

ASSESSMENT OF THE STATE OF THE COAGULATION LINK OF HEMOSTASIS IN WOMEN WHO TERMINATED NON-DEVELOPING EARLY PREGNANCY WITH MEDICATION

Fazilova M.O

Sultanov S.N

<https://doi.org/10.5281/zenodo.7257585>

Abstract. 52 women were examined on the background of medical interruption of non-developing pregnancy for up to 63 days of amenorrhea. Signs of activation of indicators of the coagulation link of hemostasis were revealed - an increase in blood clotting activity against the background of an undeveloped pregnancy and after taking mifepristone, followed by a gradual normalization of hemostatic changes and a decrease in overall blood clotting after taking misoprostol.

Key words: non-developing pregnancy, mifepristone, misoprostol, medical termination of pregnancy, coagulation link of hemostasis.

ОЦЕНКА СОСТОЯНИЯ КОАГУЛЯЦИОННОГО ЗВЕНА ГЕМОСТАЗА У ЖЕНЩИН, ПРЕКРАВШИХ НЕРАЗВИВАЮЩУЮСЯ РАННЮЮ БЕРЕМЕННОСТЬ МЕДИКАМЕНТОЗНО

Аннотация. Обследовано 52 женщины на фоне медикаментозного прерывания неразвивающейся беременности на сроке до 63 дней аменореи. Выявлены признаки активации показателей коагуляционного звена гемостаза - повышение свертывающей активности крови на фоне неразвивающейся беременности и после приема мифепристона с последующей постепенной нормализацией гемостатических изменений и снижением общей свертываемости крови после приема мизопростола.

Ключевые слова: неразвивающаяся беременность, мифепристон мизопроустол, медикаментозное прерывание беременности, коагуляционное звено гемостаза.

INTRODUCTION

The problem of non-developing pregnancy is extremely relevant in modern obstetrics and gynecology, both in clinical and social aspects. The frequency of this pathology in the structure of reproductive losses is 10-20% [3, 4]. The retention of a dead fetus in the uterus adversely affects the subsequent reproductive function of a woman. It also poses a threat not only to her health, but also to her life, due to disturbances in the hemostasis system, manifested by consumption coagulopathy and hemorrhagic complications [1, 2, 5]. It has been established that subacute DIC develops 2–3 weeks after fetal death [1, 2].

The traditional method of terminating a non-developing pregnancy is surgical simultaneous emptying of the uterine cavity [1, 5]. But in recent years, the medical method of abortion using mifepristone in combination with misoprostol has been increasingly introduced into obstetric and gynecological practice. This method is a safer and more physiological way to terminate a pregnancy on an outpatient basis up to 9 weeks inclusive [3, 6, 7]. However, this method of termination of pregnancy does not completely exclude the risk of complications [6].

And taking into account the fact that the use of hormonal contraceptives after a pharmacological abortion can affect the hemostasis system, the issue of studying the effect of antiproggestins and

prostaglandins on the coagulation link of hemostasis is significant when choosing post-abortion hormonal rehabilitation [1, 2, 4].

METHOD AND METHODOLOGY

Purpose of the study. To assess the state of the coagulation link of hemostasis in women terminating a non-developing pregnancy at an early stage with a medical method using mifepristone and misoprostol.

Materials and methods. The material for the study was 52 cases of medical interruption of NB with a period of amenorrhea up to 63 days that have passed in 2020-2021 in a day hospital of the gynecological department of the Samarkand Regional Perinatal Center.

Medical termination of pregnancy was performed according to the following scheme: a single oral dose of mifepristone 600 mg followed by the use of misoprostol at a dosage of 800 mcg 36-48 hours after taking the first drug. Hemostasiological changes were assessed in comparison with the control group - non-pregnant healthy women (n = 134, mean age 25.96 ± 5.54). The indicators of the coagulation link of hemostasis were determined using a coagulometer RAYSO RS 2201. D-dimers were determined using the enzyme immunoassay kit "D-dimer", Axis-Shield, NycoCard-reader analyzer. Soluble fibrin-monomeric complexes (SFMK) were determined by a quantitative variant of the phenanthroline test. Statistica 6 was used for statistical processing of the results.

RESULTS

When conducting a study in the coagulation link of hemostasis in women with non-developing pregnancy, the following data were obtained (Table 1).

