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ANALYSIS OF DETERMINANTS OF PREECLAMPSIA IN HIGH-RISK PREGNANT WOMEN RESISTANT TO ASPIRIN PROPHYLAXIS LITERATURE REVIEW

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Abstract
Preeclampsia (PE) occurs in 3–8% of pregnancies [1] and up to 20–25% in high-risk women [7], remaining a leading cause of maternal and perinatal morbidity and mortality [13]. Despite widespread use of low-dose aspirin prophylaxis, its effectiveness varies [9,10]. Analysis of recent data (Europe, Russia, Asia, Uzbekistan) shows that aspirin reduces PE risk by about 15% [12], while 6–17% of cases still develop [9,10]. Aspirin is an effective but limited preventive agent, with maximum benefit associated with early initiation and an individualized approach [1,7].

Keywords: Preeclampsia, aspirin prophylaxis, low-dose aspirin, high-risk pregnancy, perinatal complications, maternal complications, individualized approach.

Introduction

АНАЛИЗ ДЕТЕРМИНАНТОВ ПРЕЭКЛАМПСИИ У БЕРЕМЕННЫХ ВЫСОКОГО РИСКА, РЕЗИСТЕНТНЫХ К АСПИРИН-ПРОФИЛАКТИКЕ. ОБЗОР ЛИТЕРАТУРЫ

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Аннотация
Преэклампсия (ПЭ) встречается в 3–8% беременностей, достигая 20–25% у женщин группы высокого риска и остаётся одной из ведущих причин материнской и перинатальной заболеваемости и смертности. Несмотря на широкое применение низкодозированной аспириновой профилактики, её эффективность варьирует. Анализ данных последних (Европа, Россия, Азия, Узбекистан) показал, что аспирин снижает риск ПЭ в среднем на 15%, однако в 6–17% случаев заболевание продолжает развиваться. Аспирин является эффективным, но ограниченным средством профилактики, максимальная эффективность которого связана с ранним началом и индивидуализированным подходом.

Ключевые слова: преэклампсия, профилактика аспирином, низкие дозы аспирина, беременные группы высокого риска, перинатальные осложнения, материнские осложнения, индивидуализированный подход.

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ASPIRIN PROFILAKTIKASIGA REZISTENT BO‘LGAN YUQORI XAVF GURUHIDAGI HOMILADORLARDA PREEKLAMPSIYA DETERMINANTLARI TAHLILI. Adabiyotlar sharhi

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Annotatsiya
Preeklampsiya (PE) homiladorlikning 3–8% holatlarida uchraydi, yuqori xavf guruhidagi ayollarda esa 20–25% gacha yetadi, onalik va perinatal kasallanish hamda o‘limining yetakchi sabablaridan biri hisoblanadi. Past dozali aspirin profilaktikasining keng qo‘llanilishiga qaramay, uning samaradorligi turlicha bo‘lishi mumkin. So‘nggi ma’lumotlar (Yevropa, Rossiya, Osiyo va O‘zbekiston) tahliliga ko‘ra, aspirin preeklampsiya xavfini o‘rtacha 15% ga kamaytiradi, biroq 6–17% holatlarda kasallik rivojlanishi davom etadi. Aspirin samarali, ammo cheklangan profilaktik vosita bo‘lib, uning maksimal samaradorligi erta boshlash va individual yondashuv bilan bog‘liq.

Kalit so'zlar: preeklampsiya, aspirin profilaktikasi, past dozali aspirin, yuqori xavfli homiladorlar, perinatal asoratlar, ona asoratlari, individual yondashuv

Introduction

Preeclampsia is one of the most severe hypertensive complications of pregnancy, usually developing after the 20th week of gestation and accompanied by endothelial dysfunction, vascular spasm, and damage to the kidneys, liver, brain, and coagulation system in the maternal body [1,4]. Therefore, it may cause severe maternal complications such as eclampsia, HELLP syndrome, stroke, renal failure, and placental abruption [1,4]. According to WHO data, in the 2020 global statistics, this group of disorders accounted for approximately 10–14% of maternal deaths and ranked 3rd–4th among the leading causes [13].

From a perinatal perspective, preeclampsia and associated placental insufficiency account for up to 15–20% of preterm births and increase the risk of fetal growth restriction, low birth weight, preterm delivery, the need for neonatal resuscitation, and perinatal mortality [2,5]. Each year, approximately 2.5–3 million neonatal deaths are recorded worldwide, a significant proportion of which are associated with hypertensive disorders, including preeclampsia [13].

