MISTAKES IN THE USE OF DRUGS IN THE TREATMENT OF MASSIVE OBSTETRIC BLEEDING IN WOMEN

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Annotation. The article describes the analysis of the causes of massive obstetric bleeding, treatment features, possible errors in conservative and surgical treatment in a retrospective group of patients studied at the regional perinatal center in the city of Urgench, Khorezm region in the Republic of Uzbekistan.

Key words: massive obstetric bleeding, placental abruption, uterine atony, infusion-transfusion therapy, total hysterectomy.

Bleeding during pregnancy and childbirth is one of the leading causes of maternal mortality, as well as women's disability, the development of asthenovegetative, neuroendocrine syndromes and other diseases. According to the World Health Organization in 2017, bleeding accounted for 30.0% of the causes of maternal death, and in Uzbekistan for 2013-2015 - 25.8% (9,10,14,19).

It is known that only 62-65% of births through the natural birth canal are accompanied by physiological blood loss, 1/3 of patients lose from 500 to 1000 ml of blood, and in 3-8% of cases, the volume of blood loss exceeds 2% of the body weight of the woman in labor or more than 30% of BCC is considered massive obstetric bleeding (MAH), requiring transfusion of red blood cells and often removal of the uterus (2,11).

The main causes of bleeding are disturbances in the processes of separation of the placenta and excretion of the placenta, detachment of a normally located placenta, placenta previa, sepsis, obstetric embolism, traumatic injuries of the birth canal, uterine rupture, decreased contractile activity of the myometrium (atony of the uterus) and disorders in the hemocoagulation system, most of them are accompanied by massive obstetric bleeding (1,7,8,20).

In our republic, according to the National Committee for Confidential Investigation of Maternal Deaths (MS), with massive blood loss, inadequate treatment was carried out and in 34% of cases it was associated with a delay in the onset of surgical hemostasis and technical difficulties during hysterectomy (9).

The purpose of the research: evaluation of the effectiveness of therapeutic measures for massive obstetric bleeding in a retrospective group.

Material and methods. Analysis and evaluation of the results of treatment of massive obstetric bleeding in the retrospective group was carried out from the period 2014 to 2017. The material was collected and analyzed on the basis of the perinatal center in Urgench, studying the history of childbirth, clinical and laboratory data, the prescription sheet and the anesthesia card. Studied clinical and biochemical blood tests, if necessary, hemostasiogram, urinalysis. The retrospective group included 178 pregnant women, parturient women and puerperas who underwent massive obstetric bleeding and total hysterectomy during

childbirth and in the early postpartum period. The following methods were used to determine the volume of blood loss: visual; gravimetric - the surgical material was weighed and the volume of blood loss was calculated using the Libov formula. Conducted ultrasound examination of the fetus, abdominal cavity and, if necessary, computed tomography of the pelvic organs.

Discussion of the obtained results.

During 4 years, from 2014 to 2017, 32896 births occurred in the perinatal center in Urgench, and 178 of them ended in massive obstetric bleeding (MAH), which amounted to 0.54%, and during this period there were 5 (45.4%) cases of maternal mortality from this pathology.

The concept of the term MAC is defined by the following criteria: it is a blood loss of more than 150 ml / min, more than 50% of the BCC for 3 hours, more than 1500-2000 ml or the need for more than 10 doses of erythrocyte mass within 24 hours, as well as a decrease in hematocrit by 10% in combination with hemodynamic disorders (arterial hypotension) (2)

Of all 178 cases of MAC, 75 (42.1%) bleeds occurred during pregnancy. Of these, against the background of detachment of a normally located placenta of mild and severe degree, 64 (35.9%) cases and placenta previa amounted to 11 (6.1%). In the birth process and in the early postpartum period, against the background of hypotension and atony of the uterus, MAC was observed in 103 (57.8%) cases, of which 44 (24.7%) cases were associated with caesarean section and its complications. Over the past decade in Uzbekistan, the average static rate of caesarean section has reached up to 18.1%. According to WHO (2015), cases of surgical interventions during childbirth have become more frequent and have reached more than 30%, such data are obtained on the basis of the results of two studies in the field of population reproduction under the auspices of UNDP, UNFPA, WHO and the World Bank. However, it should be noted that the safe frequency of CS use should be no more than 10%(4).

