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THE EFFECT OF ANTIHYPERTENSIVE DRUGS ON THE COURSE OF PREGNANCY IN WOMEN WITH CHRONIC ARTERIAL HYPERTENSION

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Abstract: Hypertensive disorders during pregnancy are a major global health concern. According to the World Health Organization (WHO), the prevalence of arterial hypertension among the middle-aged population was estimated to be 20-30% in 2008. By 2021, the prevalence of hypertension among adults had increased to 25-35%, and it is projected to rise by an additional 5-10% by 2023. Notably, the prevalence of arterial hypertension during pregnancy is significantly higher, ranging from 35-45%.

Pregnancy with chronic arterial hypertension poses significant risks, including premature delivery, increased perinatal morbidity and mortality, and maternal complications. Pre-eclampsia and eclampsia, in particular, are severe complications of chronic arterial hypertension that can increase the risk of maternal death by 30-40%.

Despite the availability of standardized antihypertensive therapy guidelines for pregnant women, the early detection and effective management of chronic arterial hypertension during pregnancy remain challenging. This is crucial for preventing complications, reducing maternal and fetal mortality, and ensuring a safe and healthy pregnancy. Therefore, further research is needed to investigate the effects of antihypertensive drugs on pregnancy outcomes in women with chronic arterial hypertension.

Keywords: Arterial hypertension, Pregnancy, Pre-eclampsia, Eclampsia, Antihypertensive therapy.

Arterial hypertension is a prevalent medical condition during pregnancy, affecting 10 percent of pregnant women worldwide. Chronic arterial hypertension is diagnosed in pregnant women before or up to the 20th week of pregnancy and is observed in 5% of all pregnant women [1].

According to 2019 data from the International Society for Severity of Disease, approximately 18 million pregnant women are diagnosed with hypertension each year, and around 27,800 maternal deaths occur during pregnancy [10]. Treatment of chronic arterial hypertension in pregnant women is crucial to prevent maternal and fetal morbidity and mortality [1].

Globally, 1 in 10 pregnant women have chronic arterial hypertension, and 2% to 8% of all hypertensive pregnancies are complicated by preeclampsia and eclampsia (Abalos 2013). Preeclampsia and eclampsia, in particular, are significant acute illnesses associated with long-term disability among mothers and infants, increased risk of preterm delivery at 35 weeks, premature placental abruption, and antenatal or neonatal fetal death (Abalos 2014a; Khan 2006) [2,8]. Hypertensive diseases during pregnancy are one of the main causes of maternal and fetal mortality.

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During the early weeks of a normal pregnancy, blood pressure decreases, while in the later stages of pregnancy, blood pressure is higher than in the pre-pregnancy period (Hytten 1980; Villar 1989). These changes depend on various physiological and environmental factors, complicating the diagnosis of hypertension during pregnancy. Consequently, there are differing opinions on the definition of hypertensive disorders in pregnancy (Chappell 1999), and several classifications have been proposed (ASSHP 1993; Davey 1988; GiCord 1990; North 1999; Roberts 1993) [1].

Arterial hypertension in pregnancy is classified according to the degree of change in blood pressure, with variations based on the specific form of high blood pressure. According to the system proposed by the International Society for the Study of Hypertension in Pregnancy, arterial hypertension is diagnosed when the diastolic blood pressure is 90 mm Hg or higher on two separate occasions four hours apart, or when it is 110 mm Hg on a single measurement, or when the arterial blood pressure is equal to or greater than 160/100 mmHg at 15-minute intervals (Davey, 1988) [1,3].

The incidence of arterial hypertension in pregnant women has increased by 80% between 1995 and 2008 due to postterm delivery and the global obesity epidemic [3]. Women with chronic arterial hypertension may not perceive an increase in blood pressure during pregnancy, necessitating regular blood pressure monitoring (at least twice weekly).

