Review

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Uterine Artery Embolization in the Treatment of Postpartum Hypotonic Bleeding

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ABSTRACT Postpartum hemorrhage is a serious obstetric complication due to the threat to the life and health of a woman. One of the common causes of bleeding in the postpartum period is uterine hypotension. If conservative methods of treating hypotonic bleeding are ineffective, hemostatic compression sutures are applied to the body of the uterus, ligation/clipping of the main vessels of the uterus and (or) ligation of the internal iliac arteries. If available, endovascular uterine artery embolization (UAE) is performed. The review is devoted to the efficacy and safety of UAE in pregnant women with postpartum hypotonic bleeding, as well as to the long-term results of follow-up.

Keywords: postpartum hemorrhage; atony of the uterus; embolization of uterine arteries; long-term results; fertility

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CBV - circulating blood volume

PPH - postpartum hemorrhage

UAE - uterine artery embolization

PES - post-embolization syndrome

PR - pregnancy rate

INTRODUCTION

About 300,000 women die worldwide due to complications of pregnancy and childbirth annually [1, 2]. In the Russian Federation in 2020, the maternal mortality rate was 11.2 per 100,000 live births [3]. In the structure of maternal deaths in 2020 in the Russian Federation, bleeding (6.4%) took 3rd place after extragenital diseases (71.4%) and septic complications (8.1%) [3]. According to the literature, the global average of the share of obstetric

bleeding in maternal mortality reaches 16–27%, exceeding 50% in Asia and Africa [4–8]. In the Russian Federation, in 2020, the maternal mortality rate from hemorrhages during childbirth and the postpartum period was 0.28 per 100,000 live births [3].

One of the most common causes (64-80%) of postpartum hemorrhage (PPH) is uterine hypotension, a condition in which the tone and contractility of the uterus are sharply reduced with a preserved reflex response [9-14]. The lack of adequate and timely assistance leads to massive blood loss — a simultaneous loss of more than 1,500 ml of blood (25-30% of circulating blood volume — CBV) or more than 2,500 ml of blood (50% of CBV) in 3 hours [13, 14].

The Clinical Guidelines "Postpartum hemorrhage" (2021) draws attention to the importance of determining the volume of blood loss exclusively by the gravimetric method, using the weighing of the surgical material, and, if conditions are available, the hardware reinfusion of the autoerythrogenic suspension. In addition to a clear understanding of the nominal volume of blood loss in milliliters, its calculation as a percentage of the initial CBV of a pregnant woman is of great importance, which determines the volume and composition of infusion-transfusion therapy and surgical tactics [13].

1. CHOICE OF METHOD OF SURGICAL TREATMENT OF POSTPARTUM HYPOTONIC BLEEDING

In obstetric practice, in order to prevent hypotonic bleeding, the tactics of "active management of the third stage of delivery" are used, including the introduction of uterotonics (oxytocin, carbetocin, methylergometrine), prostaglandins immediately after delivery, early clamping and cutting of the umbilical cord, the use of controlled traction for the umbilical cord to isolate the placenta [5, 13, 15, 16].

The Clinical Guidelines "Postpartum Hemorrhage" (2021) developed a consistent algorithm of actions for bleeding [13]. At the first (non-surgical) stage, external massage and manual examination of the uterus are used, with continued bleeding, an intrauterine balloon is inserted, if it is ineffective, they switch to ligation of the internal iliac arteries or embolization of the uterine arteries (UAE), depending on the equipment of the institution, in the absence of a hemostatic effect, hysterectomy is performed [13, 16, 17].

Balloon tamponade of the uterus (balloons *Bakri*, *Folli*, *Sengstaken-Blekmor Rush* and others) has found its place in postpartum hypotonic bleeding. The method is easy to use, helps stop bleeding in uterine hypotension in 78–90% of cases, and is characterized by a minimal number of complications [5, 6, 12].

A.A. Askerov et al. it has shown that the use of uterine balloon tamponade in the treatment of hypotonic PPH contributed to a decrease in blood loss, the frequency of surgical interventions, and the need for blood transfusion [18]. In the study of T.V. Legalova and I.I. Kukarskaya hysterectomy was avoided and reproductive function was preserved in all patients with hypotonic PPH due to the use of controlled balloon tamponade of the uterus [12].

With the ineffectiveness of conservative methods of hemostasis, the choice of the type of surgical treatment is determined by the characteristics of the obstetric situation, the volume of blood loss, the equipment of the hospital, and the qualifications of the surgeon. The simplest methods are uterine ischemia by applying clamps to the uterine and ovarian arteries, as well as hemostatic compression sutures to the uterus (B-Lynch, Pereira, etc.) [4, 5].

