

Menstrual Cycle Disorders in Adolescent Girls

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Abstract

Gynecological problems in adolescents have their own characteristics. Menstrual cycle disorders such as amenorrhea, dysfunctional uterine bleeding or dysmenorrhea are relatively common in adolescents. In the early postmenarchal period, these disorders do not require specific treatment in most cases, but at the onset of pathology it requires timely and adequate approach. The authors present the basic characteristics of the normal menstrual cycle in adolescents and subsequently describe its pathological abnormalities.

Keywords: Menstrual Cycle; Adolescence; Amenorrhea; Dysfunctional Uterine Bleeding; Juvenile Metrorrhagia; Polycystic Ovarian Syndrome; Dysmenorrhea

Introduction

The menstrual cycle is the result of the cyclic hormonal activity of the endocrine system controlled by the diencephalon-hypothalamus-pituitary-ovary system. The endometrium is one of the target organs, the cyclic menstrual bleeding is an external manifestation. It is the separation of matured endometrium after secretory transformation at regular monthly intervals. The maturation of this hormonal system begins before menarche and continues long after the onset of the cycle. There are different opinions on the maturation of the hormonal regulation of the ovarian cycle, according to most authors, it occurs around the age of 21 years [1].

The normal menstrual cycle

Menarche is the culmination of previous pubertal genital development, associated with the development of secondary sexual characteristics and growth acceleration. The physiological period for the onset of the menstrual cycle is between 10 and 15 years of age, while the average age is between 12th and 13th year.

The menarcheal age is determined not only by genetic influences, body weight or body fat percentage and basal metabolic rate are also crucial for its onset. The average weight at the onset of menarche is 47,5 kg. The development of secondary sexual characteristics according to Tanner is at the onset of menarche M 2 - 3, P 2 - 3, A 1 - 2. The pubertal rearrangement of the uterus is completed, we may see follicles on the ovaries in different stages of development, Lactobacillus acidophilus can be found in the vagina.

The period of puberty is completed by the onset of menstruation and the period of adolescence begins, during which the period of sexual maturation is completed, both physical and psychological. The menstrual cycle may not be regular in this period, which lasts approximately 2 years after menarche, while this is not pathological.

The most frequent menstrual cycle is an anovulatory cycle in which a corpus luteum is not formed and progesterone is not produced in the II. half of the menstrual cycle. The endometrium undergoes changes only under the influence of estrogens - up to a pronounced hyperplasia. As estrogen levels fall, the so-called estrogen bleeding occurs. Clinically, these processes may not manifest themselves at all and the cycle may not always be irregular. The anovulatory cycle is physiological in 50% in the so-called first two years of menstrual age [2].

The normal menstrual bleeding interval is a 28 - 30 day cycle with physiological fluctuations of 21-35 days and a bleeding time of 4 - 7 days. The physiological loss of blood during menstruation is approximately 60 - 80 ml per 1 cycle, the upper limit is 100 ml. A standard for blood loss during menstruation calculated as 1% of the circulating blood or 1 ml for each kg of body weight was also reported. Bleeding during the first and second day of menses accounts for 79% of the total loss. The prerequisite for thus defined menstruation is the biphasic ovarian cycle. In it, the normoestrogenic secretion of the follicular hormone of the first phase is supplemented in the second phase by secretion of the corpus luteum hormone - progesterone.

In adolescents, cycle variability is higher than in adults (19 - 45 days) and bleeding time may vary between 3 - 7 days. More significant variations are considered to be an abnormal cycle in terms of oligo or polymenorrhea, which is due to anovulation in the first years of menarche. More than 80 ml per cycle is considered excessive blood loss. Clinically significant disorders are those that result in increased blood loss followed by anemization and weakening of the body or those associated with severe endocrinological or developmental disorder [1].

Primary amenorrhea

The most common cause of primary amenorrhea is ovarian insufficiency, congenital malformations of the inner genitals, and hypogonadotropic hypogonadism. Of the many classifications of primary amenorrhea, in our conditions, the most commonly used classification is based on levels of gonadotropic and ovarian hormones:

- Hypogonadotropic hypogonadism - anorexia, stress, hyperprolactinemia, hypopituitarism,
- Eugonadotropic eugonadism - congenital malformations of internal genitals, hymenal atresia, polycystic ovarian syndrome, pregnancy,
- Hypergonadotropic hypogonadism - ovarian dysgenesis, ovarian insufficiency, congenital adrenal hyperplasia [3].

