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Pharmacotherapy of postpartum hemorrhage: modern evidence-based approaches

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Postpartum hemorrhage (PPH) remains one of the main causes of maternal morbidity and mortality in the world. Timely pharmacotherapy is a key element of complex treatment, which contributes to reducing the risk of serious complications and fatal consequences. Modern international recommendations provide for the early use of uterotonic drugs, antifibrinolytic therapy and the individualized choice of medical treatment depending on the etiology of bleeding; however, the results of the latest research require systematization and generalization.

Aim – to conduct a systematic analysis of modern scientific data on the effectiveness, safety and evidence base of pharmacotherapy of PPH, as well as to determine modern approaches to drug treatment in accordance with international clinical recommendations.

Early use of uterotonic drugs, primarily oxytocin, is the basis of medical treatment of PPH. In case of insufficient efficiency, carbetocin, methylergometrine, prostaglandins, and misoprostol are used, taking into account the clinical situation. Early administration of tranexamic acid within the first three hours after bleeding has been shown to reduce the risk of maternal mortality. The effectiveness of pharmacotherapy depends on timely diagnosis, adherence to clinical protocols and the combination of drug treatment with other methods of emergency obstetric care.

Conclusions. A systematic analysis of modern scientific data confirms that pharmacotherapy is a defining component of the complex treatment of PPH. Early use of oxytocin as a first-line drug, timely administration of tranexamic acid, and use of alternative uterotonic agents according to the clinical situation are the most justified from the standpoint of evidence-based medicine.

The author declares no conflict of interest.

Keywords: postpartum bleeding, pharmacotherapy, oxytocin, tranexamic acid, uterotonic drugs, evidence-based medicine.

Фармакотерапія післяпологової кровотечі: сучасні доказові підходи

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Післяпологова кровотеча залишається однією з основних причин материнської захворюваності та смертності у світі. Своєчасна фармакотерапія є ключовим елементом комплексного лікування, що сприяє зниженню ризику тяжких ускладнень і летальних наслідків. Сучасні міжнародні рекомендації передбачають раннє застосування утеротонічних препаратів, антифібринолітичної терапії та індивідуалізований вибір медикаментозного лікування залежно від етіології кровотечі, проте результати новітніх досліджень потребують систематизації й узагальнення.

Мета – провести систематичний аналіз сучасних наукових даних щодо ефективності, безпеки та доказової бази фармакотерапії післяпологової кровотечі, а також визначити сучасні підходи до медикаментозного лікування відповідно до міжнародних клінічних рекомендацій.

Раннє застосування утеротонічних препаратів, насамперед окситоцину, є основою медикаментозного лікування післяпологової кровотечі. Через недостатню ефективність використовують карбетоцин, метилергометрин, простагландини та мізопростол з урахуванням клінічної ситуації. Доведено, що раннє введення транексамової кислоти протягом перших трьох годин після виникнення кровотечі знижує ризик материнської смертності. Ефективність фармакотерапії залежить від своєчасної діагностики, дотримання клінічних протоколів і поєднання медикаментозного лікування з іншими методами невідкладної акушерської допомоги.

Висновки. Систематичний аналіз сучасних наукових даних підтверджує, що фармакотерапія є визначальним компонентом комплексного лікування післяпологової кровотечі. Найбільш обґрунтованими з позицій доказової медицини є раннє застосування окситоцину як препарату першої лінії, своєчасне призначення транексамової кислоти та використання альтернативних утеротонічних засобів відповідно до клінічної ситуації.

Автор заявляє про відсутність конфлікту інтересів.

Ключові слова: післяпологова кровотеча, фармакотерапія, окситоцин, транексамова кислота, утеротонічні препарати, доказова медицина.

Introduction

Postpartum hemorrhage (PPH) remains one of the most dangerous obstetric complications and the leading cause of maternal morbidity and mortality in the world [3,5,6]. Despite the improvement of obstetric care, the introduction of modern clinical protocols and the development of intensive care, its frequency remains high, especially in low- and middle-income countries [1,3,5]. At the same time, PPH is a significant problem for countries with a developed health care system, as it is accompanied

by the development of severe hemodynamic disorders, coagulopathy, the need for blood transfusions, surgical interventions, and an increase in the duration of hospitalization [3,5,12].