Risk factors contributing to chronic arterial hypertension include:

a) Controllable factors such as an unhealthy diet (excessive salt, saturated fat, and trans fat intake, low fruit and vegetable consumption), physical inactivity, tobacco and alcohol use, and overweight or obesity.
b) Uncontrollable risk factors include a family history of chronic arterial hypertension, advanced maternal age (over 42 years), and comorbidities like diabetes or kidney disease.

Arterial hypertension in pregnant women is categorized as follows:

1. Gestational hypertension: characterized by an increase in arterial blood pressure first detected after the 20th week of pregnancy without significant proteinuria (<0.3 g/L). In 25% of cases, gestational hypertension progressing up to the 34th week of pregnancy is accompanied by preeclampsia.

2. Chronic arterial hypertension refers to high blood pressure existing prior to pregnancy or persisting beyond 20 weeks postpartum, with systolic blood pressure exceeding 140 mmHg and diastolic blood pressure exceeding 90 mmHg.

3. Preeclampsia, a serious condition characterized by high blood pressure and organ dysfunction, can develop in women with chronic arterial hypertension. The American College of Obstetricians and Gynecologists emphasizes the significance of preeclampsia as a complication following hypertension in pregnancy, even in the absence of proteinuria. Additional systemic changes such as thrombocytopenia, liver or kidney impairment, or neurological symptoms can indicate the development of preeclampsia [1,2].

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4. Eclampsia, a severe manifestation of preeclampsia, is defined by recurrent seizures in pregnant or postpartum women without underlying neurological disorders.

It is crucial to monitor blood pressure levels, with a threshold of 140/90 mmHg for diagnosing arterial hypertension according to the American College of Obstetricians and Gynecologists. However, the American College of Cardiology and the American Heart Association set slightly lower thresholds at 130/80 mmHg.

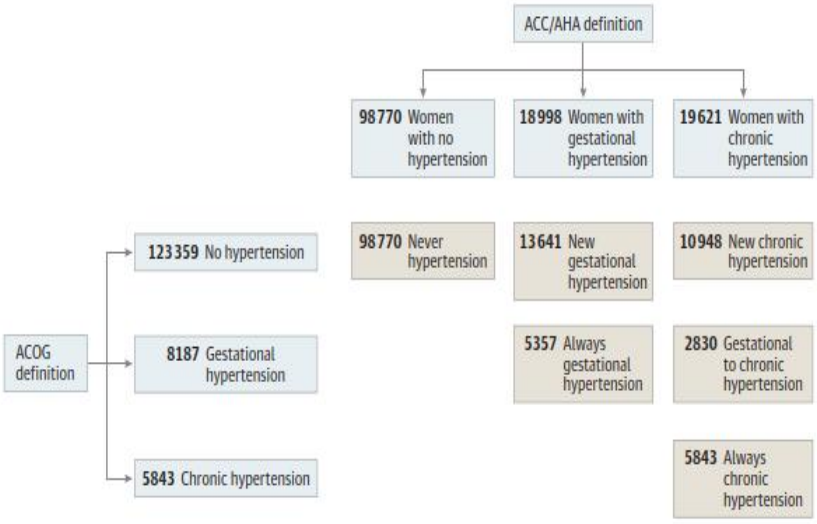
This classification system provides a framework for understanding and managing arterial hypertension in pregnant women, highlighting the importance of early detection and appropriate management to ensure optimal maternal and fetal outcomes. Arterial hypertension during pregnancy is categorized into different forms based on the timing of onset and associated complications.

According to American College of Obstetricians and Gynecologists, American College of cardiologists and American Heart Association the classification of arterial hypertension in pregnancy includes:

1. Women without hypertension
2. Women with gestational hypertension developing after 20 weeks of pregnancy
3. Women with pre-existing chronic arterial hypertension. [6]

This comprehensive approach aims to guide clinical management and improve outcomes for pregnant women at risk of hypertensive disorders.

