

## **DIAGNOSTICS AND MANAGEMENT OF NON-GRAVIDARY URGENT UTERINE BLEEDING ACCORDING TO INTERNATIONAL RECOMMENDATIONS**

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<b>ABSTRACT</b>	<b>KEY WORDS</b>
<p>Abnormal uterine bleeding (AMB) is a general term used to describe uterine bleeding that exceeds the volume and duration of normal menstruation in women of reproductive age (Fraiser I.S., Langham S., 2009). Abnormal uterine bleeding occurs in 14-25% of women of reproductive age (Adamyan L.V., Sibirskaya E.V., Koltunova I.E., 2016) and can have a significant impact on their physical, social, emotional and material quality of life.</p> <p>Abnormal uterine bleeding in reproductive age is associated with various types of functional and organic disorders of the reproductive system of women. In particular, one of the most common causes is a violation of the ratio of estrogens and progestogens that affect the target tissue - the endometrium, therefore, according to the classification of The International Federation of Gynecology and Obstetrics (FIGO), they are registered as AMK-O. According to the PALM-COEIN classification system, which is a mnemonic for structural (PALM) and non-structural (COEIN) causes of abnormal bleeding, non-gravid urgent uterine bleeding due to ovulatory dysfunction (AUB-O) is abnormal, which, according to gynecological examination and ultrasound, cannot be explained by the usual causes of bleeding (structural gynecological abnormalities, cancer, inflammation, systemic diseases, oral contraceptives or certain drugs).</p>	<p>abnormal uterine bleeding, Menorrhagia, Anemia, Polycystic Ovary Syndrome, Adolescent, Endometritis</p>

### **Introduction**

Despite the significant progress made over the past decades in various areas of obstetrics and gynecology, the problem of nongravid urgency uterine bleeding remains far from being solved.

Often, in Uzbekistan, abnormal uterine bleeding is one of the main causes of iron deficiency anemia, reduces the efficiency and quality of life of women, and also occupies one of the first places among the causes of hospitalization of women in gynecological hospitals and serves as an indication for surgical intervention.

## **Purpose of the study:**

To analyze the literature on diagnostics and management of non-gravidary urgent uterine bleeding according to international recommendations.

## **Results**

AUB can be manifested by regular, prolonged (more than 8 days) and heavy (more than 80 ml) menstrual bleeding (MBB). The causes of these bleedings are more often adenomyosis, submucosal uterine myoma, coagulopathy, functional disorders of the endometrium. Intermenstrual bleeding (IMB) against the background of a regular cycle is characteristic of endometrial polyps, chronic endometritis, ovulatory dysfunction. Irregular, unpredictable prolonged and / or profuse bleeding, more often occurring after menstruation delays, is more characteristic of hyperplasia and endometrial cancer.

To select a rational management tactic, it is necessary to establish the cause of AUB and attribute it to one of the above categories. Assessment of the amount of blood loss is carried out according to clinical indicators or a scoring scale (menstrual blood loss pictogram); an objective alkaline-hematin test is used in the conduct of scientific research.

According to international recommendations for AUB, laboratory diagnostics should include:

- determination of the level of  $\beta$ -CHG in the blood serum (with
- suspicion of pregnancy);
- examination for the presence of anemia (clinical blood test, including platelets);
- coagulogram, if a pathology of hemostasis is suspected, a consultation with a hematologist and a special examination (for von Willebrand disease - determination of factor VIII, ristocetin co-factor, factor antigen
- Willebrand).

Hormonal examination is carried out with an irregular rhythm of menstruation and the risk of hypothyroidism (determination of the level of TSH, progesterone); testing for chlamydial infection (at high infectious risk); A Pap test is performed to rule out cervical pathology.

The recommendations of the American and Canadian Colleges of Obstetricians and Gynecologists (2013) provide an algorithm for examining patients with AUB. Transvaginal ultrasound examination (ultrasound) of the pelvic organs is considered as a 1st line diagnostic procedure for assessing the state of the endometrium (higher information content in postmenopausal women). Dopplerometry provides only additional information about the nature of the pathology of the endometrium and myometrium. Sonohysterography is of high diagnostic value, which is performed when transvaginal ultrasound is insufficiently informative to clarify focal intrauterine pathology. MRI is not considered as a 1st line diagnostic procedure for AUB, it is recommended for multiple uterine myoma to clarify the topography of nodes before myoma ctomy, uterine artery embolization, FUS ablation, as well as in cases of suspected adenomyosis or in cases of poor visualization of the uterine cavity to assess the condition of the endometrium. Hysteroscopy and endometrial biopsy continue to be considered the "gold standard"

for diagnosing intrauterine pathology, primarily to exclude precancerous lesions and endometrial cancer. Recommended for suspected pathology of the endometrium, the presence of risk factors for cancer of the uterine body (obesity, polycystic ovary syndrome, diabetes mellitus, family history of colon cancer), in patients with AUB after 40 years. Office hysteroscopy and aspiration biopsy are preferred as less traumatic and more economical procedures.