The main cause of postpartum bleeding is uterine atony, but traumatic injuries of the birth canal, retention of placental tissue, and disruption of the hemostatic system also play an important role. Rapid progression of blood loss requires immediate treatment, as even a slight delay in therapeutic measures significantly worsens the prognosis for the woman in labor [5,8,12]. That is why modern approaches to the management of PPH are based on the principles of early diagnosis, standardized treatment algorithms and timely application of effective drug therapy [5,8,12].

Pharmacotherapy is a basic component of the complex treatment of PPH. According to modern international recommendations, the first-line drug remains oxytocin, the effectiveness of which has been proven by numerous randomized clinical trials [4,10,20]. In the absence of an adequate clinical effect, other uterotonic agents are used, including carbetocin, methylergometrine, prostaglandins, and misoprostol. In recent years, much attention has been paid to the use of tranexamic acid, the early administration of which is associated with a reduction in the risk of death from bleeding without a significant increase in the frequency of thrombotic complications [2,14,21].

The emergence of new results of multicenter clinical studies, updating the recommendations of international professional organizations, and the implementation of the principles of evidence-based medicine made it necessary to review modern approaches to the medical treatment of PPH [2,5,10,16]. Despite the considerable amount of accumulated scientific data, the issue of the optimal choice of pharmacological agents, the sequence of their use and the assessment of the clinical effectiveness of individual therapy schemes remain the subject of active scientific discussions. Generalization of modern evidence is important for improving clinical practice, improving the quality of obstetric care and reducing maternal mortality [3,5,8,12].

Aim – to conduct a systematic analysis of modern scientific data on the effectiveness, safety, and evidence base of pharmacotherapy of PPH, as well as to determine modern approaches to drug treatment in accordance with international clinical recommendations.

The research was carried out in the format of a systematic review of scientific literature in accordance with the principles of evidence-based medicine and the guidelines of PRISMA 2020. The information search was carried out in international scientometric databases PubMed, Scopus, Web of Science, and Google Scholar.

The systematic review included full-text articles published between 2015 and 2025 that addressed the issue of medical treatment of PPH, evaluated the efficacy and safety of pharmacological agents, or contained current clinical guidelines. Preference was given to randomized controlled trials, systematic reviews, meta-analyses, cohort studies, and international clinical guidelines. Duplicate publications, conference proceedings without full text, individual clinical cases, letters to the editor, and studies that did not meet the purpose of the review were excluded.

Methods of bibliosemantic analysis, systematization, comparison, generalization, and critical evaluation of scientific sources were used to generalize the obtained data. The synthesis of the results was carried out by qualitative analysis of the evidence base regarding the use of uterotonic drugs, tranexamic acid and other drugs in the treatment of PPH, taking into account modern approaches to evidence-based medicine.

As a result of a systematic analysis of the scientific literature, it was established that modern approaches to the pharmacotherapy of PPH are based on the principles of early medical intervention, the use of drugs with proven clinical effectiveness, and comprehensive management of patients in accordance with standardized algorithms for providing emergency obstetric care [3,5,8,12]. The analyzed studies demonstrate a high degree of agreement regarding the need for immediate treatment after the diagnosis is established, since the timely use of drugs significantly affects the volume of blood loss, the frequency of hemorrhagic shock, the need for transfusion of blood components, and the risk of maternal mortality [1–3,6].

Most studies confirm that oxytocin remains the first-line drug for the prevention and treatment of PPH. The generalization of the results of randomized controlled trials shows that its use ensures a rapid contraction of the myometrium, helps to reduce blood loss and reduces the need to use additional uterotonic agents [4,10,13,20]. At the same time, part of the works indicates that the effectiveness of oxytocin may be lower in women who re-

ceived long-term stimulation of labor, which is associated with a decrease in the sensitivity of oxytocin receptors. In such cases, the authors recommend an early transition to combined drug therapy without waiting for significant blood loss [7,13].

In the analyzed sources, considerable attention is paid to carbetocin as a modern uterotonic drug of prolonged action. The results of most clinical studies indicate that its use allows for a reduction in the need for repeated administration of uterotonics, to reduce the frequency of additional medical interventions, and to ensure longer uterine contractions compared to oxytocin [17,20]. At the same time, a number of publications emphasize that the clinical benefits of carbetocin are most noticeable among patients with a high risk of PPH, in particular, after cesarean section. At the same time, it is reported that the economic aspects of the drug's use may limit its wide implementation in routine clinical practice [5,17].

