

Advancements in Pharmacological Treatment of Pregnancy-Induced Hypertension

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Abstract: Pregnancy-induced hypertension (PIH) is a common obstetric disease characterized by clinical symptoms such as proteinuria, hypertension, and edema. It may even lead to heart and kidney failure, posing a serious threat to the life safety of pregnant women and neonates. Therefore, it is imperative to enhance hemodynamic monitoring for pregnant women and provide personalized prevention and treatment strategies. Medication plays a crucial role in managing pregnancy-induced hypertension, with diuretics, antihypertensive agents, and antispasmodics being the primary pharmacological interventions to improve the condition. This research, validated through literature review, focuses on the progress in drug research related to pregnancy-induced hypertension, aiming to contribute new insights to the clinical diagnosis and treatment of PIH.

1. Introduction

In recent years, with the gradual implementation of the two-child and three-child policies, the proportion of advanced maternal age pregnancies has continuously increased, leading to a rising risk of pregnancy-induced hypertension (PIH) and posing a serious threat to the safety of both mothers and infants [1]. The incidence of PIH in China is approximately 10%, with a higher occurrence between the 20th week of pregnancy and 2 weeks postpartum. Currently, the pathogenesis of PIH remains unclear. Clinically, the etiology of PIH is believed to be associated with genetic factors, oxidative stress reactions, placental nutritional deficiencies, and immune dysregulation [2]. Among these factors, oxidative stress theory and placental ischemia-hypoxia are key focuses of clinical research. Early prediction, detection, and intervention of PIH can promote the reduction of associated risks, aiding in the control of complications. The clinical treatment goals for PIH are the prevention of severe preeclampsia and eclampsia, the reduction of maternal and neonatal mortality rates, and the achievement of favorable perinatal outcomes [3]. To ensure the maximum safety of both mother and infant, in addition to adhering to basic treatment principles, a scientific combination of drug therapy is recommended. Calcium channel blockers, β -receptor antagonists, and diuretics are commonly used medications in the treatment of pregnancy-induced hypertension.

2. Inducing Factors of Pregnancy-Induced Hypertension

2.1 Elevated Psychological Stress in Pregnant Women

The fundamental factor influencing the development of pregnancy-induced hypertension (PIH) during pregnancy is the impact of elevated psychological stress on pregnant women themselves [4]. Generally, each woman experiences a certain level of psychological stress during their first childbirth. Due to the pain of childbirth, various discomforts during labor, and the unknown future circumstances, most women carry a psychological burden during this period. Their emotions are variable, and they are prone to anxiety [5]. Based on previous research, it has been observed that pregnant women experience anxiety, stress, and unstable temperament during pregnancy, significantly increasing the likelihood of developing pregnancy-induced hypertension.

2.2 Lack of Standardized Prenatal Examinations

Many pregnant women need to promptly understand their physical condition during pregnancy. Conducting regular prenatal examinations at specified intervals allows for the timely assessment of fetal growth and physical development based on examination results. In the presence of any abnormalities, prompt treatment can be administered with the assistance of prenatal examinations [6]. However, according to research, some pregnant women undergo fewer prenatal examinations, which can contribute to the occurrence of pregnancy-induced hypertension. Insufficient prenatal examinations make it impossible to fully understand the pregnant woman's physical condition and emotional state, hindering effective control [7]. Therefore, pregnant women should not take prenatal examinations lightly during pregnancy.

2.3 Inadequate Consumption of Fruits and Vegetables by Pregnant Women

Women require additional nutrition during pregnancy, as the fetus is growing, and their own development demands greater support from nutrition. Timely consumption of various fruits and vegetables during pregnancy, along with the intake of diverse vitamins, can enhance the resistance of both the pregnant woman and the fetus, preventing the occurrence of various diseases [8]. However, due to various reasons, some pregnant women consume fewer fresh fruits and vegetables during pregnancy, failing to promptly replenish the various nutrients needed by the body and not effectively regulating bodily functions [9]. This phenomenon is likely to contribute to the development of pregnancy-induced hypertension.

2.4 Excessive Body Weight

In general, due to misconceptions, many pregnant women believe they should consume more nutrients during pregnancy to enhance their resistance. Consequently, they excessively ingest large amounts of food, leading to an increase in their body weight and resulting in obesity [10]. Obesity is a risk factor for developing pregnancy-induced hypertension. Being overweight increases the body fat percentage in pregnant women. Once lipid balance is disrupted, it can contribute to the occurrence of symptoms associated with pregnancy-induced hypertension, leading to serious harm for pregnant women.