Treatment of AUB is carried out in a differentiated manner, in accordance with the identified pathology. In case of AUB not associated with organic pathology (AMK-O, C, E, N), drug therapy is prescribed: non-hormonal drugs [non-steroidal anti-inflammatory drugs (NSAIDs)], fibrinolysis inhibitors, drugs that reduce vascular fragility and increase the formation of fibrin thrombi), and hormonal (progestogens, COCs, antigonadotropins, aGnRH) [22].

Fibrinolysis inhibitors, in particular tranexamic acid (an inhibitor of plasminogen activation - Tranexam), are considered as non-hormonal drugs of the 1st line. Treatment of uterine bleeding with tranexamic acid was approved by the FDA (US Food and Drug Administration), in 2006. According to the FDA recommendations, the optimal daily dose is 4.0 g, the duration of administration is up to 5 days. The reduction in blood loss is 40–60% [23, 24]. A meta-analysis of 7 randomized clinical trials (RCTs) found a decrease in menstrual blood loss by 93 ml against the background of tranexamic acid (compared with placebo) and by 111.0 ml (compared with progestogens prescribed in the second phase of the menstrual cycle) [25].

For non-hormonal hemostatic therapy, NSAIDs are used (mefenamic, meclofenamic acid, ibuprofen, naproxen, etc.). The basis for their clinical use is the data on the relationship between elevated levels of prostaglandins in the endometrium and excessive menstrual blood loss. According to summary data, blood loss is reduced by 20–40% [26].

According to the international recommendations of NICE (The National Institute for Health and Care Excellence) (2007), etamsylate is ineffective in uterine bleeding (blood loss is reduced by 0–20%), and therefore it is not recommended for clinical use [3].

With AUB, COCs are used, their action is mediated by suppression of the secretion of gonadotropins, ovarian function, and inhibition of the growth of the glandular epithelium of the endometrium. Monophasic COCs [daily dose of ethinyl estradiol (EE) 100 mcg] are used for hormonal hemostasis in cases of acute AUB, as well as for subsequent anti-relapse therapy according to the contraceptive regimen. The effectiveness of COCs in OMC varies from 30 to 50% [21]. The results of studies have shown similar efficacy in the form of a 50% reduction in the volume of menstrual blood loss of tranexamic acid and COC, which includes 30 µg EE/150 µg levonorgestrel (LNG) (Oralcon) [27].

The results of 2 multicenter placebo-controlled studies, one of which was conducted in North America, the other in Europe and Australia, showed the benefits of COC (Qlaira), which includes natural estrogen - estradiol valerate (EV) and a hybrid progestogen - dienogest (DNG). A 3-month intake of the drug led to a decrease in the volume of menstrual blood loss by 71–79%, a 6-month intake - by a total of 88%, in 64% of patients, normalization of the menstrual cycle parameters was observed [28, 29]. The high efficiency of this type of therapy is associated with early proliferation of the endometrium under the influence of estrogens, an increase in the expression of progesterone receptors, and the antiproliferative effect of high doses of dienogest.

Along with COCs for the treatment of AUB, progestogens are used in cyclic and continuous modes. The results of one of the meta-analyses indicate the low effectiveness of progestogens prescribed in

the luteal phase of the cycle in the treatment of uterine bleeding compared with NSAIDs, tranexamic acid or danazol [31].

The most effective is the use of progestogens in a continuous regimen systemically or in the form of an intrauterine system that releases levonorgestrel (LNG-IUD). According to the results of a meta-analysis, the reduction in menstrual blood loss, estimated by the alkalinoheatin method, was 77–89% after 3 months of exposure to the LNG-IUD, and 97% after 6 months [32].

## Conclusion

The results of systematic reviews and meta-analyses formed the basis of the clinical recommendations of the National Institutes of Health (NICE), the American and Canadian Associations of Obstetricians and Gynecologists (2013) [3, 21] for drug and non-drug therapy of uterine bleeding. With evidence level A, LNG-IUD, long-acting progestogens, Tranexam, NSAIDs, COCs are recommended as first-line drugs. Danazol, short progestogen regimen, etamsylate is not recommended for I treat uterine bleeding.

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