



Hormonal contraception in women with hypertension

Anticoncepción hormonal en mujeres con hipertensión

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INTRODUCTION

Hormonal contraception (HC) is the method most used by women of reproductive age to avoid unplanned pregnancies.¹ Since its introduction in the decade of 1960, it is considered that 80% of women in the United States of America (USA) have used combined hormonal contraceptives (CHC) at some stage of their lives, more frequently those of oral administration, since their efficacy and relative safety allowed their widespread use.^{2,3} CHCs increase blood pressure (BP) by 2 to 5% in previously normotensive women. With the use of second-generation CHCs, the observed increase in BP was 7-8 mmHg. Currently, the trend is towards using preparations with lower doses of estrogens and developing new progestin-only pills (POP) with a more significant margin of safety that can even decrease systolic BP in hypertensive women.^{4,5}

HORMONAL CONTRACEPTION OVERVIEW

CHCs are estrogen and progestin preparations; progestin alone is the most used. According to the estrogen dose and the type of progestin, they are classified into four generations:

First generation: high-dose estrogen 150 µg and norethindrone, norethindrone acetate, or ethynediol diacetate.

Second generation: reduced the dose of estrogen to 50 µg and levonorgestrel (LNG).

Third generation: 20 to 35 µg estrogen doses and desogestrel or gestodene.

Fourth generation: maintains low doses of estrogen and drospirenone, a spironolactone analog, with anti-mineralocorticoid and antiandrogenic activity.⁶

POP contraceptives include injectable depot medroxyprogesterone acetate (DMPA), levonorgestrel-intrauterine device (LNG-IUD), and subdermal implant.⁷

CHARACTERISTICS OF THE WOMAN WITH SYSTEMIC ARTERIAL HYPERTENSION (SAH) WHO REQUIRE A CONTRACEPTIVE METHOD

Consulting for SAH in women is relatively common. In the USA, hypertension in women of reproductive age is increasing; it is reported that in approximately 1 of every four women. Less than half know their diagnosis, and only 10% receive treatment.⁸ In Mexico, according to the 2021 National Health and Nutrition Survey (ENSANUT), the prevalence of SAH in women varies according to the age group: between 20-29 years, it is 5.2%; from 30-39 years, it is 9.8%, and in those between 40-49 years, it is up to 25.2%.⁹ Choosing the correct contraceptive method for women with SAH is important because CHC increases BP, cerebrovascular event (STROKE) risk, and acute myocardial infarction (AMI). The American College of Gynecology and Obstetrics (ACOG) supports the USA Medical Eligibility Criteria for the Use of Contraceptives (USMEC)¹⁰ and recommends considering four characteristics: a) age of the patient, with emphasis on women 35 years of age and older; b) risk factors for Cardiovascular Disease (CVD), it is necessary to investigate

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dyslipidemia, diabetes, overweight or obesity, smoking, physical activity and a family history of premature CVD; c) precise measurement of BP, to confirm the diagnosis of SAH and its classification; d) degree of hypertension.

Mortality in women between 35 and 44 who present a high rate of obesity, smoking, less physical activity, and increased CHC consumption is increasing.^{11,12}

EFFECTS OF HORMONAL CONTRACEPTIVES ON HYPERTENSION

The effect of estrogens on BP is complex and can vary depending on the woman’s age, health status, and hormonal balance. It is estimated that in women with SAH who use CHC, the relative risk of AMI is multiplied by 12 compared to those who do not use this method.¹⁰ Women with established SAH who use CHC have a higher risk of stroke than normotensive non-users.¹³ The use of POP contraceptives, as well as the copper IUD does not have a significant effect on BP or CVD risk.¹⁰

CHC act on BP through the renin-angiotensin-aldosterone system (RAAS), increasing hepatic

production of angiotensinogen, and renal and adrenal production of renin and aldosterone, which causes an increase in sodium reabsorption and volume circulating with the subsequent elevation of BP (Figure 1).^{13,14}

On the other hand, possible pathways through which estrogens can induce BP elevation have been proposed, including activation of molecular signaling pathways such as endothelin-1 (ET-1) and accumulation of superoxide anions in the rostral ventrolateral medulla of the brain, as well as increased sensitivity and flow of calcium channels in smooth muscle cells mediated by the phosphorylation pathway of the myosin light chain (MLC) and the MLC kinase (CLMK) (Figure 1).¹⁴