Low-dose aspirin is one of the most extensively studied pharmacological agents for the prevention of preeclampsia and, according to international recommendations, is usually used at a dose of 75–150 mg/day, while U.S. guidelines recommend 81 mg/day [1,12]. It is initiated after the 12th week of gestation, optimally before the 16th week [1,7]. This is because spiral artery remodeling and placental formation represent a critical stage, and the physiological reorganization of uteroplacental blood circulation occurs precisely during this period [2]. Therefore, aspirin prophylaxis is particularly recommended for women with a history of preeclampsia, multiple pregnancy, chronic hypertension, pregestational diabetes, kidney disease, systemic lupus erythematosus, or antiphospholipid syndrome [1,12].

Studies: Recent studies confirm that low-dose aspirin plays an important role in the prevention of preeclampsia; however, they show that its effectiveness is not the same in all populations [9,10,12].

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Randomized clinical trials and cohort observations conducted in different regions have determined that the effect of aspirin depends on dose, timing of initiation, biomarker status, individual patient characteristics, and the background of underlying diseases [9,10].

In European studies, particularly in a large cohort analysis conducted in Sweden (2025) (n=13,828), preeclampsia was identified in 812 cases (8.9%) among 9,141 women who received 75 mg of aspirin, and in 443 cases (9.5%) among 4,687 women who received 150–160 mg, demonstrating that a higher dose is not superior to a lower dose. This is explained by the "saturation effect" of platelet COX-1 blockade, that is, beyond a certain dose, additional administration of the drug does not increase effectiveness [10].

In a randomized study conducted in Spain (StopPRE, 2023) (n≈936), among women with normal biomarkers (sFlt-1/PlGF ≤38) receiving 150 mg of aspirin, participants were divided into two groups at 24–28 weeks: early preterm preeclampsia was observed in 7 cases (1.48%) among 473 women who discontinued aspirin, and in 8 cases (1.73%) among 463 women who continued it. As a conclusion, it was determined that if biomarkers are normal, early discontinuation of aspirin does not increase the risk [9].

In an observational study conducted in Russia (2024), 88 high-risk pregnant women were studied, of whom preeclampsia was identified in 7 cases (11.3%) among 62 women who received 150 mg of aspirin early (from 14–16 weeks), whereas it was identified in 8 cases (30.8%) among 26 women who did not receive aspirin, indicating an absolute reduction of 19.5%. Severe preeclampsia was recorded in 3 cases (4.8%) in the aspirin group and in 6 cases (23.1%) in the control group (reduction of 18.3%). Fetoplacental insufficiency was observed in 9 cases (14.5%) in the aspirin group and in 14 cases (53.8%) in the control group. From the fetal side, fetal growth restriction was identified in 5 cases (8.0%) in the aspirin group and in 10 cases (38.5%) in the control group; intrauterine hypoxia in 12 cases (19.4%) and 14 cases (53.8%); and preterm birth in 7 cases (11.3%) and 6 cases (23.1%), respectively. The aim of the study was to evaluate the real clinical effectiveness of aspirin prophylaxis, and it was shown that when 150 mg of aspirin is initiated at 14–16 weeks, it significantly reduces maternal and perinatal complications [10,12].

Asian studies demonstrated significant heterogeneity. In the APPEC randomized study conducted in China (n=898), 100 mg of aspirin did not show significant effectiveness in reducing preeclampsia (16.8% vs 17.1%). In contrast, in a randomized study conducted in India (n=178), 150 mg of aspirin was considerably more effective than 75 mg, reducing the incidence of preeclampsia from 17% to 6.5% (absolute −10.5%, relative ≈62%). These differences may be associated with population characteristics, BMI, genetic factors, and drug metabolism [9,10].

In the 2024 clinical protocol of the Ministry of Health of the Republic of Uzbekistan, aspirin prophylaxis is recommended for high-risk pregnant women at a dose of 150 mg/day from 11–14 weeks of gestation until 36 weeks, which is consistent with international evidence. However, due to the lack of large randomized clinical trials at the local level, these recommendations are mainly based on international data [1,7,12].

Overall, general meta-analyses (USPSTF 2021) show that low-dose aspirin reduces the risk of preeclampsia by an average of 15%, preterm birth by 20%, intrauterine growth restriction by 18%, and perinatal mortality by 21% in high-risk pregnant women. However, in individual studies, these

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indicators vary within a wide range — in some cases, a reduction from 0% (no effect) up to 60% has been observed [12].

At the same time, all studies confirm that aspirin prophylaxis does not provide complete protection. Preeclampsia still developed in 6–17% of women who received aspirin. This situation is explained by the following determinants: late initiation of the drug, insufficient dosage, high BMI and obesity, chronic hypertension and metabolic diseases, angiogenic imbalance (sFlt-1/PlGF), inflammatory and immune mechanisms, as well as poor adherence to therapy [9,10].

In conclusion, aspirin is an effective but limited means of preeclampsia prevention, and its maximum benefit is achieved through early initiation, optimal dose selection, and individualized risk-based patient selection [1,7,12].

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