Mini-Review

Dysmenorrhea in Adolescents and Young Adults: Etiology and Management

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Abstract. Dysmenorrhea is the most common gynecologic complaint among adolescent and young adult females. Dysmenorrhea in adolescents and young adults is usually primary (functional), and is associated with normal ovulatory cycles and with no pelvic pathology. In approximately 10% of adolescents and young adults with severe dysmenorrhea symptoms, pelvic abnormalities such as endometriosis or uterine anomalies may be found. Potent prostaglandins and potent leukotrienes play an important role in generating dysmenorrhea symptoms. Nonsteroidal anti-inflammatory drugs (NSAID) are the most common pharmacologic treatment for dysmenorrhea. Adolescents and young adults with symptoms that do not respond to treatment with NSAIDs for 3 menstrual periods should be offered combined estrogen/progestin oral contraceptive pills for 3 menstrual cycles. Adolescents and young adults with dysmenorrhea who do not respond to this treatment should be evaluated for secondary causes of dysmenorrhea. The care provider's role is to explain about pathophysiology of dysmenorrhea to every adolescent and young adult female, address any concern that the patient has about her menstrual period, and review effective treatment options for dysmenorrhea with the patient.

Key Words. Dysmenorrhea—Adolescents—Young adults

Introduction

The Menstrual Cycle in Adolescents

Menarche, the onset of menstrual periods, marks an important point in life for the female adolescent, as it symbolizes the entrance into womanhood. In 1997, Herman-Giddens and colleagues examined pubertal development and age of menarche of young girls seen in pediatric practices throughout the United States.[1] The majority of girls were Caucasian (90.4%) and 9.6% were African-American. Mean age of breast development was 8.87 years in African-American girls and 9.96 years in Caucasian girls. Mean menarchal age was 12.2 years in African American girls and 12.9 years in Caucasian girls. These findings revealed that young girls begin the pubertal process earlier than previously reported.[2] The findings also indicated that the age of menarche in the USA has remained stable among Caucasian girls and has slightly decreased among African American girls over the past 40 years.

In adult women, most of the cycles are ovulatory and regular, lasting between 21 and 35 days. During the first half of the cycle (follicular phase) pulsatile GnRH secretion from the hypothalamus stimulates secretion of luteinizing hormone (LH) and follicle-stimulating hormone (FSH) from the anterior pituitary gland. FSH and LH stimulate development of a dominant follicle in the ovaries. The estrogen produced by the ovaries is capable of exerting a positive stimulatory feedback on LH release, leading to LH surge around day 14 of the cycle. Ovulation occurs approximately 12 hours after the LH surge. If ovulation has occurred, progesterone is secreted from the corpus luteum during the second half of the cycle (luteal phase) with a peak around 8 days after the LH surge. While the luteal phase is constant and lasts 14 days, the number of days required for follicular growth and maturation in the follicular phase may vary, leading to slight variability in cycle length among women. Regression of the corpus luteum results in a decrease of both progesterone and estrogen, triggering a synchronous sloughing of the endometrial lining (menstruation). The average blood loss during the menstrual period is 40 mL, with a normal range between 25 and 69 mL.[3] Most of the blood loss occurs during the first few days of the menstrual period, which generally lasts from 2 to 7 days.

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In adolescents, the positive stimulatory feedback mechanism of estrogen on LH does not mature, and the LH surge does not occur, until 2−5 years after menarche. As a consequence, 50−80% of the cycles are anovulatory and irregular during the first 2 years after menarche, and approximately 10−20% of cycles remain anovulatory up to 5 years after menarche. The length of the interval between the onset of menses and the establishment of ovulatory cycles is associated with the age of menarche, with earlier menarche correlating with a shorter interval.[4] The eventual attainment of ovulatory cycles by the teenagers leads to normal, repetitive menstrual bleeding. While dysmenorrhea (menstrual cramps and other menstruation-associated symptoms) is less common during the first 2−3 years after menarche, when most of the menstrual cycles are anovulatory, it becomes more prevalent during mid and late adolescence, with the establishment of ovulatory menstrual cycles.[5]