Figure 1. Cross-Classification of Women From ACOG to ACC/AHA Category Resulting in 6 Possible Groups



ACOG indicates American College of Obstetrics and Gynecology; ACC/AHA, American College of Cardiology/American Heart Association. Study terms for reclassification include: new chronic hypertension (no ACOG hypertension and ACC/AHA chronic hypertension), gestational to chronic hypertension (ACOG gestational hypertension and ACC/AHA chronic hypertension), new gestational hypertension (no ACOG hypertension, ACC/AHA gestational hypertension), always chronic hypertension (ACOG and ACC/AHA chronic hypertension), always gestational hypertension (ACOG and ACC/AHA gestational hypertension), and never hypertension (no ACOG or ACC/AHA hypertension).

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Antihypertensive therapy can be administered at any stage of pregnancy and during post-pregnancy lactation. Recommended antihypertensive drugs include methyldopa (oral), nifedipine (oral), labetalol (IV or oral), and enalapril.

When using antihypertensive drugs, it is essential to monitor blood pressure every 10-20 minutes, with the target range being 130-140 mmHg for systolic and 80-90 mmHg for diastolic pressure. Falling below these critical limits may lead to complications due to inadequate fetal perfusion.

In cases of severe hypertension, **labetalol** is administered intravenously at a dose of 10-20 mg, with a maximum daily dose of 1200 mg. **Nifedipine** rapidly lowers arterial blood pressure, but frequent monitoring is not recommended due to the potential for critical fetal changes, such as increased heart rate.

Various studies have investigated the mechanism of action and use of antihypertensive drugs during pregnancy in women with chronic arterial hypertension. One such study was conducted by Thomas Easterling in two public hospitals in Nagpur, India. The study included pregnant women aged 18 and above at 28 weeks, with severe chronic arterial hypertension. The primary objective was to assess blood pressure control and adverse outcomes within 6 hours after receiving oral medications, including nifedipine, labetalol, or methyldopa. A total of 2307 pregnant women were included in the study, with 1413 individuals being excluded due to various reasons such as refusal to participate, complications like preeclampsia and eclampsia, and childbirth. Following the exclusion of 1413 participants due to various reasons such as refusal to participate, complications like preeclampsia and eclampsia, and childbirth, the remaining women in the study were divided into three groups: the first group received nifedipine, the second group received labetalol, and the third group received methyldopa. As a result of the study, 11 women (4%) in the nifedipine group, 10 women (3%) in the labetalol group, and 11 women (4%) in the methyldopa group discontinued treatment (due to delivery or transfer). The remaining 894 (39%) women were randomly assigned to the treatment group and included in the treatment analysis: 298 (33%) women received nifedipine, 295 (33%) women received labetalol, and 301 (33%) women received methyldopa. The primary outcome showed that significantly more women in the nifedipine group discontinued treatment compared to those in the methyldopa group (249 [84%] women vs 230 [76%] women; p=0·03). However, no difference was found between the nifedipine and labetalol groups (249 [84%] women vs 228 [77%] women; p=0·05), and similar results were obtained in the comparison between the labetalol and methyldopa groups (p=0·80). During the study, seven serious adverse events (1%) were reported: one female (<1%) in the labetalol group and six (1%) neonates (one (<1%) in the nifedipine group, two newborns in the labetalol group, and three (1%) newborns in the methyldopa group) were stillborn. In this study, all three oral antihypertensive drugs lowered blood pressure in most patients. In cases of severe hypertension, the use of nifedipin with labetalol in combination has been more effective than the single use of nifedipin. All three oral antihypertensive drugs - methyldopa, nifedipine, and labetalol - were designated as early treatment options. [5]

In conclusion, this comprehensive study of antihypertensive drugs in women with chronic arterial hypertension and their correct usage for treating the disease will greatly reduce

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complications observed in mothers and children, thereby contributing to improved maternal and child health outcomes.

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