hormone can directly act into the vascular wall, changing the elemental factor inducing the function of endothelial DY. This transformation has the potential to induce thromboembolism even as a stroke (do Carmo Souza, Borges, & Mourão, 2018). As is known, stroke is the leading cause of death and disability in the world 6.

Data obtained from basic health research Faubion, Casey, & Shuster (2012) shows the prevalence rate of stroke in East Java as much as 9.1% based on the diagnosis of health providers, and about 16% based on symptoms and signs. The prevalence of stroke in the city of Surabaya tends to increase from 0.7% in 2007 to 16.2% in 2013 (YI, & Primadi, 2020).

This study aims to identify the characteristics of female ischemic stroke patients with history as users of hormonal contraception at the general hospital Dr. Soetomo Indonesia from March to May 2019.

**METHOD**

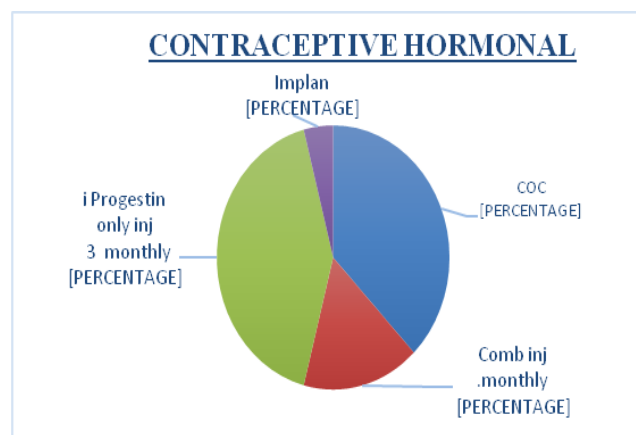
This research uses the descriptive observational method. Research subjects were patients aged 25-70 years who were diagnosed with ischemic stroke at the neurological clinic Dr. Soetomo Public Hospital, Indonesia. Also, there is a sampling of 50 patients who suffer from ischemic stroke with a history of hormonal contraceptive use several years before the disease comes. The variables used in this study were: age, occupation, how many years used HC, and how many years after stopping HC they suffered from ischemic stroke.

**Table 4. Family Medical Records**

No.	Family Medical Records	Number (n=48)	Percentage (100%)
1.	Hypertension	24	50%
2.	Heart disease	7	15%
3.	Diabetes mellitus	11	23%
4.	Stroke	6	12%

**Table 5. Years after stopping the use of HC for stroke episodes**

Category	Frequency (n=50)	Percentage (100%)
<12 yrs	34	68%
>12 yrs	16	32%



**Fig. 1. Contraceptive Hormonal Records**

**Table 1** shows that the cases often happen to 'Middle Age Begins' group with 40%, followed by 'Middle Age Ends' group with 32% and Young Adults Begins Group being the lowest one (4%).

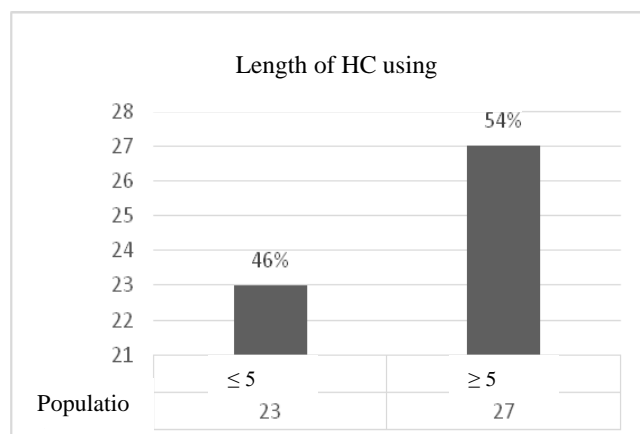
**Table 2** indicates that most patients with no formal occupations were housewives with a percentage of 42%, while the lowest percentage was a civil servant at 8%.

**Table 3** shows that hypertension is the most common disease diagnosed before the stroke occurred (40%), followed by Hypercholesterolemia (30%). While heart disease and Diabetes mellitus being the lowest one with 15% respectively.

**Table 4** shows that hypertension was the highest percentage of family medical records that occurred (58%), followed by diabetes mellitus (23%). While heart disease and stroke were the lowest with 15% and 12% respectively.

From **Table 5** we know that the year after stopping HC for the first episode of an ischemic stroke was 11, 08 ± 8,169 years.

**Figure 1** shows that the majority of previous or current respondents were using progestin-only injection (42%).



**Fig. 2.** The length of hormonal contraception using

**Figure 2** explains that 54% of respondents had been using hormonal contraception for more than 5 years, while others were less than 5 years.