Prevalence and Treatment Patterns of Dysmenorrhea

Dysmenorrhea is the most common gynecologic complaint and the leading cause of recurrent short-term school or work absenteeism among female adolescents and young adults.[5] Despite the high prevalence of dysmenorrhea in adolescents and young adults, many girls either do not seek medical advice or are under-treated. In one study, a majority (98%) of adolescents used nonpharmacologic methods such as heat, rest, or distraction to treat dysmenorrhea, with perceived effectiveness of 40% or less.[6] In other studies from different populations, 30−70% of girls reported at least occasionally self-medicating with over-the-counter (OTC) pain medications.[7−9] However, 57% of those who self-medicated with OTC preparations used sub-therapeutic doses.[9] Only 54% of adolescents knew that certain medications could relieve menstrual cramps,[8] and 27% of girls were unable to recognize any of three non-steroidal anti-inflammatory drugs (NSAID) listed as possible treatments for dysmenorrhea.[10]

Dysmenorrhea Symptoms and Risk Factors

While lower abdominal cramping is the most common dysmenorrhea symptom, many adolescents suffer from other menstruation-associated symptoms, such as headaches and vomiting (Fig. 1). Symptoms typically accompany the start of menstrual flow or occur within a few hours before or after onset, and last for the first 24−48 hours. Severity of dysmenorrhea symptoms positively correlates with early menarche and with increased duration and amount of menstrual flow.[7,11] Low fish consumption correlated with dysmenorrhea severity in two studies.[11,12] In addition, cigarette smoking may increase duration of

Fig. 1. Dysmenorrhea symptoms.

dysmenorrhea, presumably because of nicotine induced vasoconstriction.[13] Premenstrual symptoms, which are more common starting in the third decade of life, are less common in adolescent girls and are often alleviated by adequate treatment of dysmenorrhea.

Pathophysiology of Primary Dysmenorrhea

The majority of dysmenorrhea in adolescents and young adults is primary (or functional), is associated with a normal ovulatory cycle and with no pelvic pathology, and has a clear physiologic etiology.[5,14] After ovulation there is a buildup of fatty acids in the phospholipids of the cell membranes. The high intake of omega-6 fatty acids in the western diet results in a predominance of the omega-6 fatty acids in the cell wall phospholipids.[15] After the onset of progesterone withdrawal before menstruation, these omega-6 fatty acids, particularly arachidonic acid, are released, and a cascade of prostaglandins (PG) and leukotrienes (LT) is initiated in the uterus (Fig. 2). The inflammatory response, which is mediated by these PG and LT, produces both cramps and systemic symptoms such as nausea, vomiting, bloating, and headaches. In particular, the prostaglandin F2α, cyclooxygenase (COX) metabolite of arachidonic acid, causes potent vasoconstriction and myometrial contractions, leading to ischemia and pain.[14]

Chan and Hill measured PGF2α activity in menstrual fluid from tampons and found that PG activity was twice as high in the dysmenorrheic as in the eumenorrheic women.[16] Similar findings were reported by Rees et al.[17] Lundstrom and Green examined endometrial specimens taken from both dysmenorrheic and eumenorrheic women during the menstrual period and found that women with dysmenorrhea receiving no medication had endometrial PGF2α levels four times higher than the eumenorrheic women on the first day of the menstrual period.[18] While the PG pathway has been extensively investigated in dysmenorrhea, there is a paucity of data regarding the LT
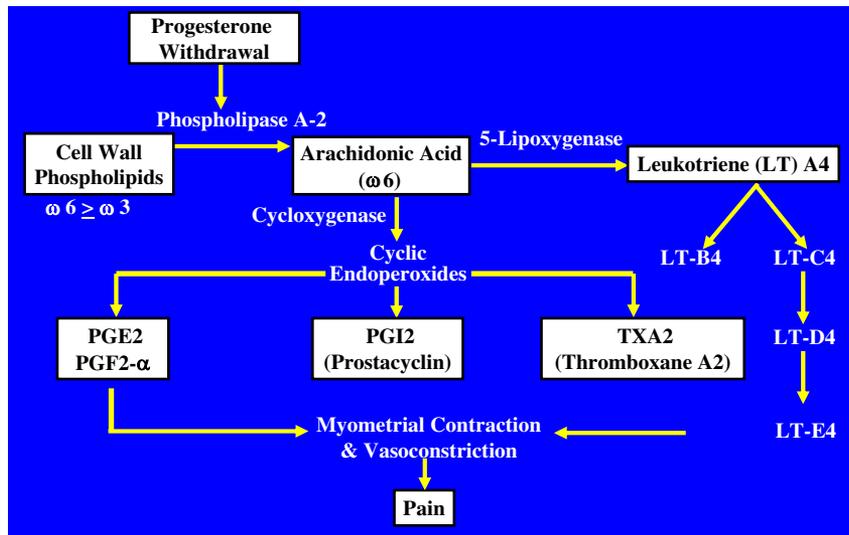
Fig. 2. Pathophysiology of Dysmenorrhea.