RECOMMENDATIONS FOR THE USE OF CONTRACEPTIVES IN WOMEN WITH SAH

The appropriate type of contraception for women with this comorbidity should consider the age and the severity of SAH. According to the USMEC guide, recommendations are classified into four categories (Figure 2):

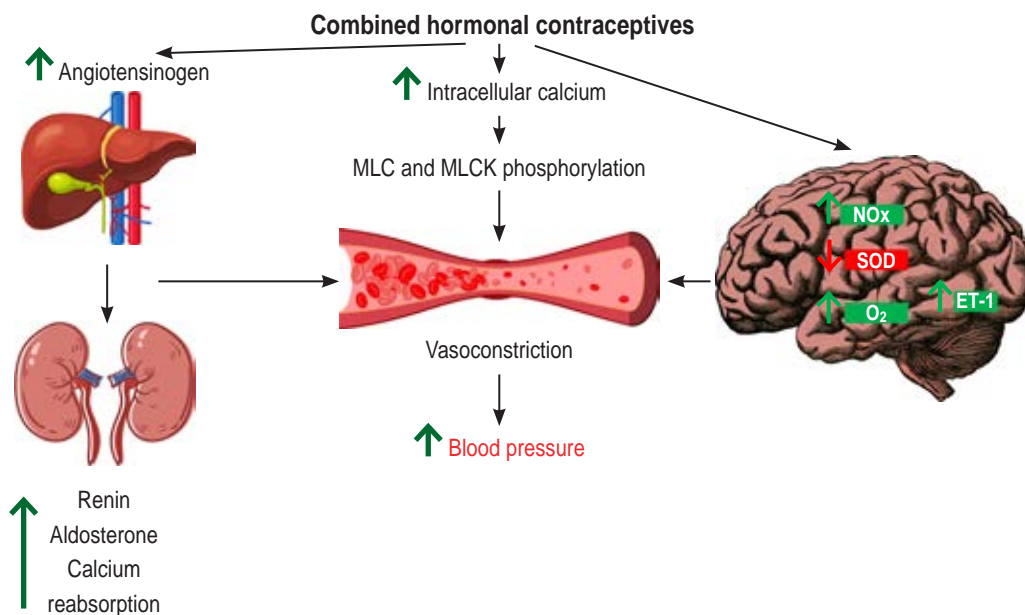


Figure 1: Effects of combined hormonal contraceptives on blood pressure. This scheme summarizes the mechanisms proposed at the systemic level generating vasoconstriction, causing elevation of blood pressure. MLC = myosin light chain. MLCK = myosin light chain kinase. ET-1 = endothelin-1. NOx = oxides of nitrogen. SOD = superoxide dismutase.