Table 1

The state of the coagulation link of hemostasis in women who interrupted NP medically

Index	Control group, n = 134	Against the background of NP, n = 52	After taking Mifepristone, n =44	After taking misoprostol, n=25
AVR, s	97,02 ± 19,97	97,00 ± 11,76	95,88 ± 13,30	104,38 ± 11,69*
APTT, s	28,00 ± 3,80	30,38 ± 3,26*	29,44 ± 4,05	29,68 ± 3,17
PO	1,07 ± 0,09	1,09 ± 0,08	1,10 ± 0,10	1,05 ± 0,04
PTI, %	92,78 ± 10,49	93,35 ± 7,97	92,59 ± 7,81	98,11 ± 4,51*
INR	1,08 ± 0,10	1,07 ± 0,08	1,09 ± 0,11	1,02 ± 0,06
TV, s	16,00 ± 1,77	14,99 ± 1,19*	15,10 ± 1,32	15,50 ± 0,68
FH, g/l	3,15 ± 2,25	3,44 ± 0,83	3,13 ± 0,43	3,30 ± 0,61
RFMK, g/l	2,09 ± 4,71	4,92 ± 5,75*	1,86 ± 2,99	2,33 ± 3,03
AT III, %	112,70 ± 14,09	105,86 ± 6,69	105,75 ± 9,41	113,00 ± 4,54
IRP, %	101,29 ± 16,39	100,00 ± 8,66	103,17 ± 7,89	95,00 ± 2,15
D-dimer, µg/ml	0,11 ± 0,04	0,12 ± 0,05	0,11 ± 0,04	0,10 ± 0,00
Hb, g/l	125,22 ± 14,99	124,73 ± 8,91	124,83 ± 8,06	120,36 ± 9,06

*Note: * - a significant difference between the parameters of coagulation hemostasis in women who interrupted NB medically from the state of hemostasis in the control group (healthy non-pregnant women).*

Against the background of a non-developing pregnancy, an increase in activated partially thromboplastin time (APTT) was recorded, in comparison with the value of this indicator in persons in the control group (30.38 ± 3.26 and 28.00 ± 3.80 , respectively). On the first day after taking mifepristone, there was a shortening of the APTT from 30.38 ± 3.26 s to 29.44 ± 4.05 s, and after taking misoprostol, some prolongation of the APTT to 29.68 ± 3.17 s was again recorded. Against the background of non-developing pregnancy, an increase in the concentration of soluble fibrin-monomer complexes (SFMC) by 2.3 times was determined, compared with the control group, which indicates the activation of continuous intravascular blood coagulation. Thrombin time (TT) in the group of women before medical abortion was 14.99 ± 1.19 s, after taking mifepristone, the value of this indicator was extended to 15.10 ± 1.32 s, and after misoprostol - up to 15.50 ± 0.68 s, and in the control group this indicator was higher (16.00 ± 1.77 s).

The concentration of fibrinogen (FG) changed within the reference values, there was a decrease in FG after taking mifepristone from 3.44 ± 0.83 g/l to 3.13 ± 0.43 g/l, followed by an increase in its concentration to 3.30 ± 0.61 g/l under the action of misoprostol. It was also found a decrease in the level of Antithrombin III by 6.5% before termination of pregnancy, with a subsequent increase in its level to the values of the control group. Activation of the fibrinolytic system was noted - the maximum value of the plasminogen reserve index (PRI) was registered the next day after taking mifepristone. The value of the D-dimer level was maximum against the background of non-developing pregnancy, then it consistently decreased during the termination of pregnancy from 0.12 ± 0.05 $\mu\text{g/ml}$ to 0.10 ± 0.00 $\mu\text{g/ml}$. The level of hemoglobin in the study group against the background of non-developing pregnancy was 124.73 ± 8.91 g/l, and after taking misoprostol, its concentration in blood plasma decreased to 120.36 ± 9.06 g/l, which can be explained by blood loss in during the termination of pregnancy.

Conclusions. On the basis of the obtained data of the study conducted against the background of medical interruption of a non-developing pregnancy, signs of activation and dissociation of the indicator of the coagulation link of hemostasis were revealed. A shortening of the APTT after taking Mifepristone indicates both the activation of the internal mechanism of plasma coagulation and an increase in the overall blood clotting in general. Thrombin time was shortened as much as possible against the background of non-developing pregnancy, then gradually increased during the course of medical abortion, but did not reach the values of the control group, which indicates tension in the hemostasis system.

This suggests the predominance of the intrinsic mechanism of plasma coagulation during medical abortion prior to misoprostol. This condition is probably associated with the activating effect of mifepristone on the internal mechanisms of blood coagulation against the background of a decrease in the intake of tissue factor into the bloodstream as a result of mifepristone-induced detachment of a dead fetal egg, and a significant lengthening of AVR after taking misoprostol is associated with a decrease in blood clotting factors against the background of blood loss induced by misoprostol.

