

Pharmacotherapy of Ovulatory Dysfunctional Uterine Bleeding: An Update Review

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Abstract

Abnormal uterine bleeding (AUB) is a kind of common gynecological diseases with a higher incident rate, usually results in great physical, emotional, sexual, social and financial burdens of patients and patients' family. Due to complexity of clinical symptoms of AUB patients, different treatment methods are often required for AUB treatment. In this review, firstly we introduced the pathogenesis of AUB, and different treatment methods for AUB patient treatment was also summarized, we hope that this review could make some useful suggestions for clinical medical staff.

Keywords: AUB; Pharmacotherapy; Pathogenesis; Medicine Selection

Introduction

Abnormal uterine bleeding (AUB) is a common women clinical disease during their reproductive years, which has almost 14% incidence rate in the world; it could impair patients' quality of life by resulting in significant physical, emotional, sexual, social and financial burdens [1]. The terminology of AUB has been established by the International Federation of Gynecology and Obstetrics (FIGO) Menstrual Disorders Working Group in 2011 and then has been adopted worldwide [2]. Usually, AUB was describe as a spectrum of symptoms, such as heavy menstrual bleeding (HMB), intermenstrual bleeding and a combination of both heavy and prolonged menstrual bleeding. AUB is also a common clinical gynecological endocrine disease in women during their reproductive years, usually resulted in heavily physical and mental health.

From the perspective of traditional Chinese Medicine, AUB was classified as "BengLou", and the main cause was 'LaoShangXueQi', 'ZangFuSuShang', 'JingXueShiChang', many articles have been reported Traditional Chinese Medicine including Chinese herbs and acupuncture could provide individual and effective therapeutic strategies for AUB patients [4]. In this review, we will introduce the pathogenesis of AUB and introduced the pathogenesis of AUB, and summarized different treatment methods for AUB patient treatment, which may provide some useful treatment strategy for AUB.

The pathogenesis of AUB

Normal ovulation requires the normal function of the complete hypothalamic pituitary ovarian gonadal axis, dysfunction of any link or organic disease can cause temporary or long-term ovarian dysfunction and lead to abnormal ovulation. Usually, there are three kind of ovulatory disorders including the anovulatory, rare ovulation, and the luteal function insufficiency [5]. The anovulatory mainly caused by the dysfunction of hypothalamic-pituitary-ovarian axis (HPO axis), usually occurred in adolescent girls and menopausal transition period

women, could result in AUB. Furthermore, the polycystic ovary syndrome (PCOS), obesity, higher prolactin blood disease, thyroid and adrenal disease could also result in AUB in reproductive age women; those women will perform menstruation frequency, length and the amount of bleeding abnormal and excessive proliferation of endometrial and irregular peeling [6-8].

Treatment methods for patients with AUB

In clinic, different types of AUB patients usually adopt different treatment methods. Usually, acute-AUB patients with fertility demand were usually treated by the combined oral contraceptives (COS), shedding the endometrium, shaving, hysteroscopic examination of biopsy and total abdominal hysterectomy treatment is a better choice for AUB patients with those highly complex and without fertility demand; for those chronic-AUB patients, combined oral contraceptives, high performance synthetic progesterone and shedding the endometrium were usually used according to their age and physiological condition [3].

In the period of acute hemorrhage, stop bleeding and correct anemia and adjust the cycle after hemostasis to prevent endometrial hyperplasia and recurrence of AUB are necessary for AUB treatment. Choices of suitable treatment methods for patients with AUB usually should be according to the age of the patients, the degree of bleeding, the degree of anemia, and whether there are fertility demand [9]. For example, patients under the age of 35 with cardiovascular disease, or hypertension, or venous thromboembolism, or breast cancer, or smoking should be suggested to take intravenous or oral estrogen [10]; for adolescent AUB, because the fine regulation of HPO axis is not mature, resulting in anovulation or oligo ovulation and progesterone deficiency, progesterone intimal exfoliation, short-acting COC treatment and natural progesterone or dexamethasone are recommended [11].

The common causes of AUB during childbearing period are PCOS, hyperprolactinemia, obesity, abnormal thyroid function. Short-acting COC therapy, progesterone intimal exfoliation and efficient synthesis of progesterone intimal atrophy are recommended in the bleeding period, and diagnostic curettage, hysteroscopy and endometrial pathological examination should be considered as important methods to stop bleeding timely. To adjust the cycle, for those who have fertility requirements can be given to promote ovulation, such as oral clomiphene, letrozole and choose the regular withdrawal method of natural progesterone or dexamethasone which does not affect pregnancy. For patients without fertility requirements can choose LNG-IUS; or use short-acting COC for a long time, which can reduce the incidence of malignant tumors [12]. Usually, the high-efficiency synthetic progestogen therapy is suitable for patients in childbearing age and menopausal transition period, the representative drug of the high-efficiency synthetic progestogen therapy is norethisterone; and common auxiliary hemostatic drugs including tranexamic acid, non-steroidal anti-inflammatory drugs, ethamsylate, vitamin K, testosterone propionate [15].

The main cause of AUB during menopausal transition is ovarian dysfunction to ovarian failure, resulting in oligo-ovulation or anovulation. When choosing drugs, it is necessary to consider safer treatments and drugs that have less impact on the whole body. During the bleeding period, it is recommended to use progesterone endometrial prolapse method, efficient synthesis of progesterone endometrial atrophy method, appropriate consideration of diagnostic curettage or hysteroscopy, endometrial pathological examination; adjust the cycle recommended LNG-IUS, can be long-term and effective protection of endometrium, significantly reduce menstrual bleeding, or the use of natural progesterone or progesterone, reduce the risk of cardiovascular disease and breast cancer. For patients with clear symptoms of estrogen deficiency, sequential treatment of natural estrogen with progesterone or dexamethasone is recommended [13].

Most patients with AUB caused by luteal insufficiency are asymptomatic; patients with common bleeding in follicular phase, luteal phase, peri-ovulatory phase, or after excluding organic causes, such as less bleeding can tolerate or do not use drugs. If the AUB patients without fertility requirements, short-acting COC (low-dose estradiol) can be used to control the cycle. For those with fertility requirements, clomiphene or letrozole can be used as appropriate to promote ovulation to improve follicular development and luteal function [14].

Besides western medicine treatment, traditional Chinese medicine also has good applications in AUB treatment. Studies have shown that motherwort injection can improve endometrial condition, stop bleeding quickly, and improve blood routine and coagulation function [16], Yuzhizhixue Granule combined with ferrous fumarate is effective to alleviate anemia which caused by excessive menstruation [17]. Yangxue Danggui Capsule combined with mifepristone can significantly improve the serum estrogen level of patients, inhibit endometrial hyperplasia, and improve the clinical efficacy of mifepristone in perimenopausal AUB [18]. Besides Chinese herbal medicines, many studies have shown that acupuncture could regulate the hypothalamic-pituitary system and the hormone level of the target gland, thus making the endometrial blood vessels shrink to achieve the purpose of hemostasis and has a significant effect on dysfunctional uterine bleeding [19].

Conclusion

AUB could lead to secondary anemia, endometrial hyperplasia and other complications, which will cause serious economic burden to patients and their families. Due to complexity and unclear pathogenesis of AUB, the appropriate treatment methods should be selected according to the actual situation of patients. The current treatment methods for AUB mainly include western medicine and traditional Chinese medicine, the combined treatment of traditional Chinese medicine and western medicine may be a better choice to alleviate the symptoms of AUB and to avoid side effects which caused by any single therapy method.

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Conflicts of Interest

The author declares that there is no conflict of interests in this review.

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