Or, a classification based on the presence and nature of secondary sexual characteristics is used:

- Primary amenorrhea with secondary sexual characteristics sufficiently and properly developed, where developmental disorders of the inner genitals are most common (for example - aplasia of the vagina, uterus, gynatresia),
- Primary amenorrhea with secondary sex traits insufficiently or not developed,
- Primary amenorrhea with secondary sexual characteristics with signs of the opposite sex, where there may be various causes from mild form of adrenogenital syndrome to disorder of gender differentiation [2].

Secondary amenorrhoea

Secondary amenorrhoea is defined as the absence of menstruation in the length of 3 menstrual cycles 6 months after the stabilization of the normal menstrual cycle. In adolescence, menstrual cycle is more labile and more responsive to external influences than in adult women. Also, greater mental stress, lifestyle changes, physical stress (especially in female athletes) often manifest themselves as secondary amenorrhoea in girls. Elderly adolescents should also be aware of pregnancy, even if the girl denies sexual intercourse. In young women, premature ovarian failure (POF) may be the cause of oligomenorrhoea or even secondary amenorrhoea in rare cases. It may be due to autoimmune ovarian damage, especially within the so-called polyglandular autoimmune syndrome [4].

Treatment of secondary amenorrhea

There is no need for treatment in adolescents up to 2 years after menarche. In the later period, hyperestrogenic disorders are treated with gestagens in the II. phase of the menstrual cycle. Preference is given to oral preparations - progesterone at a dose of 200 - 300 mg/day during the 17th - 26th day of the menstrual cycle. Hypoestrogenic disorders are treated with individualized hormone replacement therapy, or with concurrent interest in contraception, with 30 µg ethinylestradiol contraceptive [5].

Anorexia nervosa

It is the most serious cause of oligohypomenorrhea to secondary amenorrhea. It is a primary psychogenic form of hypothalamic dysfunction. It arises as a result of deliberate weight loss, in which the patient has a self-perception disorder and an unrealistic idea of her obesity. Menstrual cycle disorders usually occur at a rapid 15% weight reduction or reduction below 22% body fat. Severe hypoestrogenism is manifested by atrophy of genitals and breasts with the development of osteoporosis. The disease is accompanied by functional hypothyroidism, with bradycardia and cold intolerance. Blood levels of FSH, LH and estradiol are low, and a prepubertal response to GnRH secretion returns, which can be verified by a GnRH test. The basis is psychological-psychiatric treatment. The gynecologist must start hormone replacement therapy to prevent the progressive irreversible development of osteoporosis, which develops after 6 months of amenorrhea [2].

Polycystic ovary syndrome (PCOS)

It is another possible cause of oligomenorrhea or even amenorrhea in adolescents. The incidence of PCOS among adolescents is between 11 and 26%, with approximately 50% of these patients being obese. Due to the increasing number of obese adolescent girls in developed countries, this syndrome can be expected increasingly among girls shortly after menarche. According to the androgenic pre-exposure hypothesis, PCOS begins already during intrauterine life, but is only beginning to manifest clinically during adolescence with maturation of the hypothalamic-pituitary-ovarian axis. Although PCOS is not difficult to diagnose in adulthood, it may be easily overlooked in adolescence, as the NIH and ESHRE/ASRM criteria of 2006 are not specific to this age group.

- In adolescence, about half of menstrual cycles are anovulatory for 1 - 2 years from menarche,
- Transient hyperandrogenemia or acne are normal characteristics of puberty,
- Multiple follicular ovaries are a physiological ultrasound image in adolescence,
- Since transvaginal ultrasound examination cannot be used in adolescent virgin girls; the sensitivity of transabdominal examination is lower.

Overlooking of these symptoms may result in a late diagnosis and thus a late onset of treatment.

The PCOS phenotype spectrum in adolescents is broad. Adolescents may have no clinical or biochemical signs of hyperandrogenism in dysfunctional polycystic ovaries or may have 1 or more characteristics. Some adolescent PCOS patients have normal levels of androgens with mild hirsutism compared to adults.