The important role of bilateral ligation of the internal iliac arteries is not denied. This technique is effective in almost all patients with hypotonic bleeding [4, 7, 9].

Kurtser M.A. et al. in their study showed that after ligation of the internal iliac arteries, 56.4% of patients additionally lost up to 300 ml of blood. The authors confirmed that vascular ligation can be undertaken when embolization is ineffective and does not require laparotomy, while the reverse sequence of measures is extremely difficult or impossible [9].

Wang C.Y. et al. conducted a comparative analysis of the effectiveness of bilateral ligation of the internal iliac arteries and UAE in 40 patients with hypotonic postpartum hemorrhage. It was found that the efficiency of vessel ligation was 88.9%, there were no postoperative complications. At the same time, two patients who underwent UAE died of DIC (disseminated intravascular coagulation). The authors concluded that ligation of the internal iliac arteries is safer for massive blood loss accompanied by consumption coagulopathy and should be performed as soon as possible when an indication for emergency obstetric care appears [19].

If organ-preserving surgical methods are ineffective, hysterectomy is performed, which additionally increases the volume of intraoperative blood loss by 500-1000 ml. The frequency of emergency postpartum hysterectomy performed for PPH in the world is from one to three cases per 1000 births [5, 20], in Russia it is 1.11 and 1.07 per 1,000 births in 2019 and 2020, respectively, in Moscow it is 0.15 and 0.11 per 1,000 births, respectively [3].

Dahlke J.D. et al. compared 4 protocols for the treatment of massive postpartum hemorrhage: American College of Obstetricians and Gynecologists (ACOG), Royal Australian and New Zealand College of Obstetricians and Gynecologists (RANZOG), Royal College of Obstetrician and Gynecologists (RCOG) and Society of Obstetricians and Gynecologists of Canada (SOGC). All experts emphasized the need for minimal aggression and preservation of fertility, although representatives of the UK considered it appropriate to switch to hysterectomy earlier under the motto "better sooner than later" [21].

Kurtser M.A. et al., on the contrary, recommended to avoid hysterectomy in PPH if possible, which increases total blood loss and can lead to the death of a woman [9].

2. UTERINE ARTERY EMBOLIZATION AS AN ALTERNATIVE TO HYSTERECTOMY FOR OBSTETRIC BLEEDING

2.1. Efficacy and safety of uterine artery embolization

For more than 30 years, the UAE method has been used in emergency obstetrics for the treatment of postpartum hemorrhage [10, 22–24]. This minimally invasive and effective intervention, which requires additional equipment and qualified personnel, is used in case of failed conservative hemostasis, allows bleeding to be controlled and avoid hysterectomy [10, 25, 26].

Uterine artery embolization is successfully used not only for hypotonic postpartum hemorrhage, but also for placental anomalies, injuries of the soft birth canal, arteriovenous malformation of the uterine body. The indication for selective UAE may be the ineffectiveness of hemostasis after hysterectomy due to coagulopathy [19, 23, 24, 27–29].

In Russia, in order to arrest postpartum hemorrhage, UAE was first used by M.A. Kurtser in 2006 at the Family Planning and Reproduction Center. In the study of M.A. Kurtser et al. it was shown that vascular embolization is an effective and safe way to stop postpartum hemorrhage, as well as a method of choice that promotes rapid hemostasis. The authors proved that UAE is the method of choice for hypotonic postpartum hemorrhage, refractory to conservative therapy, and only in the absence of the effect of UAE is it reasonable to attempt bilateral ligation of the internal iliac arteries [9].

In the domestic literature, there are only a few works on the role of UAE in the treatment of hypotonic bleeding, which forced us to resort to the analysis of foreign studies on this topic [10].

According to *Ikeda A. et al.*, patients with postpartum hemorrhage before surgery needed a comprehensive examination, including computed tomography (CT), which makes it possible to judge the need for UAE by the presence of arterial bleeding, its location, and the shape of the uterine cavity [30]. As shown in the study, if signs of bleeding from a blood vessel (extravasates) were dobserved in the lower segment of the uterus, it is possible to perform balloon tamponade; and when the source of bleeding is located in the upper part of the uterus, UAE is required [30]. At the same time, the Clinical guidelines "Postpartum hemorrhage" (2021) clearly indicate that patients with PPH as an instrumental examination are sufficient to conduct an ultrasound examination [13].