## DISCUSSION

According to the age distribution of stroke patients, this research is in line with basic national health research which the most stroke cases often occur in Indonesia is ischemic, found on 45-75 years age group, even stroke disease also occurs in the reproductive period before 40 (Røttingen, et al. 2013). Theoretically with increasing age, there will be a gradual aging process, where almost all organs including the brain and blood will degenerate. MICT myocardial is a major risk factor for cerebrovascular disease (CVA) (Smith et al. 2011). CVA such as stroke a few years ago usually occurs in post-reproductive age (for example when reaching climacteric age), but now it is not uncommon in young people. Evidence of this shift may be caused by different lifestyles nowadays such as smoking, alcohol consumption, junk food, lack of exercise, air and water pollution, etc.

By type of work, most respondents work as housewives followed by private workers and the least are civil servants (6,2%). This result is in line with other studies in 2004 where housewives were the most frequent cases (30,4%) followed by private workers (24, 8%). However, not only housewives are at high risk for having a stroke, but other factors such as a people with a history of hypertension and a family history of stroke, heart disease, and hypertension can also be triggers.

Diabetes mellitus also contributes to the development of atherosclerosis (Idris, Thomson, & Sharma, 2006). However, according to Adler et al. (2003) diabetes mellitus is not a stroke factor, several other factors influence to trigger a stroke so the relationship between diabetes mellitus and stroke is still difficult to prove (Adler, et al. 2003).

The risk of suffering from hypertension is very high if the family has a history or hereditary hypertension. If one

of our parents has a history of hypertension, then throughout our lives, we have a 25% chance of having hypertension as well (Triyanto, 2014).

In the study of Kasner SE, et al., (2006) which states that a person with a family history of stroke is more likely to suffer from diabetes and hypertension (Kasner, et al. 2006). The tendency for hypertension in the family can also be related to the similarity of eating patterns between parents and children.

Past medical history and family illness are among the risk factors associated with stroke. But history and family illness are not the main risk factors that cause strokes. Family history may also be closely related to diet and lifestyle by the family such as lack of exercise, tendency to be obese, stress management, and changes in diet so that families become at risk for the development of heart disease, hypertension, diabetes mellitus and even stroke (Zaenurrohman, & Rachmayanti, 2017).

Until now there has been no research that states with certainty how long it takes from the use of hormonal contraception until there is a change in the body's homeostasis to cause an ischemic stroke because there are several important factors that influence the rapid and slow stroke processes, such as age >35 years, hypertension, smokers and alcohol consumption, physical activity, and lifestyle patterns of a person (Carlton, Banks, & Sundararajan, 2018).

Saifuddin stated that progesterone-only injections are preferred because they only need to be re-injected every 2-3 months and do not require invasive procedures such as an IUD or implant insertion. This contraception is also considered effective, practical, the price is relatively cheap and safe to use for all women of productive age (Saifudin, et al. 2008)

Regarding the risk of ischemic stroke, Sacco et al. (2017) state that some published data show there is no increased risk of ischemic stroke associated with hormonal contraceptive use of the type of progesterone, although there is still debate about whether progestogens have an impact on venous thromboembolic risk, progestogens do not appear to significantly affect the risk of arterial events (Sacco, et al. 2017). Studies conducted by Hussain (2004) also state that progesterone-only is the recommended method for women who are at risk of coronary heart disease in the presence of other risk factors such as hypertension (Hussain, 2004). In contrast to progesterone, Kemmerren et al. (2002) state that active estrogen can promote thrombosis, apparently because this hormone reaches the liver in high concentrations in portal blood and changes the formation of clotting factors in the liver (Kemmerren, et al. 2002).

Although according to this discussion it is mentioned that the use of the hormone progesterone in contraception seems unlikely to have a detrimental effect on hemostasis and does not show a significant risk of ischemic stroke, further studies are still needed on the

use of hormonal contraception as a risk factor for ischemic stroke to match the development of ischemic stroke and can complement data that enhances the overall picture of research.

In his study, raújo, TL de et al. (2017) concluded that there were no correlation between the occurrence of ischemic stroke with the duration of hormonal contraceptive use, both current and previous users (do Carmo Souza et al. 2018). This is not in line with studies that suggest that women who have used oral contraceptives, the risk is relatively adjusted for age in developing hypertension.

## CHARACTERISTICS

The characteristics of hormonal contraceptive users in ischemic stroke patients are as follows: the majority of the age group is early age (46-55 years) with most of them working as housewives, hypertension is a history of previous illnesses, most patients with the hereditary disease suffer, the highest proportion used hormonal contraception for more than 5 years with the most frequent type of use is the injection of progesterone only, and the average respondent stopped using hormonal contraception lower than 12 years before the occurrence of ischemic stroke.