pathway. Previous studies have shown that human uterine tissue has the capacity to synthesize and metabolize LT,[19] and LT receptors have been detected in uterine tissue.[20] Rees et al found that the highest LT values were present in uterine tissue obtained (during hysterectomy) from adult women with a complaint of dysmenorrhea.[19] Nigam et al found a close correlation between menstrual flow LT-C_4/D_4 levels and the severity of dysmenorrhea symptoms in adult women with primary dysmenorrhea.[21] In a preliminary study, we found an increase in urinary LT-E_4 in adolescent girls with dysmenorrhea,[22] further indicating a possible involvement of these potent vasoconstrictors and inflammatory mediators in generating symptoms of dysmenorrhea in adolescents.

Pathophysiology of Secondary Dysmenorrhea
Secondary dysmenorrhea refers to painful menstruation associated with pelvic abnormalities, which may be seen in about 10% of adolescents and young adults with dysmenorrhea. Secondary dysmenorrhea is more likely to be associated with chronic pelvic pain, midcycle pain, dyspareunia, and metrorrhagia.

Endometriosis. Endometriosis is the most common cause of secondary dysmenorrhea in adolescents and young adults. It is defined as the presence and growth of uterine glands and stroma outside the uterine cavity. The majority of endometriosis implants are located in the pelvis, with the ovaries being the most common site. Other common endometriosis sites include the pelvic peritoneum, anterior and posterior cul-de-sac, uterosacral ligaments, pelvic lymph nodes, cervix, uterus, vagina, vulva, rectosigmoid colon, and appendix. Rare sites of implantation include the

umbilicus, surgical scars, bladder, kidneys, lungs, and extremities. The incidence of endometriosis in adolescents has been reported to be between 45% and 70% in a referral population presenting with chronic pelvic pain.[23] The youngest reported patient to have biopsy-proven endometriosis was 10 years of age.[24] The 6.9% incidence of endometriosis in first-degree relatives of women with the disease compared with the 1% incidence in a control population, implies a possible polygenic multifactorial model of inheritance.[25]

The most widely accepted theory about the development of endometriosis is the Sampson's theory of retrograde menstruation. Deficient cell-mediated immunity with impaired clearing of endometriotic cells from aberrant locations has also been implicated. Other theories of origin include the Meyer's theory of multipotential cells undergoing metaplasia, and the Halban's theory of hematogenous and lymphatic dissemination of endometrial cells. Abnormal local hormonal activity and potent inflammatory mediators are also involved in the pathophysiology of endometriosis.

Endometriosis is an estrogen-dependent disorder. Immunohistochemical studies have located estrogen receptor expression and increased expression of aromatase in epithelial and stromal cells of endometriotic tissues and peritoneum.[26,27] Thus, while aromatase activity is not detectable in normal endometrium, it is expressed inappropriately in endometriosis, leading to a rise in local biosynthesis of estrogen. This acquisition of steroidogenic capacity may permit the ectopic endometrial tissues to survive despite the lack of ovarian steroids during menstruation. In addition, aberrant expression of cytokines such as interleukin-1

and tumor necrosis factor-alpha may influence the establishment and proliferation of these ectopic endometrial implants.[28] Immunohistochemical studies have shown that the COX-2 expression is upregulated in endometriotic lesions,[29] and this increase in COX-2 is most likely secondary to the increase in estrogen.[30] The increased COX activity results in production of PG such as PG E_2, which, in turn, is a potent inducer of aromatase expression and activity in endometriotic stromal cells.[31] Another abnormality that contributes to the rise of estrogen in endometriosis is a deficient 17beta-hydroxysteroid dehydrogenase (17β-HSD) type 2 expression which impairs the inactivation of estradiol to estrone.[32] This 17β-HSD type 2 deficiency may also be viewed as a defective action of progesterone, which fails to induce this enzyme in endometriotic tissue. Thus, the positive feedback loop in endometriosis consists of high local level of estrogen, which induces transcription of COX-2 and synthesis of PG E_2, resulting in further expression and activity of aromatase, and further increase in estrogen (Fig. 3). The accumulation of estrogen and PG results in a potent inflammatory process and pelvic pain.

