

ANNOTATION
of the dissertation work Medubayeva Madina on the topic: "Optimization
of approaches to differentiated management of pregnant women with
chronic and gestational arterial hypertension"
submitted for the degree of Doctor of Philosophy (PhD) in the
specialty 6D110100 - "Medicine"

Relevance

Arterial hypertension in pregnant women is one of the main causes leading to complications for both the mother and the fetus. Every year, more than 50 thousand women die during pregnancy due to complications associated with AH.

Most international communities dealing with the problem of AH in pregnant women agree that BP should not exceed 140/90 mm Hg. However, there is no consensus on target BP levels for chronic and gestational AH. The lack of consensus on target BP levels entails another problem, differences of opinion on the criteria for initiating antihypertensive therapy.

Over the past 20 years, international paradigms on BP levels in pregnant women with hypertension, at which it was necessary to initiate antihypertensive therapy, have changed at least twice. In the early 2000s, the recommended BP level was no higher than 120/80 mm Hg and, accordingly, antihypertensive therapy was prescribed early. Experts called this "strict" BP control. In subsequent years, a number of studies have shown that "strict" control has no advantages over "soft" control, when target BP levels in pregnant women remain higher – up to 140/90 mm Hg. It is worth noting that the recommended BP levels were the same for both chronic and gestational hypertension.

Despite the relevance of this problem at the global level, there is no evidence of modifiable risk factors for chronic and gestational hypertension, which creates difficulties in their control at the primary health care level, although the differences in the etiology and pathogenesis of the formation of chronic and gestational hypertension are obvious. There is a theory that gestational hypertension is closer to gestosis in its pathogenesis (placental factors, endothelium, etc.), while chronic hypertension occurs during a longer process even before pregnancy. There are many studies that confirm a reliable link between risk factors such as obesity, smoking, dyslipidemia and heredity on the development of hypertension. However, it remains unclear to what extent these factors specifically affect the development of complications during pregnancy with chronic or gestational hypertension, and what preventive measures are necessary to prevent their development.

Despite the great attention paid to the problem of hypertension in pregnant women by research and practical medicine, there remains inconsistency in classification, indications for the appointment of additional methods of blood pressure monitoring, target blood pressure levels, criteria for the initiation of hypotensive therapy, leading to disagreements in patient management. An even more debatable and controversial issue is the differentiated management of pregnant women depending on the type of hypertension.

Purpose of the Study

To optimize approaches to differentiated management of pregnant women with chronic and gestational hypertension to prevent adverse pregnancy and childbirth outcomes.

Research objectives:

1. To identify risk factors for complications of pregnancy and childbirth in women with chronic and gestational hypertension in the Central Asian population.
2. To evaluate the effectiveness of office and out-of-office methods of blood pressure monitoring and to determine indications for daily blood pressure monitoring in pregnant women with hypertension.
3. To evaluate the relationship between blood pressure levels and the state of uteroplacental blood flow in chronic and gestational hypertension against the background of different antihypertensive therapy regimens.
4. To determine the relationship between the development of BMD disorders in pregnant women with chronic and gestational hypertension and morphological changes in the placenta.
5. To develop recommendations on the specifics of managing pregnant women with chronic and gestational hypertension.

Subject and object of the study

Retrospective analysis of documentation on 728 pregnant women (257 with chronic hypertension, 271 with gestational hypertension and 200 with physiological pregnancy). The prospective cohort study included 190 pregnant women: chronic hypertension-55, gestational hypertension-55 and 80 with physiological pregnancy. The group of pregnant women who were managed according to the developed algorithm included chronic hypertension - 25, gestational hypertension - 25.

Research methods:

1. Clinical (collection of clinical and anamnestic data)
2. Calculation of body mass index
3. Instrumental research methods (office BP, 24-hour BP monitoring, home BP monitoring, Doppler, echocardiography)
4. Laboratory research methods (conducted according to the protocol)
5. Morphological study of the placenta
6. Statistical (statistical processing of the obtained data)

Scientific novelty

1. In Kazakhstan, for the first time, a targeted and in-depth study was conducted aimed at studying the influence of risk factors for the development of hypertension on the development of complications during pregnancy and childbirth, differentially for pregnant women with chronic and gestational hypertension.
2. New data were obtained indicating the undoubted need for 24-hour BP monitoring based on the readings of the average morning BP obtained during home BP monitoring.
3. For the first time, an algorithm for differentiated management of pregnant women with chronic and gestational hypertension was developed and implemented depending on the initial weight, levels of average morning blood pressure, and the presence of non-dipper at different stages of pregnancy.

Practical significance

The proposed differentiated approach to the complex of examinations of pregnant women with hypertension allows to reduce the routine implementation of ABPM, which reduces the psycho-emotional stress in women.

The algorithm we developed for the combined treatment of pregnant women with chronic hypertension in the presence of obesity, high morning BP values with DMAP and non-dippers made it possible to achieve target BP levels and reduce the frequency of complications during pregnancy and childbirth.

Key Points for Defense:

1. Predictors such as obesity and excessive weight gain during pregnancy increase the risk of complications during pregnancy and childbirth in women of the Central Asian population, causing violations of the BMD in pregnant women with chronic hypertension more often than in gestational hypertension.
2. In pregnant women with chronic hypertension, high values of average morning BP, obtained based on DMAP at 28-30 weeks of pregnancy, are an indication for ABPM.
3. In pregnant women with chronic hypertension, if indicated, the use of combined hypotensive therapy reduced the frequency of BMD violations by 3 times compared to the administration of dopegit in a "soft" mode or "on demand".
4. The conducted Doppler studies do not reveal the full picture of changes in the placentas that are detected during their morphological study.
5. The algorithm for differentiated management of pregnant women depending on the type of hypertension that we developed is a safe and effective way to reduce the frequency of BMD violations in pregnant women with hypertension.