Suspicion of PCOS should occur in adolescents with:

- Moderate to severe hirsutism or hirsutism equivalent (refractory acne or androgenic alopecia),
- Moderate hirsutism or obesity with any of the other symptoms of PCOS, such as irregular menstruation,
- Irregular menstrual cycle that persists for more than two years after menarche or severe dysfunctional uterine bleeding,
- Uncontrollable obesity independent of the degree of hirsutism or the presence of an irregular menstrual cycle,
- Girls with a history of premature pubarche, which is a precursor to PCOS.

Clinical symptoms of PCOS in adolescents

Hirsutism is one of the main symptoms of PCOS. Hirsutism or one of its equivalents, e.g. acne, alopecia, hidradenitis suppurativa or hyperhidrosis appear in 75% of adolescents with PCOS. Hirsutism involves excessive terminal body hair in androgen-dependent areas. It should be distinguished from hypertrichosis, which is generalized body hair growth even in areas that we do not consider to be androgen-dependent. Hirsutism can be perfidious especially at the beginning of the disease when it can be considered a physiological sign of puberty.

Menstrual cycle irregularities also occur in approximately 75% of PCOS patients. However, it may be a physiological phenomenon in puberty. Nonetheless, if these problems persist after 2 years from menarche, PCOS can be considered as one of the possible causes.

Adolescents with PCOS may also have the following symptoms:

- Menarche after the 15th year of life,
- Secondary amenorrhea lasting more than 90 days,
- Missing of 4 menstrual cycles during the year,
- Frequent dysfunctional uterine bleeding.

Adolescents with irregular menstrual cycles have higher plasma levels of androgens than adolescents with regular cycles. Since menstrual cycles are largely anovulatory within 1 - 2 years after menarche, even their regularity does not guarantee ovulation in this period. Hyperandrogenemia in adolescents persists until adulthood, with the first clinical signs appearing even 3 years after menarche.

In laboratory parameters for PCOS in adolescents, we find increased free testosterone levels, increased total testosterone levels, reduced SHBG levels, normal or elevated DHEAS levels, normal or elevated LH levels. Sampling should be done in the follicular phase of the cycle, preferably between day 4 and 10 of the cycle.

Treatment of PCOS in adolescents

PCOS treatment is as variable as its characteristics and symptoms. Some components of treatment are standard, others need to be adapted according to the patient.

Weight loss of 5% in obese adolescents has a significant benefit in improving hirsutism, acne, menstrual cycle normalization and the return of ovulation. Equally, weight loss also has a positive effect on the treatment of diabetes in these patients.

Combined hormonal contraception is the first line of treatment for adolescent PCOS patients. When using this form of contraception, menstrual cycle irregularities are normalized and androgen levels are reduced. According to the FDA (Food and Drug Administration), preparations containing a combination of ethinylestradiol/norgestimate, ethinylestradiol/drospirenone are recommended for adolescents. In addition to the antiandrogenic effect, drospirenone also has a mineralocorticoid effect, which also causes partial weight reduction. Ethinylestradiol levels in adolescents are, according to many studies, sufficient and recommended at 20 µg. Combined hormonal contraception normalizes androgen levels within a few weeks. The minimum recommended duration of use is 6 months. Since hair reduction can be observed about 9 months after the start of treatment, it is recommended to maintain this treatment for at least 6 - 9 months with good compliance. Before starting treatment, it is important to get family and personal medical history and possible contraindications of this treatment [6].

Inositol in the treatment of PCOS in adolescents

Inositol is a cyclic sugar alcohol. Due to its cyclic structure with the presence of 6 hydroxyl groups it forms a total of 9 stereoisomers. Myo-inositol is the most represented isomer in biological systems. It is usually grouped into a group of B complex vitamins, although organisms (both prokaryotic and eukaryotic) are able to synthesize it. The question remains whether it is sufficient.

Myo-inositol is one of the so-called insulin sensitizers. Thus, its potential association is not only in the pathogenesis of type 2 diabetes and gestational diabetes, but also with PCOS.

In 2009, Zacche, *et al.* found that after 6 months of daily administration of 4g myo-inositol, LOS, testosterone, free testosterone, basal insulin levels and skin manifestations of hyperandrogenemia decreased in PCOS patients. In patients with PCOS independent of BMI, androgen levels decreased as a result of reduced insulin resistance and ovarian function was improved - thereby improving oligomenorrhea and return of ovulation [7]. The manufacturer states the dosage - 1 sachet per day, i.e. 2g. However, in the studies, in the case of hirsutism and acne treatment, a higher dose of 2 sachets per day is recommended, i.e. 2 x daily 2g for 3 months. Currently, this increased dosage is recommended for treatment to reduce the symptoms of hyperandrogenism [8].