3. Prevention Analysis of Pregnancy-Induced Hypertension

3.1 Prevention

Aspirin is a white crystalline or crystalline powder that can alleviate blood hypercoagulability, prevent platelet aggregation, and inhibit thrombus formation. Simultaneously, aspirin can block the activity of cyclooxygenase-1, reduce the synthesis of thromboxane A₂, thereby improving local blood circulation [11]. Pregnancy-induced hypertension is more common in the middle and late stages of pregnancy. Pregnant women with this condition may experience systemic small artery spasm, leading to luminal narrowing, increased peripheral resistance, and endothelial damage.

Endothelial damage can induce platelet aggregation and promote the formation of small blood vessel thrombi. Thromboxane, formed and released by platelet aggregation, stimulates the vascular wall, intensifies vascular constriction or spasm, increases peripheral resistance, and causes sustained elevation of blood pressure. It forms the basis of preeclampsia and eclampsia [12]. Low-dose enteric-coated aspirin prevents platelet aggregation and helps avoid the formation of blood clots in small blood vessels. In addition, it can prevent vasoconstriction or spasm caused by thromboxane and increase the sensitivity of blood vessels to active substances. In particular, it can dilate blood vessels, reduce peripheral circulatory resistance, and control blood pressure levels in pregnant women with hypertension [13].

3.2 Health Education for Expectant Mothers

Strengthening the understanding and health education of pregnant women and conducting regular prenatal examinations at hospitals are essential. During pregnancy, many first-time expectant mothers may have misconceptions about pregnancy and lack sufficient experience in health education [14]. Therefore, it is crucial to enhance their understanding and provide health education to pregnant women, encouraging them and their families to prioritize these aspects. This effort aims to raise awareness of pregnancy-induced hypertension, guide and supervise pregnant women to undergo regular prenatal examinations at hospitals, promptly identify various adverse factors, and ensure timely and scientifically guided treatment [15]. Empowering pregnant women with various prenatal care knowledge helps enhance their self-awareness and ability to protect themselves.

3.3 Attention to Dietary Intake during Pregnancy

During pregnancy, it is crucial to ensure the timely intake of various nutrients. Pregnant women should also have a correct understanding of the intake of various nutrients during pregnancy, adhering to established standards. They should avoid consuming highly nutritious foods excessively and strive to maintain a healthy weight while ensuring proper nutrient absorption in their bodies [16]. It is advisable to incorporate a balanced diet that includes a variety of fresh fruits and vegetables to prevent excessive nutrient intake, which can lead to weight gain and potential health issues. Pregnant women should make food choices based on their individual conditions, selecting suitable options for a well-rounded and nutritious diet [17].

3.4 Counseling Pregnant Women with Adverse Psychological States

Pregnant women often experience psychological stress and emotional burdens during pregnancy. It is essential to provide timely psychological counseling to pregnant women, guiding their thought processes and alleviating their emotional stress. A positive and healthy mindset greatly contributes to the healthy growth of the fetus. Pregnant women should adhere to a healthy sleep schedule and avoid

staying up late [18]. Ensuring good sleep quality helps reduce the occurrence of various adverse emotions. It is important for pregnant women to prioritize adequate rest based on a healthy daily routine [19].

4. Treatment Drugs for Pregnancy-Induced Hypertension

4.1 Antispasmodic Drugs

Systemic small artery spasm is a pathological feature of pregnancy-induced hypertension (PIH), making antispasmodic treatment not only a fundamental therapeutic approach but also the primary principle in drug treatment. The goal of antispasmodic treatment is to promote the dilation of spasming small arteries, improving blood supply to major organs and the placenta [20]. Magnesium sulfate is a common antispasmodic drug, and its therapeutic status in pregnancy-induced hypertension remains irreplaceable. Magnesium sulfate can release magnesium ions in the patient's body, reducing acetylcholine formation, lowering the risk of spasms, and thereby preventing the development of the disease [21].

Furthermore, Mg^{2+} can compete with Ca^{2+} , stimulating the endothelium to release calcitonin, promoting vasodilation. In comparison to normal pregnant women, pregnant women with hypertension exhibit a significantly decreased intracellular Mg^{2+} concentration. Additionally, Mg^{2+} can alleviate cerebral cell hypoxia, improve maternal systemic oxygen metabolism, reduce the body's sensitivity to angiotensin, thereby lowering blood pressure. Wu Hailong et al. suggested that magnesium sulfate can improve symptoms such as spasms and inadequate perfusion caused by blood pressure, but it lacks ideal effectiveness in blood pressure control and is prone to recurrence [22].