## REFERENCES

- Adler, A. I., Stevens, R. J., Manley, S. E., Bilous, R. W., Cull, C. A., Holman, R. R., & UKPDS Group. (2003). Development and progression of nephropathy in type 2 diabetes: the United Kingdom Prospective Diabetes Study (UKPDS 64). *Kidney international*, 63(1), 225-232.
- Carlton, C., Banks, M., & Sundararajan, S. (2018). Oral contraceptives and ischemic stroke risk. *Stroke*, 49(4), e157-e159.
- Dewata, L., Prasetyo, B., Yuliati, A., & Wahyuhadi, J. (2017). Hormonal Contraceptive Exposure and Risk Factors for Meningioma in Soetomo Hospital 2012–2016. *Advanced Science Letters*, 23(4), 3291-3294.
- do Carmo Souza, R., Borges, G. F., & Mourão, D. M. (2018). Contracepção oral e fatores de risco em mulheres brasileiras: revisão integrativa. *Academus Revista Científica da Saúde*, 3(1), 92-105.
- Ea, O., Ajani, E. N., & Nenna, M. G. (2015). Constraints to Brood and Sell Poultry Production among Farmers in Enugu State, Nigeria. *Current Research in Agricultural Sciences*, 2(2), 73-80.
- Faubion, S. S., Casey, P. M., & Shuster, L. T. (2012). Hormonal contraception and migraine: clinical considerations. *Current pain and headache reports*, 16(5), 461-466.
- Hussain, S. F. (2004). Progestogen-only pills and high blood pressure: is there an association?: A literature review. *Contraception*, 69(2), 89-97.
- Idris, I., Thomson, G. A., & Sharma, J. C. (2006). Diabetes mellitus and stroke. *International journal of clinical practice*, 60(1), 48-56.
- Jusuf, M. I., Machfoed, M. H., & Keman, S. (2016). Infarction Stroke Risk Prediction Model for Indonesian Population: A Case-Control Study. *Bangladesh Journal of Medical Science*, 15(2), 269-274.
- Kasner, S. E., Chimowitz, M. I., Lynn, M. J., Howlett-Smith, H., Stern, B. J., Hertzberg, V. S., ... & Sila, C. A. (2006). Predictors of ischemic stroke in the territory of a symptomatic intracranial arterial stenosis. *Circulation*, 113(4), 555-563.
- Kemmeren, J. M., Tanis, B. C., van den Bosch, M. A., Bollen, E. L., Helmerhorst, F. M., van der Graaf, Y., ... & Algra, A. (2002). Risk of Arterial Thrombosis in Relation to Oral Contraceptives (RATIO) study: oral contraceptives and the risk of ischemic stroke. *Stroke*, 33(5), 1202-1208.
- Lestari, S. W, Khairunissa, S.T, Midoen, Y.H, Hestiantoro, A., Tanojo, T.D, Itishom, R. (2019).An update of Male contraception: A review of cellular perspective. *J Glob Pharma Technol*. 11(1):219–30.
- Mir, D., Ardabilgazar, A., Afshariyamchlou, S., & Sachmechi, I. (2018). Malignant Hypertension in Association with Low Estrogen Dose Oral Contraceptives: Case Report and Review of Literature. *Cureus*, 10(7).
- Roach, R. E., Helmerhorst, F. M., Lijfering, W. M., Stijnen, T., Algra, A., & Dekkers, O. M. (2015). Combined oral contraceptives: the risk of myocardial infarction and ischemic stroke. *Cochrane Database of Systematic Reviews*, (8).
- Röttingen, J. A., Regmi, S., Eide, M., Young, A. J., Viergever, R. F., Årdal, C., ... & Terry, R. F. (2013). Mapping of available health research and development data: what's there, what's missing, and what role is there for a global observatory?. *The Lancet*, 382(9900), 1286-1307.
- Sacco, S., Merki-Feld, G. S., Aegidius, K. L., Bitzer, J., Canonico, M., Kurth, T., ... & Mitsikostas, D. D. (2017). Hormonal contraceptives and risk of ischemic stroke in women with migraine: a consensus statement from the

- European Headache Federation (EHF) and the European Society of Contraception and Reproductive Health (ESC). The journal of headache and pain, 18(1), 108.
- Saifudin, A. B., Afandi, B., Baharudin, M., & Soekir, S. (2008). Practical Handbook on Contraception Services. Jakarta: Yayasan Bina Pustaka Sarwono Prawirohardjo.
- Smith Jr, S. C., Benjamin, E. J., Bonow, R. O., Braun, L. T., Creager, M. A., Franklin, B. A., ... & Lloyd-Jones, D. M. (2011). AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update: a guideline from the American Heart Association and American College of Cardiology Foundation. *Circulation*, 124(22), 2458-2473.
- Triyanto, E. (2014). Pelayanan keperawatan bagi penderita hipertensi secara terpadu. Yogyakarta: Graha Ilmu.
- YI, P. N., & Primadi, A. (2020). Comparison of antibiotic prescriptions in adults and children with upper respiratory tract infections in Bangka Tengah primary health care centers. *Journal of Basic and Clinical Physiology and Pharmacology*, 30(6).
- Zaenurrohmah, D. H., & Rachmayanti, R. D. (2017). Relationship Between Knowledge and Hypertension History with Blood Pressure Control in Elderly. *Jurnal Berkala Epidemiologi*, 5(2), 174-184.