Dysfunctional uterine bleeding

Dysfunctional bleeding is defined as abnormal uterine bleeding without evidence of structural pathology. In adolescence, dysfunctional bleeding is also referred to as juvenile metrorrhagia (metrorrhagia juvenilis) and is one of the most common problems in this age group.

The onset of the disorder is sometimes very inconspicuous, often underestimated not only by parents but also by doctors and can lead to serious health disorders or even life threatening condition. The maximum incidence is perimenarcheal and around the second year of menstruation, more often in asthenic girls with a smaller uterus, where due to the frequent reactivity of the endometrium, an increased amount of estrogen receptors in the endometrium can be assumed. In prolonged bleeding, the patient chronically anemizes, which can lead to secondary disorders of hemocoagulation or hypotonia of uterine muscles due to hypoxia.

Causes of juvenile metrorrhagia

The main cause is anovulation, in which, under the influence of hyperestrogenism, uncorrected by progesterone, the endometrium is excessively proliferated until a relative estrogen deficiency occurs which is no longer able to fully maintain the hyperproliferated endometrium. Mucosal necrosis occurs with bleeding (a so-called estrogen bleeding). The endometrium separates irregularly, and in other places it grows again and the bleeding continues.

Endometritis is not a separate cause of bleeding. However, in protracted dysfunctional bleeding, even very discrete endometrial inflammatory changes potentiate the course of juvenile metrorrhagia. In the pre-disease period of juvenile metrorrhagia, it is possible to detect a febrile illness - especially in the upper respiratory tract, chronic tonsillitis, urinary tract infection. The usual hormonal treatment is not successful in such cases.

Although haemocoagulation disorders are often diagnosed before puberty, it is often the case that strong bleeding during menarche or heavy bleeding after menarche is the first sign of severe coagulopathy. In such cases, gynecologist and haematologist collaboration is required to manage profuse bleeding during menses [2].

Diagnosis of juvenile metrorrhagia

The most important element is a thorough medical history - bleeding for more than 7 days, more than 5 pads a day. For this reason, we require a thorough menstrual calendar management in adolescents. In gynecological examination we find normal palpation findings, diagnosis of anovulation and hyperestrogenism is determined easily and quickly by hormonal cytology. Blood screening is crucial.

Criteria for treatment:

- Hemoglobin < 100 g/l with acute bleeding: urgent hormonal bleeding arrest followed by separation of the endometrium and prevention of relapses,
- Hemoglobin <100 g/l without acute bleeding: combined hormone therapy followed by prevention of relapses,

- Hemoglobin 100g - 120 g/l: stopping of bleeding: gestagen or combined hormone therapy,
- Hemoglobin > 120 g/l: hormone-free cycle monitoring, serum iron examination eventual supplementation, check-ups every 3 months.

Treatment of juvenile metrorrhagia

Treatment of juvenile metrorrhagia consists of four components:

- Bleeding arrest,
- Separation of irregular endometrium,
- Adjustment of blood count,
- Prevention of relapses.

In the past, the so-called hormonal shock (hormone curettage) was used to stop bleeding. This was a simultaneous intramuscular administration of estrogen and progesterone, which was repeated the next day. This treatment has almost always stopped bleeding for 2 - 5 days. Then, so-called withdrawal bleeding, usually in menses strength, occurred. Estrogens promote mucosal proliferation and thereby stop bleeding, while progesterone administered concurrently provides secretory transformation of the endometrium, which precipitates rapidly and with small blood loss after the hormonal levels fall. Progesterone also has a beneficial effect on pathologically enhanced fibrinolysis in irregular endometrium. The disadvantage of this procedure is the short interval between previous acute and subsequent separation bleeding. At present, the scheme is not used for the unavailability of a particular estrogen preparation.

Currently, a combined oral contraceptive - single-phase (levonorgestrel) with a standard dose of 30 µg of ethinylestradiol is used to stop acute dysfunctional bleeding in adolescents:

- 2x 1 tbl for 10 days - moderate intensity bleeding,
- 3 - 4x 1 tbl for 5 - 10 days - strong intensity bleeding,
- 3 - 4x 1 tbl for 4 days... 3x 1 tbl for 3 days ... 2x 1 tbl for 2 weeks - acute bleeding with severe anemia.