Combining magnesium sulfate with labetalol in the treatment of pregnancy-induced hypertension has been found to effectively control blood pressure levels, homocysteine, and high-sensitivity C-reactive protein levels. It promotes improved fetal blood flow and reduces the incidence of premature birth and distress. However, several studies have reported that excessive and prolonged doses of magnesium sulfate may lead to toxicity. Moreover, high concentrations of magnesium ions may further inhibit the medullary respiratory center, leading to respiratory arrest.

4.2 Antihypertensive Drugs

4.2.1 Calcium Channel Blockers

Calcium channel blockers help inhibit calcium influx, promoting relaxation of vascular smooth muscle. Nifedipine and amlodipine can achieve significant antihypertensive effects, improving clinical manifestations such as dizziness, headache, and proteinuria [23]. Amlodipine belongs to the dihydropyridine class of calcium channel blockers, assisting in vasodilation of smooth muscle and improving peripheral vascular spasm, thereby achieving the goal of lowering blood pressure.

4.2.2 Adrenergic Receptor Blockers

Labetalol is a widely used adrenergic receptor blocker. As a salicylamide derivative, labetalol plays a crucial role in both β receptors and α receptors. Its antagonistic effect on β_1 receptors helps promote vasodilation, reduce cardiac load, improve oxygen consumption, increase cardiac ejection fraction, and enhance placental blood flow [24]. Simultaneously, labetalol can block central and peripheral renin, slow down the heart rate, and reduce myocardial contractility, thereby exerting antihypertensive effects.

The European Society of Cardiology, the European Society of Hypertension, and the Joint Committee for the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure in the

United States recommend labetalol as a first-line drug for treating pregnancy-induced hypertension. The Canadian Association of Obstetricians and Gynecologists suggests listing it as a second-line drug. Reports indicate that labetalol has a slight impact on cerebral blood flow and oxygen metabolism in patients with pregnancy-induced hypertension, which may not be significant but can help alleviate headache symptoms. Studies have found that, compared to monotherapy, the combination of labetalol and nifedipine, under routine treatment, achieves more desirable outcomes in the intervention of severe pregnancy-induced hypertension in pregnant women. Additionally, it can effectively control blood pressure levels while reducing the risk of adverse complications after medication on a reduced dosage basis.

4.2.3 Diuretics

Diuretics reduce maternal blood volume, increase blood concentration, and exacerbate fetal hypoxia symptoms. Therefore, diuretics are typically only used in patients with severe complications of pregnancy-induced hypertension, such as acute pulmonary edema, acute heart failure, etc. Some researchers conducted an analysis on 148 pregnant women with pregnancy-induced hypertension and concomitant coronary heart disease [25]. On the basis of vasodilation treatment, they were given aspirin and spironolactone. Clinical results indicate that this approach promotes improvements in coagulation function, ventricular remodeling, and ventricular hypertrophy in pregnant women with pregnancy-induced hypertension and concomitant coronary heart disease.

4.3 Analgesic Drugs

Intense pain during childbirth can lead to various secondary physiological changes, triggering negative emotions such as tension, anxiety, and resistance, enhancing stress responses, causing hormonal imbalances, and increasing catecholamine secretion. The elevation of blood pressure in pregnant women can result in increased oxygen consumption and ventilation. Prolonged excessive ventilation can lead to respiratory alkalosis, reduced placental blood supply, and intrauterine fetal hypoxia [26]. In addition, parturients release a large amount of catecholamines during the delivery process, causing restricted rhythmic uterine contractions and stress reactions that are not conducive to protecting the health of both mother and baby. Therefore, the use of targeted analgesic drugs to assist in the delivery of pregnant women with hypertension is particularly important.

According to Liang Gang et al., in the case of intermittent epidural administration combined with patient-controlled analgesia, low-concentration ropivacaine (0.06%) and sufentanil (0.5 µg/ml) can meet the analgesic needs of pregnant women with hypertension, reduce the dosage of ropivacaine in the second stage of labor, and provide advantages over 0.1% ropivacaine + 0.5 µg/ml sufentanil compared to sufentanil alone [27].