Basically, MAC occurred before the age of 30 in 97 (88.9%). The average age of pregnant women was 26.8±2.3 years. Among pregnant women with MAC, there were -46.8% housewives, employees -28.3%, workers -14.6%, students -6.4% and medical workers - 3.6%. By nationality, patients with MAC were: Uzbeks - 71.5%, Russians - 13.7%, Koreans - 6.4%, other nationalities - 5.5%, i.e. mostly pregnant women of local nationality prevailed. Among pregnant women with MAC, there were primigravidas - 23.3%, multi-pregnancy - 76.6%, as well as preterm births - 28.5%, and urgent - 71.4%, of all births induced - 12 cases (6.7%) due to preeclampsia of mild severity. Thus, MAC occurs at any fertile age, mainly during repeated pregnancy, and no relationship with the profession was found.

Out of 178, 63 (35.3%) patients had a metabolic syndrome i.e. morbid obesity, body mass index was more than 32, which today is considered as one of the risk factors for bleeding. When analyzing the anamnestic data, it was revealed that 3 (1.6%) women had uterine myoma, one woman had previously undergone myomectomy. In 67 (37.6%) patients, there was a history of inflammatory diseases of the uterus and appendages, which also plays a role in subsequent abnormal placentation during pregnancy (10,11). Almost every third patient had a history of endometrial curettage, and the average number of procedures was 1.5±0.5. 13 (7.3%) women had bleeding during previous births, for which they were transfused with donor blood components (er.mass). Three patients had antenatal fetal death in a previous pregnancy in the third trimester.

The volume of bleeding in the retrospective group, registered against the background of detachment of a normally located placenta of mild and severe degree in 64 (35.9%) cases, averaged 1890.0 ± 150.0 (p>0.05) and against the background of placenta previa in 11 (6.1%) patients, averaged 2450.0 ± 200.0 (p>0.05). In two women who underwent hysterectomy, the volume of blood loss due to placenta previa was significantly greater, and amounted to 5000.0 ml. In the labor process and in the early postpartum period against the background of hypotension and atony of the uterus, the average amount of blood loss was 2050.0±120.0 (p>0.05) in 103 (57.8%) cases.

Thus, speaking about the volume of blood loss, it should be said that it varied from 1550.0 to 5000.0 ml depending on obstetric pathology and averaged 2410.45± 520.55 ml. Interoperative blood loss in the amount of 750±110.0 (p>0.05), ml was observed in a patient who initially underwent a caesarean section, and when the operation was expanded to hysterectomy, blood loss increased to an average of 1650.0 ±150.0 (p>0.05), and the duration of the operation before total hysterectomy was 144.0±15.0 min (p>0.05).

All patients with MAC underwent a volumetric surgery to remove the uterus, of which low supravaginal amputation of the uterus (subtotal hysterectomy) - in 14 (7.8%); extirpation of the uterus (total hysterectomy) - in 164 (92.1%). Total hysterectomy with severe DIC in the stage of hypocoagulation was accompanied by ligation of the internal iliac artery - in 68 (38.2%) cases, it should be noted that in 41 (23.0%) patients, an organ-preserving operation was performed from the beginning as “ligation of three great vessels” and “hemostatic sutures on the B-Lynch uterus”, however, due to the lack of effect, the volume of the operation expanded to extra pathology of the uterus. During the operation of extirpation of the uterus in 6 (3.3%) cases, both appendages were removed due to hemorrhage and necrosis of the ovaries, and in 14 (7.8%) cases, only appendages were removed. Analyzing the situation with surgery for MAC, I would like to note that in 32 (17.9%) surgical intervention was performed on time, in 26 (14.6%) surgical care was started one hour late, in 112 (62.9%) - two hours, in 7 (3.9%) - three hours and in 1 (0.5%) - 5 hours due to expectant tactics and due to an attempted organ-preserving operation.