Approval of the Dissertation:

The main provisions of the work were presented at the IX Congress of Cardiologists of the Republic of Kazakhstan with international participation (Almaty, 2017), the 60th Anniversary International Scientific and Practical Conference of Young Scientists and Students (Astana, 2018), the X Congress of the Association of Cardiologists and the V Congress of Therapists of the Republic of Kazakhstan, the VIII Congress of the Association of Cardiologists of the Turkic World and the conference of the "Society of Arrhythmologists of the Silk Road Countries" dedicated to the 40th anniversary of the WHO Alma-Ata Declaration on Primary Health Care (Almaty, 2018), European meeting on hypertension and cardiovascular protection (Barcelona, 2018), Russian National Congress of Cardiologists 2018 (Moscow, 2018), international conference on emergency medicine dedicated to the memory of Doctor of Medical Sciences, Professor, Corresponding Member of the National Academy of Natural Sciences of the Republic of Kazakhstan A. Z. Dyusupov (Semey, 2024), European meeting on Hypertension and cardiovascular protection (Berlin, 2024).

The results of the study are presented in 15 scientific publications, including 10 abstracts, 5 scientific articles. Of these, 1 work in the publication of the Scopus rating agency, 3 articles in journals recommended by the Committee for Control in the Sphere of Education and Science of the Republic of Kazakhstan and 1 article in a peer-reviewed foreign journal.

On the topic of the dissertation, 1 certificate protected by the copyright of the Republic of Kazakhstan was received (№ 17385 dated 11.05.2021).

The results of the work were implemented based on the treatment and diagnostic center of City Multidisciplinary Hospital № 2 and the consultative and diagnostic department of Multidisciplinary City Hospital № 3.

Conclusions

1. Predictors that increase the risk of complications in women of the Central Asian population (initial obesity and excessive weight gain during pregnancy) cause BMD disorders in pregnant women with CAH 3 times more often than in GAG. In pregnant women with CAH with initial obesity, weight gain during the entire pregnancy should not exceed 9.8 kg. In pregnant women with GAG with initial obesity, weight gain did not show a direct effect on the development of BMD disorders.
2. In pregnant women with CAH with average morning SBP/DBP $\geq 133/86$ mm Hg according to DBPM at 28-30 weeks of pregnancy, ABPM should be performed, since high morning BP values obtained with DBPM indicate the presence of a non-dipper and increase the risk of BMD disorders. In pregnant women with GAG, no direct relationship was found between morning BP readings and non-dipper at 28–30 and 34–36 weeks of pregnancy. However, all pregnant women with GAG with impaired BMD (n=8) had high readings of average daily SBP/DBP $\geq 132/82$ mm Hg at 28–30 weeks according to DBPM. In this regard, it is recommended to determine indications for ABPM in pregnant women with GAG based on average daily BP readings.
3. The use of dopegit ≥ 500 mg per day, including combination therapy in pregnant women with CAH, reduced the incidence of BMD disorders by 3 times compared to the administration of dopegit < 500 mg per day and "on demand" (5.8% and 22.2%, respectively). When using dopegit ≥ 500 mg per day in pregnant women with GAG, a decrease in the incidence of BMD disorders was also noted, compared to dopegit < 500 mg per day, however, the results obtained are not so significant.
4. The conducted Doppler studies do not reveal the full picture of changes in the placentas that are detected during its morphological study. The incidence of BMD disorders in pregnant women with CAH during Doppler (28.1%) is 2 times less compared to placental insufficiency (PI), established based on morphology (52.7%). A similar picture was revealed by Doppler (9.9%) of pregnant women with GAG, the frequency of BMD violations was lower compared to PN, established based on morphology (30.9%). Based on the obtained results, it can be concluded that all pregnant women with AG, a priori, need to carry out prevention of BMD violations.
5. Pregnant women with CAH with initial obesity - 23 (41.8%), who were monitored without weight gain control in 12 (52.2%) cases had BMD violations, while in pregnant women with CAH with initial obesity - 9 (36.0%), who were monitored according to the algorithm with weight gain control up to 9.8 kg, the frequency of BMD violations was 1 (4.0%) case. In pregnant women with CAH with initial obesity, there was no direct connection between the development of BMD violations and weight gain during pregnancy. The use of a combined treatment according to the algorithm in pregnant women with CAH with high morning BP values according to DMAP, the presence of a non-dipper according to ABPM allowed to reduce the frequency of BMD violations by 6 times compared to pregnant women with CAH, which were managed without the

algorithm (4.0% and 25.5%, respectively). The use of the algorithm in pregnant women with GAH also showed a positive result, so the frequency of IMD violations in pregnant women with GAH, which were managed without the algorithm, was almost 2 times higher compared to the management according to the algorithm (14.5% and 8.5%, respectively).

Practical recommendations

The proposed differentiated approach to the complex of examinations of pregnant women with hypertension will reduce the routine implementation of ABPM, which will reduce the psycho-emotional stress in women.

The algorithm we have developed for the combined treatment of pregnant women with CHG in the presence of obesity and non-dippers allows achieving target blood pressure levels and will reduce the frequency of complications during pregnancy and childbirth.

Volume and structure of the dissertation

The dissertation is presented on 126 pages of typewritten text. The dissertation consists of an introduction, a literature review, a chapter on materials and research methods, results, conclusion, findings, a list of references, practical recommendations, and an appendix. The work is illustrated with 43 tables and 21 figures. The bibliographic index includes 154 literary sources.