The severity of pain from endometriosis involves several factors. These include the location of the lesion, depth of invasion, and stretching or scarring of tissue. In particular, women with deep implants tend to have more active disease and more severe pain.[33] However, the presence of symptoms does not always predict the extent of endometriosis.[34]

Reproductive Tract Anomalies and Other Causes of Secondary Dysmenorrhea. In the adolescent age group the distinct possibility of a mullerian anomaly must also be considered. The patient may have a didelphic uterus with unilateral obstruction resulting in pelvic pain that may or may not be cyclic. In particular, an early age of presentation of endometriosis is often associated with a genital outflow obstruction. In one study by Goldstein et al, congenital anomalies of the reproductive tract were noted in 11% of teenagers with endometriosis.[35] Adhesions, pelvic inflammatory disease, abscess, ectopic pregnancy,

miscarriage, ovarian cyst, and, rarely, ovarian neoplasm are also included in the differential diagnosis of secondary dysmenorrhea.

Treatment of Dysmenorrhea

Non-pharmacological Approach

Interventions such as herbal preparations,[36] transcutaneous nerve stimulation,[37] acupuncture,[38] exercise,[39] and topical heat therapy[40] have been reported to improve dysmenorrhea in some studies. A low-fat vegetarian diet was associated with a decrease in dysmenorrhea duration and intensity in young adult women.[41] Dietary supplementation with omega-3 fatty acids had a beneficial effect on dysmenorrhea symptoms in adolescents in one study.[42] Increasing dietary omega-3 fatty acids intake leads to production of less potent prostaglandins and less potent leukotrienes, which may have accounted for the reduction in menstrual symptoms observed in adolescent girls in that study.

Non-steroidal Anti-inflammatory Drugs

The most common pharmacological treatments for dysmenorrhea are NSAIDs. NSAIDs inhibit cyclooxygenase, leading to a reduction in prostaglandin production. The resulting lower level of prostaglandin leads to less vigorous contractions of the uterus, and, therefore, to less discomfort. While most NSAIDs inhibit only cyclooxygenase, meclofenamate sodium (a fenamate NSAID) has been shown in vitro to inhibit both cyclooxygenase and lipooxygenase pathways.[43] Chan and Dawood found that PGF2α decreased and pain improved in a small number of dysmenorrheic women treated with NSAIDs.[44] Subsequent larger, randomized, placebo-controlled studies have shown several NSAID preparations, including naproxen sodium, zomepirac sodium, mefenamic acid, ketoprofen, ibuprofen, and diclofenac, to be effective treatments for primary dysmenorrhea.[45−50] While Owen found a trend favoring fenamates over ibuprofen, indomethacin, and naproxen,[51] Roy found no significant clinical difference between mefenamic acid and ibuprofen,[52] indicating that there is no clear-cut advantage of one NSAID over another in the treatment of dysmenorrhea. DuRant et al randomized 45 girls with a mean age of 15 years to five naproxen sodium dosing regimens for the treatment of dysmenorrhea. By the third treatment month, a loading dose of 550 mg was associated with more improvement of dysmenorrhea symptoms than the regular dose of 275 mg.[53] This suggests that a loading dose of NSAID (typically twice the regular dose) should be used as initial treatment for dysmenorrhea, followed by a regular dose as needed.
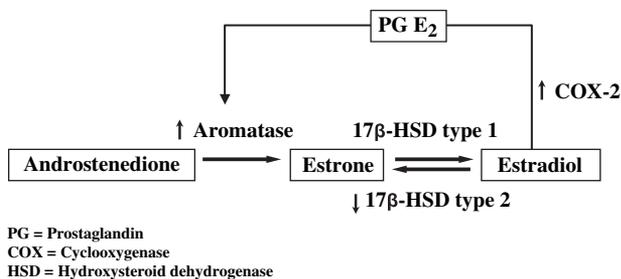

PG = Prostaglandin
COX = Cyclooxygenase
HSD = Hydroxysteroid dehydrogenase

Fig. 3. Pathophysiology of Endometriosis.