The activation of the internal mechanism of blood coagulation (through the activation of the Hageman factor) against the background of a decrease in procoagulant (external) mechanisms is

also evidenced by a decrease in the level of RFMK after taking Mifepristone, which is associated with the action of the Hageman factor and calcium ions, resulting in cross-polymerization of fibrin monomers with the formation of insoluble fibrin, thereby reducing the concentration of RFMK. At the same time, abortion itself has a stress-induced effect, activating the sympathoadrenal system, which, through a number of factors (kallikrein-kinin system, hyperadrenelinemia, hypercalcemia, and others), activates the internal mechanisms of plasma coagulation. In addition, medical interruption of NB is characterized by a tendency to reduce the activity of the antithrombin and fibrinolytic blood systems.

CONCLUSION

Thus, against the background of a non-developing pregnancy, activation of the internal mechanism of blood coagulation is observed, which is directly related to the stressful effect of abortive intervention and to the direct activating effect of mifepristone on plasma coagulation. The subsequent decrease in overall blood clotting that occurs after taking misoprostol is probably associated with the emptying of the uterine cavity from the fetal egg, accompanied by bleeding of varying intensity and volume. And, consequently, all women who have undergone medical abortion for a non-developing pregnancy should be attributed to the risk group for thrombohemorrhagic complications, despite the high efficiency of this method and its atraumatic nature.

REFERENCES

1. Amanova A. M. Medical methods for terminating missed pregnancy in the first trimester // Bulletin of KSMA them. I. K. Akhunbaeva. 2016. No. 1. S. 36-39.
2. Grigoryeva N. V. The state of the coagulation link of hemostasis in non-developing early pregnancy depending on the duration of the delay of the dead fetal egg in the uterine cavity / Grigorieva N. V., Bagirov R. N. // Proceedings of the III All-Russian Conference of Young Scientists "Science and innovations of the 21st century". Surgut: ITs SurGU, 2016. Vol. II. 258 c. pp. 121-124.
3. Karpova I. A., Polyakova V. A., Grigoryeva N. V., Aksent'eva A. V., Bagirov R. N. Peculiarities of changes in the coagulation link of hemostasis against the background of medical interruption of a non-developing early pregnancy, V. A. Platitsin, E. V. Zolotukhina, N. N. Buslaeva // University Medicine of the Urals. 2016. No. 4. S. 5-7.
4. Karpova I. A. Pathogenetic rationale for the correction of hemostatic changes against the background of contraceptive hormonal systems / I. A. Karpova, V. A. Polyakova, A. M. Chernova, V. A. Platitsin, R. N. Bagirov // Academic Journal of Western Siberia. 2016. Vol. 12, No. 1.
5. Nemanova S. B. The effect of a complex effect on the hemostasis system of drugs (antigestagens and prostaglandins) used to terminate pregnancy in a short period / S. B. Nemanova et al. // Journal of Obstetrics and Women's Diseases. 2011. T. LX, No. 1. S. 47-55.
6. Polyakova V. A. The results of the effectiveness of medical termination of pregnancy using one tablet of mifepristone / V. A. Polyakova, O. Kh. Kuzakberdieva, I. A. Karpova, T. P. Shevlyukova // University science: a look into the future " Proceedings of the International Scientific and Practical Conference Dedicated to the 81st Anniversary of the Kursk State Medical University and the 50th Anniversary of the Pharmaceutical

- University. In 3 volumes. Edited by V. A. Lazarenko, P. V. Tkachenko, P. V. Kalutsky, O. O. Kurilova. 2016. S. 40-42.
7. Bettahar K., Boisrame T., Cavillon V. et all. Medical induced abortion // J Gynecol Obstet Biol Reprod (Paris). 2016.
 8. Зокирова Н. и др. Оптимизация ведение женщин с пузырным заносом //Журнал вестник врача. – 2014. – Т. 1. – №. 01. – С. 89-93.
 9. Каримова М., Асатулаев, А., & Тугизова, Д. (2022). Оценка эффективности различных методов лечения больных с местнораспространенным раком молочной железы. Журнал вестник врача, 1(04), 69–70. извлечено от https://inlibrary.uz/index.php/doctors_herald
 10. Тугизова Д. И., Джураев М. Д., Каримова М. Н. ФАКТОРЫ ПРОГНОЗА ПРИ РАКЕ ШЕЙКИ МАТКИ, АССОЦИИРОВАННЫЕ С БЕРЕМЕННОСТЬЮ.
 11. Тугизова Д. И., Каримова М. Н., Рахимов Н. М. ТАКТИКА ВЕДЕНИЯ БЕРЕМЕННЫХ С ИНВАЗИВНЫМ РАКОМ ШЕЙКИ МАТКИ (ЛИТЕРАТУРНЫЙ ОБЗОР) //ЖУРНАЛ БИОМЕДИЦИНЫ И ПРАКТИКИ. – 2022. – Т. 7. – №. 3.