Following the discontinuation of treatment, bleeding is expected to occur within 3 days. The advantage is a longer bleeding interval from a previous acute bleeding. This provides time to regenerate the patient's overall condition, especially adjusting the blood count parameters prior to separation bleeding. Following the management of acute bleeding attack, progesterone treatment of approximately 3 to 6 months must follow in the second half of the cycle to prevent relapses [2,9,10].

Dysmenorrhea

Dysmenorrhoea is divided into primary, which is without association with macroscopic pelvic pathology and secondary, in which anatomical or macroscopic pathology is present. In the pathophysiology, abnormal formation of endometrial prostaglandin, leukotrienes, vasopressin, the presence of a pathological process in the pelvis or a psychological factor is contemplated. Primary dysmenorrhoea usually occurs 6 to 12 months after menarche - with the onset of ovulation. It is reported that up to 88% of adolescent girls diagnosed with primary dysmenorrhoea will experience their first painful menstruation within the first 2 years after menarche.

If the first painful menstruation arrives later than two years after menarche, it is very likely that it will be a secondary dysmenorrhea. One of the most serious causes of secondary amenorrhoea is endometriosis. Endometriosis may be asymptomatic or may appear as pelvic pain or dyspareunia in addition to secondary dysmenorrhea. Its seriousness lies in the potential problems of getting pregnant in adulthood, so it is necessary to think about it in time. Janssen., *et al.* (2013) report the incidence of endometriosis in up to 70% of dysmenorrhea adolescents [11].

Conclusion

In adolescent girls, we tolerate minor disorders of the menstrual cycle, especially if they are up to 2 years from menarche. However, we must never allow bleeding to be too frequent, long and strong, and lead to patient anemia. Successful treatment of menstrual disorders in this group requires a thorough assessment of the nature of the disturbances taking into account the age of the patient. The treatment of these disorders is not always the responsibility of a gynecologist and often requires interdisciplinary collaboration with a hematologist, endocrinologist or geneticist. Preventing relapses and long-term patient care is an important moment in maintaining her reproductive health.

Bibliography

1. Nižňanská Z., *et al.* "Poruchy menštruačného cyklu v adolescentnom veku". *Gynekológia Pre Prax* 2.2 (2002): 93-98.
2. Hynková M and Hynek K. "Menštruačný cyklus a jeho poruchy u dievčat". *Mod Gynek Porod* 10.4 (2001): 419-423.
3. Rosenfield RL. "Clinical review: Adolescent anovulation: maturational mechanisms and implications". *Journal of Clinical Endocrinology and Metabolism* 98.9 (2013): 3572-3583.
4. Fait T. "Poruchy menštruačného cyklu". *Mod Gynek Porod* 9.9 (2000): 347.
5. Benjamins L. "Practice Guideline: Evaluation and management of abnormal vaginal bleeding in adolescents". *Journal of Pediatric Health Care* 23.3 (2009): 189-193.
6. Vuguin PM. "Interventional studies for polycystic ovarian syndrome in children and adolescents". *Pediatric Health* 4.1 (2010): 59-73.
7. Zacche MM., *et al.* "Efficacy of myo-inositol in the treatment of cutaneous disorders in young women with polycystic ovary syndrome". *Gynecological Endocrinology* 25.8 (2009): 205-213.
8. Sysák R. "PCOS z pohľadu gynekológa". In: Borovský M, Payer J. *Gynekologická endokrinológia*. Bratislava: Herba (2006): 53-64.
9. Nižňanská Z. "Hormonálna liečba v gynekológii detí a dospelých". In: *Hormonálna liečba v gynekológii*. Bratislava: SAP (2005): 11-20.
10. Borovský M and Krištúfková A. "Diferenciálna diagnostika porúch menštruačného cyklu". *Ambulantná Terapia* 7.1 (2009): 18-22.
11. Janssen EB., *et al.* "Prevalence of endometriosis diagnosed by laparoscopy in adolescents with dysmenorrhea or chronic pelvic pain: a systematic review". *Human Reproduction Update* 19.5 (2013): 570-582.

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