The analysis of the results of studies devoted to the use of prostaglandins showed that misoprostol is an effective alternative drug in cases of insufficient effectiveness of oxytocin or the absence of the possibility of using injectable uterotonic agents [18–20]. Most authors note its availability, ease of use and stability at room temperature, which is an important advantage for medical institutions with limited material and technical support [18,19]. At the same time, it was established that the use of misoprostol is more often accompanied by the development of short-term adverse reactions, among which chills, increased body temperature, nausea, and vomiting predominate [18–20].

The conducted analysis also proved that the use of methylergometrine provides a rapid uterotonic effect, but its use is limited due to the possibility of developing cardiovascular side effects [5,8,20]. In most studies, it is indicated that the drug is not recommended for patients with preeclampsia, arterial hypertension, or other severe cardiovascular pathology. In this regard, its use is mainly considered a component of the second line of drug therapy after assessment of possible risks [5,8,20].

A separate block of analyzed publications was devoted to tranexamic acid. Summarizing the results of multicenter clinical studies confirmed that early administration of the drug, preferably within the first three hours after the development of bleeding, significantly reduces the risk of death from blood loss, reduces the need for hemotransfusion and the frequency of emergency hysterectomy [2,14–16]. At the same time, the majority of authors did not find a statistically significant increase in the frequency of thromboembolic complications if the recommended dosage regimens were followed. It has been established that the greatest clinical effect of tranexamic acid is observed when it is used simultaneously with uterotonic drugs as part of complex treatment [2,14,21].

The analysis of literary sources also showed that the effectiveness of pharmacotherapy depends not only on the choice of the drug, but also on the organization of medical care. Most studies report improvement in clinical outcomes when using standardized algorithms for management of postpartum bleeding, which involve simultaneous drug therapy, infusion-transfusion support, laboratory monitoring of the hemostatic system, and continuous assessment of the patient's hemodynamic status [5,8,12]. The authors note that the implementation of such algorithms contributes to shortening the time to the start of treatment, reducing the volume of blood loss and the frequency of severe obstetric complications [3,5,8,12].

The results of a systematic review indicate the growing role of a personalized approach to the medical treatment of PPH. Modern studies emphasize the need to take into account the cause of bleeding, the mode of delivery, the presence of concomitant diseases, individual risk factors and the clinical condition of the woman when choosing the optimal regimen of pharmacotherapy [3,5,6]. This approach provides the possibility of timely correction of treatment tactics, increases the effectiveness of medical intervention and contributes to the improvement of treatment results.

The results of the conducted systematic review are consistent with modern international clinical recommendations, according to which pharmacotherapy is the basis of PPH treatment and should be started immediately after diagnosis [5,8,12]. The analysis of literary sources shows the high consistency of the positions of international professional organizations regarding the use of oxytocin as a first-line drug. Despite the emergence of new uterotonic drugs, oxytocin remains the «gold standard» due to its high efficiency, relative safety and significant clinical experience of its use [4,10,20].

At the same time, the results of modern research demonstrate a gradual expansion of the possibilities of drug treatment of PPH. Carbetocin is characte-

rized by a longer effect and allows for reducing the need for repeated administration of uterotonic drugs, which is especially important in patients with a high risk of developing massive blood loss [17,20]. However, the economic availability of the drug remains one of the factors that limit its widespread introduction into clinical practice, especially in countries with limited financing of the health care system. In this regard, most authors support the feasibility of a differentiated approach to the choice of uterotonic therapy, taking into account the clinical situation and resource provision of the medical institution [5,12,17].

In recent years, special attention has been paid to tranexamic acid, the effectiveness of which has been confirmed by the results of large international clinical studies. Unlike uterotonic drugs, its mechanism of action is aimed at inhibiting fibrinolysis, which allows for the stabilization of the formed thrombus and reduces subsequent blood loss [2,14,21]. The generalization of scientific data shows that the maximum therapeutic effect is achieved when the drug is administered within the first three hours after the development of bleeding. A later appointment significantly reduces clinical effectiveness, which emphasizes the need for early diagnosis and quick treatment decisions [2,15,21].

The analysis also confirms that drug therapy should not be considered in isolation. Most modern clinical guidelines emphasize the need for comprehensive management of patients with postpartum bleeding, which includes assessment of hemodynamic status, early initiation of infusion-transfusion therapy, laboratory monitoring of hemostasis indicators, mechanical methods of bleeding control, and, if necessary, timely surgical intervention [5,8,12]. It is the multidisciplinary approach that provides the most favorable clinical results and reduces the risk of multiple organ failure and maternal mortality [3,5,8].