Angiography is an accurate diagnostic method that allows assessing the characteristics of the blood supply to the pelvic organs and identifying the source of bleeding [24, 27]. According to *Dinc G. et al.*, vascular extravasation was the most common (100%) angiographic sign of postpartum hypotonic bleeding [28]. At the same time, *Aoki M. et al.* did not consider contrast agent extravasation to be the main angiographic sign of PPH, as it was observed only in 15 patients with uterine atony and bleeding (45%) [31].

An analysis of literature data on the technical aspects of X-ray endovascular intervention showed that for the purpose of hemostasis in postpartum hypotonic bleeding, the authors more often used gelatin sponges with a diameter of 500 to 1000 microns, dry particles of polyvinyl alcohol, gel foam, N-butyl-2-cyanoacrylate (NBCA), glue and *Gelfoam* [24, 27, 32]. The uterine artery, internal iliac and inferior mesenteric arteries were more often embolized [27, 28, 33].

According to modern concepts, emergency UAE is a safe and highly effective method of hemostasis in life-threatening postpartum hypotonic bleeding. According to various authors, the clinical success rate was 72.7–91.3% [19, 26–29, 31, 33, 34].

Liu Z. et al., in a meta-analysis of 14 studies involving 956 patients with hypotonic postpartum hemorrhage, showed that UAE significantly reduced blood loss during labor (893.39 ml; 95% CI: 581.13–1205.65), reduced operation time (37.19 min; 95% CI: 29.96–44.42) and length of hospital stay (5.36 days; 95% CI: 4.97–5.76) compared with patients who underwent hysterectomy: 1255 ml; 56.12 min; 7.13 days, respectively (p < 0.001) [35].

Spreu A. et al. managed to preserve the uterus in all 16 patients who underwent UAE for hypotonic bleeding, while hysterectomy was inevitable in 2 out of 22 women with PPH (9.1%) who received uterine compression sutures and did not undergo UAE. The levels of hemoglobin, fibrinogen and platelet count after treatment were higher in the UAE group (96.73 \pm 2.78 g/l, 149.67 \pm 17.23 \times 10 °/l and 4.67 \pm 0.42 g/l, respectively) than in the group of patients who did not undergo UAE: 90.77 \pm 3.22 g/l (p =0.19), 109.00 \pm 11.84 \times 10 °/l (p =0.01) and 4.04 \pm 0.40 g/l (p =0.31) [26].

The ineffectiveness of the interventional technique is often associated with the peculiarities of the vascular anatomy of the small pelvis. According to *Aoki M. et al.*, the presence of anastomosis of the uterine and ovarian arteries (blood flow type *A*) was the cause of ongoing hypotonic bleeding after UAE. The authors concluded that patients with type A require selective embolization of the ovarian branches of the uterine arteries in addition to UAE [31].

Lee S. M. et al. showed that the inefficiency of UAE may also be associated with the type of embolizing agent, for example, the effect is often absent when using a gelatin sponge in patients with severe coagulopathy [22].

Lai B.M. et al. revealed other significant factors of failed embolization in postpartum hemorrhage: platelet count before embolization ($84.5\pm21.2\times10^{9}$ /l; p=0.036) and maternal age (37.0 ± 3.7 years; p=0.019). Since a low platelet count before intervention and a late reproductive age of the mother are associated with a higher likelihood of embolization failure, these patients, according to the authors, require careful post-embolization monitoring [33].

Re-bleeding after successful UAE may be caused by recanalization of a previously embolized artery due to restoration of hemodynamics and occurrence of episodes of increased blood pressure [24]. According to *Choi W. et al.*, recanalization is the main source of recurrent bleeding after UAE (60.6%) performed for hypotonic bleeding [34].

Along with the evaluation of effectiveness, the question of the safety of endovascular intervention is always raised.

According to *Zhang X.Q. et al.*, the main complication after UAE performed for postpartum hypotonic bleeding is post-embolization syndrome (PES) [27]. Post-embolization syndrome (PES) is a complex of subjective and laboratory abnormalities that occurred after UAE (pain, nausea and/or vomiting, fever, fatigue, discomfort, leukocytosis, hypertransaminasemia) [36].

The main pathogenetic mechanism for the development of PES is myometrial ischemia [37]. Ischemic damage to the muscular layer of the uterus after UAE is similar to myocardial ischemia, in which chemical mediators such as lactate and adenosine are released, stimulating sensitive receptors. To avoid myometrial ischemia in recent years, doctors are increasingly abandoning the aggressive technique, which is characterized by embolization until complete stasis of contrast in the uterine artery [36].