The clinical picture in MAC is due to the loss of blood as the volume of circulating plasma. A decrease in the level of hemoglobin (below 60 g/l) occurs with blood loss > 35-40.0% of the BCC and causes the development of hypoxia of the tissue organs. A decrease in the concentration of the components of the blood coagulation system occurs when blood loss is > 50% of the BCC, which leads to depletion of the hemostasis system, the development of DIC, hemorrhagic shock, aggravation of the condition of the puerperal and often death.

The analysis carried out in a retrospective group, out of 178 cases - in 5 (2.8%) pregnancy and childbirth ended in maternal mortality. When these 5 cases were analyzed, only 3 (60.0%) of them were registered with an obstetrician-gynecologist, but 2 (40.0%) were not registered in the primary care. Of the three registered somatic diseases, such as UTI (chronic pyelonephritis), hepatitis, acute respiratory viral infections and iron deficiency anemia of moderate severity were established.

The gestational age of 37-40 weeks was in 4 (80.0%) of the deceased and in 1 (20.0%) the gestational age was 35 weeks, and she died from central placenta previa accompanied by MAC, hemorrhagic shock, DIC and multiple organ failure incompatible with life. The pregnant woman was admitted to the hospital in an extremely serious condition, with a blood loss of more than 2000.0 ml, and at the final stage of the total hysterectomy operation she died on

the operating table. In the structure of maternal mortality, 2 (40.0%) had detachment of a normally located placenta of severe degree, 1 (20.0%) had uterine rupture, and 1 (20.0%) had atonic postpartum hemorrhage. It should be noted that the patients who died from uterine rupture with central placenta previa were not registered in the primary care, since both were abroad and they arrived at home after 34 weeks of pregnancy.

In the traditional group, 178 patients with MAC underwent intensive therapy: infusion-transfusion, plasma, blood transfusion with correction of DIC - syndrome, i.e. multicomponent correction. An analysis of the volumes and qualitative composition of infusion and transfusion therapy in the treatment of MAC showed that the volume of crystalloid solutions (0.9% sodium chloride) averaged 3350.50±1050.40 ml (from 2000 to 5000 ml), the volume of a solution of hydroxyethyl starch (HES) 6% refortan, hekaton averaged 1800.0±150.0 ml. The composition of the injected infusion media should be balanced and close to that of blood plasma, however, the parameters for infusion media are not applicable to a 0.9% aqueous solution of sodium chloride. Studies have shown that due to the excess of 1.5 times the content of chlorides in saline, compared with blood plasma, massive volemic support of this environment leads to hyperchloremia associated with a two-fold increase in mortality. In the case of timely (in the first 10-30 minutes) adequate intensive therapy, the outcome in hemorrhagic shock is usually favorable (2). However, the main intensive therapy with crystalloids was started with a delay of 55.4 ± 10.6 min and 2.5 times more than expected.

With MAC, bleeding volumes are significant, there is a rapid consumption of coagulation and anticoagulation factors. If the volume of blood loss is more than 30-35% of the BCC, a rapid introduction of donor fresh frozen plasma (FFP) should be started in a volume of at least 20 ml/kg of body weight (6). On average, FFP was transfused in volumes of 1650.17±384.83 ($p>0.05$) on the first day, 950.12±150.20 on the second day ($p>0.05$), until complete correction of DIC. Due to an organizational issue, sometimes waiting tactics, the plasma transfusion was delayed by 87.5 ± 10.2 minutes.