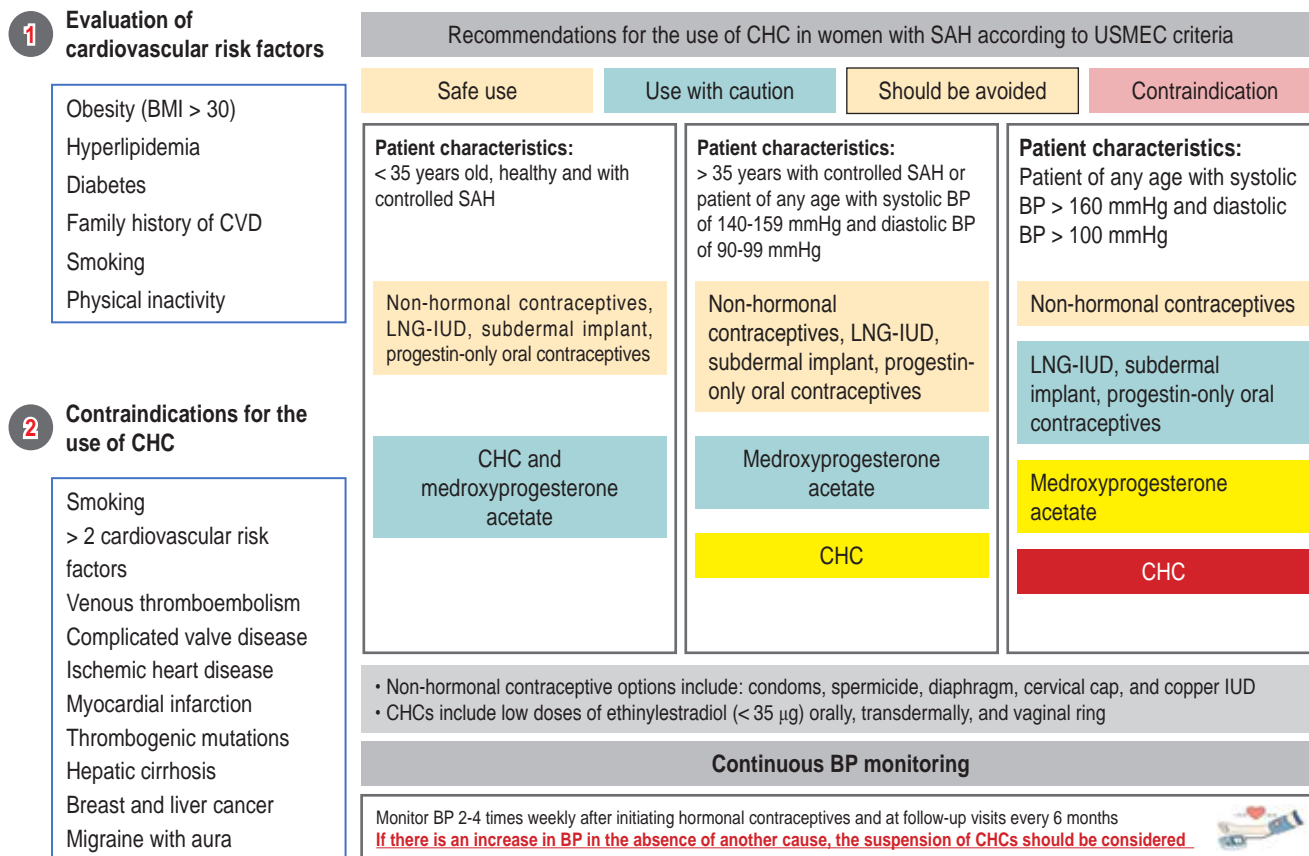


Figure 2: Recommendations for the use of CHC in women with SAH according to the USMEC criteria. Adapted from Shufelt C.¹³ CHC = combined hormonal contraceptives. CVD = cardiovascular disease. LNG-IUD = levonorgestrel intrauterine device. SAH = systemic arterial hypertension. BP = blood pressure. BMI = body mass index.

1. In healthy women under 35 years of age with controlled SAH, it is recommended to use non-hormonal contraceptives (condoms, spermicides, diaphragm, copper IUD), POP, LNG-IUD, and subdermal implant (**category 1**: safe use). If the patient does not accept or tolerate POP, CHC or DMPA is allowed (**category 2**: use with caution).¹³
2. Non-hormonal contraceptives, POP, LNG-IUD, and subdermal implant (**category 1**) are recommended in women over 35 years of age with controlled SAH or patients of any age with systolic pressure of 140-159 mmHg and diastolic pressure of 90-99 mmHg. CHC should be avoided (**category 3**).^{10,15}
3. In patients of any age with systolic pressure ≥ 160 mmHg and diastolic pressure ≥ 100 mmHg, the recommendation

is non-hormonal contraceptives (**category 1**), POP, LNG-IUD, and subdermal implant (**category 2**) may be recommended, DMPA should be avoided (**category 3**), CHC are contraindicated (**category 4**).^{13,15}

Although few women develop SAH after starting CHC use, blood pressure at follow-up visits should be measured, and discontinuation of the hormonal method should be considered if blood pressure increases significantly without other apparent causes.¹⁰

CONCLUSIONS

SAH is common in women older than 35. In this group of patients, it is common to observe overweight, obesity, smoking, decreased physical activity, and other factors that increase

the risk of CVD. Even though the absolute risk is low, CHCs increase the risk of stroke and AMI in women with SAH, so choosing the appropriate contraceptive method is relevant. In women with SAH, the US medical eligibility criteria (USMEC) recommend using non-hormonal contraceptives, POP oral contraceptives, LNG-IUD, and subdermal implants. Further studies are required to understand the safety profiles of non-oral hormonal preparations and ultra-low dose in women with SAH.

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