Along with the positive results, the analysis of the literature revealed a number of unresolved issues. Different studies used different criteria for assessing the massiveness of blood loss, different drug dosage regimens, and heterogeneous clinical groups of patients, which makes it difficult to directly compare the obtained results [10,14–16,21]. In addition, part of the research was conducted in highly specialized medical centers, which may limit the possibility of extrapolation of their conclusions to institutions with less resource provision [1,11].

Optimizing combined pharmacotherapy regimens, determining the most effective sequence of drug use, personalizing treatment taking into account risk factors, and searching for new pharmacological agents with greater efficacy and a better safety profile remain promising directions for further research. Equally important is the implementation of uniform standardized treatment algorithms, regular training of medical personnel, and ensuring the availability of modern medicines in maternity hospitals of various levels. Comprehensive implementation of these measures will contribute to increasing the effectiveness of PPH treatment, improving the quality of obstetric care, and further reducing maternal morbidity and mortality.

Conclusions

A systematic analysis of modern scientific literature confirmed that PPH remains one of the most dangerous obstetric complications, and timely pharmacotherapy is a determining factor in reducing maternal morbidity and mortality. Summarizing the results of research shows that the most reasonable strategy of medical treatment is the early use of uterotonic drugs, primarily oxytocin, which remains the first-line drug according to modern international clinical recommendations. In the absence of a sufficient clinical effect, it is advisable to use carbetocin, methylergometrine, misoprostol and other uterotonic agents, taking into account the clinical situation, concomitant pathology and possible contraindications.

It has been established that the inclusion of tranexamic acid in the complex treatment scheme, especially when it is administered within the first three hours after the onset of bleeding, reliably improves clinical results, reduces the volume of blood loss, the need for hemotransfusions, and the risk of fatal consequences. The effectiveness of pharmacotherapy largely depends on early diagnosis, strict adherence to standardized treatment algorithms, individualization of drug therapy and its combination with other methods of emergency obstetric care. Further improvement of clinical protocols, expansion of the evidence base regarding optimal treatment regimens, and introduction of modern international recommendations into the practice of obstetric hospitals will contribute to increasing the effectiveness of treatment of PPH and improving maternal and perinatal outcomes.

The author declares no conflict of interest.