In 38 (21.34%) patients with MAC, before and during surgery, a full-fledged infusion therapy was performed with the introduction of up to 15 mg/kg of body weight of tranexamic acid (Hemotran), repeating every 6-8 hours until complete hemostasis, however, in 96 (53.9%) patients, this drug was administered in an insufficient dose of 500 mg once a day, and in 44 (24.7%) patients, it was not used at all. due to the lack of this drug. As a means of normalizing the fibrinolysis system, tranexamic acid (gemotran) is used - a synthetic amino acid that competitively inhibits plasminogen; its efficiency is 15-20 times higher than that of aminocaproic acid (17.18). The action of tranexamic acid is carried out by inhibiting the lysin-binding sites of plasminogen, due to which this proenzyme does not turn into plasmin and cannot bind to fibrin. Also, tranexamic acid (gemotran) inhibits the production of kinins and other active peptides, which provides the anti-allergic and anti-inflammatory effect of this drug (18). When using this antifibrinolytic agent, there was no increase in the risk of thrombotic complications.

To achieve the maximum effect of tranexamic acid (gemotran), it is necessary to select the appropriate dose of the drug. This antifibrinolytic agent is administered immediately before the incision on the anterior abdominal wall at a dose of 10-15 mg/kg of body weight intravenously rapidly in saline solution (20-30 ml). Unfortunately, for unknown reasons, this drug was not used at all in the retrospective group with MAC in 44 (24.7%) patients, both in the therapeutic and prophylactic doses (13).

In 87 (48.7%) patients in an insufficient dose of 100-150 thousand. used inhibitors of proteolysis, mainly aprotinin (kontrykal). Although there is no evidence base for the use of aprotinin for the treatment of MAC, however, there are a lot of articles reflecting the effectiveness of this drug in the treatment of DIC, suppressing the fibrinolytic activity of the blood and inhibiting the effect of fibrinolysis, thereby preventing the progression of intravascular coagulation (8,14)

It should be noted that in this group, in 13 (7.3%) patients, rFVIIa (Coagil) was administered at a rate of 90 μg/kg, with the development of a severe form of hypocoagulation, refractory to therapy with FFP and fibrinolysis inhibitors (15). The volume of blood loss averaged 2354.4±465.4 ml. After the introduction of rFVIIa (Coagil), these patients showed a significant decrease in the rate and volume of bleeding, which allowed these patients to perform a total hysterectomy with ligation of the internal iliac artery.

When discussing blood transfusion, it should be noted that the transfusion of erythrocyte-containing blood components contributes to the restoration of globular volume in MAC. Recently, the procedure of intraoperative reinfusion of autoerythrocytes has played a large positive role, which allows minimizing the use of donor erythrocytes, and in some cases completely eliminating them, preventing possible blood transfusion complications and improving the outcome of surgery for MAC (12).

In the study group, all 178 patients with MAC underwent transfusion of donor red blood cells. It should be noted that only 34 (19.1%) patients underwent full, timely and sufficient transfusion, and 144 (80.8%) patients underwent this procedure with a delay of 1 to 5 hours, and in insufficient quantities. 2 (1.1%) had a post-transfusion complication that required resuscitation, and one of them was transferred to the hemodialysis unit.

Conservative treatment of MAC, such as pelvic arterial embolization, staged, stepwise uterine devascularization, and/or hypogastric artery ligation, has become a reliable and effective alternative to hysterectomy. Although further long-term and subsequent studies are still needed, and these procedures, according to foreign researchers, do not worsen subsequent fertility and pregnancy outcomes, these operations were not performed by the patient in the traditional group under study (15,16).

Thus, analyzing 178 birth histories accompanied by MAK, in the period from 2014 to 2017 in the regional perinatal center in Urgench, they came to the following conclusion:

1. The frequency of massive obstetric bleeding in the studied retrospective group was 0.54%, and in the structure of maternal mortality 45.4%.

2. The main causes of massive obstetric hemorrhage were postpartum uterine atony in 103 (57.8%) patients, detachment of a normally located placenta in 64 (35.9%) patients and placenta previa in 10 (6.1%) patients. The amount of blood lost averaged 2410.45± 520.55 ml.

3. Mistakes made during clinical examination, surgical, conservative treatment and organizational issues led to 5 cases of maternal death and deterioration in the quality of life of a woman in the study group.

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