4.4 Combined Use of Multiple Drugs

Yu Lei et al. analyzed the clinical efficacy of sustained-release nifedipine combined with intravenous magnesium sulfate in the treatment of pregnancy-induced hypertension [28]. They believe that the combination of nifedipine and magnesium sulfate can promote relaxation of peripheral vascular smooth muscle, reduce vascular resistance, and improve uterine artery blood flow. The main adverse reactions in both groups were drowsiness and gastrointestinal reactions. Nifedipine is a calcium channel blocker used in the clinical treatment of pregnant women with pregnancy-induced hypertension. It does not cause harm to the fetus through the placental barrier and has a certain level of safety.

Ma Xiaolian et al. discussed the role of Nemothoracoplasty combined with magnesium sulfate

injection in the clinical treatment of hypertensive disorders during pregnancy [29]. The results indicated that the overall effective rate in the combination group was 95.74%, significantly higher than the 82.22% in the magnesium sulfate group ($P<0.05$). At the same time, both systolic and diastolic blood pressure in the combination group were lower than those in the magnesium sulfate group ($P<0.05$). Adverse reactions such as dizziness, hypotension, and gastrointestinal discomfort were mainly observed in both groups.

Qi Zheng selected 90 pregnant women with hypertensive disorders during pregnancy as the analysis sample [30]. The control group was treated with magnesium sulfate combined with nifedipine, while the study group was treated with magnesium sulfate combined with nifedipine and compound Danshen injection. After treatment, it was found that the study group had lower levels of urinary protein, fibrinogen, positive rate of blood glucose, plasma viscosity, whole blood high shear viscosity, whole blood medium shear viscosity, whole blood low shear viscosity index, and adverse pregnancy outcomes compared to the control group ($P<0.05$). This suggests that the three-drug combination is helpful in controlling the positive rate of urinary protein, promoting the improvement of hemorheological indicators, and significantly improving the condition of pregnant women with hypertensive disorders. Compared with the two-drug regimen, the three-drug regimen is helpful in preventing adverse pregnancy outcomes such as preterm birth and postpartum hemorrhage. The addition of compound Danshen injection on the basis of magnesium sulfate combined with nifedipine can achieve definite therapeutic effects. The reason may be that these three drugs have complementary effects. Although magnesium sulfate can inhibit neuromuscular transmission, promote relaxation of vascular smooth muscle, and vasodilation to improve fetal hypoxia, its antihypertensive effect is insufficient. Therefore, nifedipine is needed for treatment, as it has a rapid antihypertensive effect. The application effectiveness of the three-drug combination needs further confirmation through large-sample studies.

Yan Lingling et al. discussed the therapeutic effects of levamlodipine besylate tablets combined with phentolamine in the treatment of hypertensive disorders during pregnancy [31]. The results revealed that the levels of red blood cell hematocrit, 24-hour urinary protein, resistance index, systolic blood pressure, diastolic blood pressure, blood viscosity, and the incidence rate of adverse pregnancy outcomes were significantly lower than those in the levamlodipine besylate tablet group ($P<0.05$). This indicates that the combination therapy of levamlodipine besylate tablets and phentolamine can achieve certain clinical efficacy in the treatment of hypertensive disorders during pregnancy.

5. Conclusion

In summary, hypertensive disorders during pregnancy constitute a major cause of adverse outcomes for both pregnant women and neonates. Prenatal screening and healthcare initiatives have created favorable conditions for the early prevention, diagnosis, and treatment of hypertensive disorders during pregnancy. Despite the diverse array of clinical treatment options for these disorders, there remains a lack of effective and safe therapeutic agents. Therefore, it is imperative to continue enhancing our understanding of the pathogenesis of hypertensive disorders during pregnancy and to improve clinical efficacy through personalized interventions.

Simultaneously, proactive optimization of pregnancy management is crucial in the prevention and treatment of hypertensive disorders during pregnancy. This involves maximizing efforts to mitigate the risks associated with these disorders, thereby assisting patients in achieving favorable outcomes. Currently, due to the absence of groundbreaking clinical trials for antihypertensive drugs during pregnancy, there is a lack of unified international standards for these medications. The application value of relevant drugs needs to be substantiated through large-sample, multicenter, prospective, controlled experiments. This approach will provide scientifically sound evidence in evidence-based

medicine, continuously refining the treatment strategies for hypertensive disorders during pregnancy.

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