Ruiz Sanchez E. et al. described a case of uterine necrosis after UAE performed for hypotonic bleeding in a 37-year-old female patient. On the 16th day, she sought a consultation due to a recurrence of fever. According to magnetic resonance imaging, a diagnosis of uterine necrosis was established. An abdominal hysterectomy was performed [38].

Wang C.Y. et al. reported two deaths in patients with hypotonic uterine bleeding [19]. It is well known that in patients with massive blood loss after childbirth and unstable hemodynamic parameters, when choosing a method of treatment, preference should be given to ligation of the internal iliac arteries, rather than embolization of the uterine vessels.

2.2. The results of dynamic monitoring of patients with hypotonic postpartum hemorrhage who underwent uterine artery embolization

The next step in studying the role of UAE in the treatment of obstetric bleeding was the study of its effect on the possibility of the onset and bearing of subsequent pregnancies [25, 27, 39].

With regard to reproductive function, the opinion of most authors is the same: UAE does not affect fertility and pregnancy outcomes in women in the future [26, 39, 40]. However, data on the pregnancy rate (PR) after UAE are very contradictory and do not reveal the features of the gestation period.

Lai B.M. et al. reported that only 2 patients (6.1%) became pregnant after UAE, but one of them had an ectopic pregnancy [33]. In a study by *Aguilar-Crespo A. et al.* normal menstruation was restored in 21 patients (64%) who underwent UAE due to hypotonic bleeding; became pregnant in subsequent years 6 (18.2%) [29].

Sentilhes L. et al. analyzed reproductive function in 68 patients who underwent UAE for hypotonic bleeding. In 17 patients (25%), one ectopic and 25 uterine pregnancies were observed, the latter ended in 4 miscarriages, 2

abortions and 19 births. Pregnancies (in 19 patients) proceeded without complications. PR and pregnancy outcomes did not differ between patients undergoing embolization and uterine-sparing surgery [40].

A review of the literature by *Soro M.P.* found that UAE performed for postpartum hypotonic hemorrhage did not adversely affect the menstrual cycle, fertility, and subsequent pregnancies, and the PR, according to the literature, was high and reached 70–80% [25] . *Toguchi M. et al.* confirmed a high PR (60.9%; 14 of 23) after UAE, the birth rate was 71.4% (10 of 14) [41].

At the same time, it is impossible not to ignore the deviations of reproductive function and adverse outcomes of subsequent pregnancies identified after UAE by a number of foreign authors. Thus, *Toguchi M. et al.* found that patients who underwent UAE for postpartum hemorrhage were later diagnosed with ovarian dysfunction (4.9%), endometritis (16.2%), and Asherman's syndrome (1.6%) [41].

Imafuku H. et al. conducted an analysis of the course of subsequent pregnancies and outcomes of childbirth in patients with postpartum hemorrhage and blood loss of more than 2,000 ml, treated with and without UAE. It was found that in patients with a history of UAE due to hypotonic bleeding, compared with the group of women in labor who had PPH in the past, but UAE was not used, during childbirth there were significantly more: the volume of blood loss (1,581 ml and 1,021 ml, respectively; p < 0.01) and the frequency of rebleeding (35.7% and 9.4%, respectively; p < 0.05). At the same time, there were no significant differences between the two groups in the incidence of preterm birth, hypertensive disorders, and fetal growth retardation [42].

A high risk of developing abnormal placentation and/or recurrence of massive postpartum hemorrhage in subsequent pregnancies after the use of UAE for hypotonic bleeding was also noted by other authors [25, 27, 41, 42].

Thus, according to *Imafuku H. et al.*, placenta ingrowth occurred in 7 out of 14 patients who underwent UAE (50%), while none of the 32 observed in whom standard surgical methods were used for the treatment of PPH had this complication did not develop [42]. In a study by *Toguchi M. et al.* the incidence of placenta ingrowth after UAE performed for PPH was lower, accounting for 17.7% (11 of 62) [41].

Saiga A. et al. found that the frequency of intrauterine synechia was significantly higher in the group of patients in whom a gelatin sponge suspension was used as an embolizing agent (83.3%), compared with those observed who received the same substance, but in the form of a filling material (0%; p < 0.001) [43].

CONCLUSION

Hypotonic hemorrhage, being the most common and most formidable complication of the postpartum period, remains the focus of attention of obstetricians around the world.

The search for modern methods of hemostasis, corresponding to the principles of efficiency, safety and expediency is of greatest interest. The similar criteria are met by uterine artery embolization, which has taken its rightful place in the treatment of hypotonic bleeding. Further efforts of scientists will be aimed at analyzing the long-term results of the use of endovascular organ-preserving techniques, their impact on the reproductive potential and quality of life of women.

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