References/Література

1. Ammerdorffer A, Rushwan S, Timms R, Wright P, Beeson L, Devall AJ et al. (2022, Jun). Quality of oxytocin and tranexamic acid for the prevention and treatment of postpartum hemorrhage in Kenya, Nigeria, South Africa, and Tanzania. Int J Gynaecol Obstet. 158; Suppl 1: 46-55. doi: 10.1002/ijgo.14197.
2. Bienstock JL, Eke AC, Hueppchen NA. (2021, Apr 29). Postpartum Hemorrhage. N Engl J Med. 384(17): 1635-1645. doi: 10.1056/NEJMra1513247.
3. Brenner A, Ker K, Shakur-Still H, Roberts I. (2019, Nov). Tranexamic acid for post-partum haemorrhage: What, who and when. Best Pract Res Clin Obstet Gynaecol. 61: 66-74. doi: 10.1016/j.bpobgyn.2019.04.005.
4. De Silva M, Mizzi G, Potts E, Webb J, Thyer E, Naidoo N. (2024, Apr). Tranexamic acid versus oxytocin for primary postpartum Haemorrhage in the out-of-hospital setting: A systematic review with implications for rural practice. Aust J Rural Health. 32(2): 227-235. doi: 10.1111/ajr.13103.
5. Diop A, Abbas D, Ngoc NTN, Martin R, Razafi A et al. (2020, Mar 6). A double-blind, randomized controlled trial to explore oral tranexamic acid as adjunct for the treatment for postpartum hemorrhage. Reprod Health. 17(1): 34. doi: 10.1186/s12978-020-0887-2.
6. Ducloy-Bouthors AS, Jude B, Duhamel A, Broisin F, Huissoud C, Keita-Meyer H et al. (2011). Mandelbr High-dose tranexamic acid reduces blood loss in postpartum haemorrhage. Crit Care. 15(2): R117. doi: 10.1186/cc10143.
7. Elbohoty AE, Mohammed WE, Sweed M, Bahaa Eldin AM et al. (2016, Sep). Randomized controlled trial comparing carbetocin, misoprostol, and oxytocin for the prevention of postpartum hemorrhage following an elective cesarean delivery. Int J Gynaecol Obstet. 134(3): 324-328. doi: 10.1016/j.ijgo.2016.01.025.
8. Gallos ID, Papadopoulou A, Man R, Athanasopoulos N, Tobias A, Price MJ et al. (2018, Dec 19). Uterotonic agents for preventing postpartum haemorrhage: a network meta-analysis. Cochrane Database Syst Rev. 12(12): CD011689. doi: 10.1002/14651858.CD011689.pub3. Update in: Cochrane Database Syst Rev. 2025 Apr 16; 4: CD011689. doi: 10.1002/14651858.CD011689.pub4.
9. Giouleka S, Tsakiridis I, Kalogiannidis I, Mamopoulos A, Tentas I et al. (2022, Nov). Postpartum Hemorrhage: A Comprehensive Review of Guidelines. Obstet Gynecol Surv. 77(11): 665-682. doi: 10.1097/OGX.0000000000001061.
10. Günaydın B. (2022, Dec). Management of Postpartum Haemorrhage. Turk J Anaesthesiol Reanim. 50(6): 396-402. doi: 10.5152/TJAR.2022.21438.
11. Jones AJ, Federspiel JJ, Eke AC. (2023, Feb). Preventing postpartum hemorrhage with combined therapy rather than oxytocin alone. Am J Obstet Gynecol MFM. 5(2S): 100731. doi: 10.1016/j.ajogmf.2022.100731.
12. Koch DM, Rattmann YD. (2019, Nov 7). Use of misoprostol in the treatment of postpartum hemorrhage: a pharmacoepidemiological approach. Einstein (Sao Paulo). 18: eAO5029. doi: 10.31744/einstein_journal/2020AO5029.
13. Pacheco LD, Clifton RG, Saade GR, Weiner SJ, Parry S, Thorp JM Jr et al. (2023, Apr 13). Tranexamic Acid to Prevent Obstetrical Hemorrhage after Cesarean Delivery. N Engl J Med. 388(15): 1365-1375. doi: 10.1056/NEJMoa2207419.
14. Parry Smith WR, Papadopoulou A, Thomas E, Tobias A, Price MJ, Meher S et al. (2020, Nov 24). Uterotonic agents for first-line treatment of postpartum haemorrhage: a network meta-analysis. Cochrane Database Syst Rev. 11(11): CD012754. doi: 10.1002/14651858.CD012754.pub2.
15. Sentilhes L, Vayssière C, Deneux-Tharaux C, Aya AG, Bayoumeu F, Bonnet MP et al. (2016, Mar). Postpartum hemorrhage: guidelines for clinical practice from the French College of Gynaecologists and Obstetricians (CNGOF): in collaboration with the French Society of Anesthesiology and Intensive Care (SFAR). Eur J Obstet Gynecol Reprod Biol. 198: 12-21. doi: 10.1016/j.ejogrb.2015.12.012.
16. Sentilhes L, Winer N, Azria E, Sénat MV, Le Ray C, Vardon D et al. (2018, Aug 23). Tranexamic Acid for the Prevention of Blood Loss after Vaginal Delivery. N Engl J Med. 379(8): 731-742. doi: 10.1056/NEJMoa1800942
17. Torloni MR, Siaulys M, Riera R, Cabrera Martimbianco AL, Leite Pacheco R, Latorraca COC et al. (2021, Jun 3). Timing of oxytocin administration to prevent post-partum hemorrhage in women delivered by cesarean section: A systematic review and metanalysis. PLoS One. 16(6): e0252491. doi: 10.1371/journal.pone.0252491.
18. Vallera C, Choi LO, Cha CM, Hong RW. (2017, Jun). Uterotonic Medications: Oxytocin, Methylergonovine, Carboprost, Misoprostol. Anesthesiol Clin. 35(2): 207-219. doi: 10.1016/j.anclin.2017.01.007.
19. Winikoff B, Dabash R, Durocher J, Darwish E, Nguyen TN, León W et al. (2010, Jan 16). Treatment of post-partum haemorrhage with sublingual misoprostol versus oxytocin in women not exposed to oxytocin during labour: a double-blind, randomised, non-inferiority trial. Lancet. 375(9710): 210-216. doi: 10.1016/S0140-6736(09)61924-3.
20. Wormer KC, Jamil RT, Bryant SB. (2024, Jul 19). Postpartum Hemorrhage. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2026 Jan–. PMID: 29763164.

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