Specific cyclooxygenase type 2 (COX-2) inhibitors may also relieve dysmenorrhea symptoms.[54] These specific COX-2 inhibitors spare prostaglandins produced by COX-1 which are essential for the integrity of the gastric mucosa. Celecoxib (Celebrex®) is the only available COX-2 inhibitor approved by the US Food and Drug Administration (FDA) for treatment of primary dysmenorrhea. Currently, it is approved for treatment of patients ≥ 18 years. The recommended dosage of celecoxib (Celebrex®) is 400 mg initially, followed by 200 mg every 12 hours as needed during the menstrual period.

Not all adolescents and young adults with dysmenorrhea respond to NSAIDs, and some of those who do respond report only partial relief.[51,55] One possible explanation is that most NSAIDs inhibit only cyclooxygenase and do not affect the production of other inflammatory mediators such as leukotrienes. However, in a recent study, treatment with the leukotriene receptor antagonist montelukast (Singulair®), in the FDA approved dose (for asthma) and commencing immediately before the menstrual period, failed to improve dysmenorrhea symptoms in adolescents.[56] Occasionally, adolescents who do not respond to NSAIDs may have psychogenic causes of dysmenorrhea. Most important, adolescents who do not respond to NSAIDs may have secondary organic causes of dysmenorrhea.

Oral contraceptive pills. Combined oral contraceptive pills (OCP) are a widely used treatment for primary dysmenorrhea in women. OCPs are perhaps an ideal treatment for adolescent dysmenorrhea: they are safe during adolescence, have health benefits important to adolescents such as improvement in acne, and could prevent unintended pregnancy.

OCPs prevent or improve dysmenorrhea directly by limiting endometrial growth and reducing the amount of endometrial tissue available for PG and LT production, and indirectly by inhibiting ovulation and subsequent progesterone secretion. The observed decrease in menstrual fluid PG and LT during OCP use[44,57] and the observed inconclusive serum levels of these inflammatory mediators[58,59] are consistent with a change in local uterine production of PG and LT. Ekstrom et al found a decrease in intrauterine pressure and improvement in pain on the first day of menstrual bleeding following treatment with low-dose OCP.[60,61] Taken together, these studies suggest that OCPs may decrease pain by decreasing PG and LT production as well as by decreasing intrauterine pressure.

Many studies have reported an association between OCP use and decreased dysmenorrhea. While one study suggested that OCPs consisting of a potent progestin (such as levonorgestrel) might be more beneficial in treatment of dysmenorrhea,[62] other studies showed OCPs with less potent progestins to be beneficial as well.[63,64] Overall, the consistency of OCPs effect across populations and with different pill formulations[63–67] supports the use of OCPs in the treatment of dysmenorrhea.

Girls on OCP who continue to experience menstrual symptoms or exacerbation of a medical condition (asthma, arthritis, seizure) during the active pill-free interval may be considered for extension of the duration of active hormones to more than 21 days. Studies in adult women with menstrual-related problems showed that an extended cycle regimen (allowing menses every 3 or more months) was easier to follow, well tolerated, and efficacious in reducing menstrual symptoms.[68,69] A new combined OCP (Seasonale®) consisting of active pills for 84 days of continued use was approved by the FDA in September 2003. The main concerns with the extended cycle regimen are: a potential decrease in endometrial stability, a possible deleterious effect on lipid profile, and the question of long-term safety with increased hormonal load.[70]

Injectable long-acting hormonal contraceptives. The injectable contraceptive depot medroxyprogesterone acetate (DMPA) is a progestin-only, long-acting, effective, and convenient contraceptive method. It is available in two formulations: the intramuscular formulation (Depo-Provera®, 150 mg DMPA/1 ml) approved by the FDA in 1992, and the subcutaneous formulation (Depo-subQ Provera 104®, 104 mg DMPA/0.65 ml) approved by the FDA in 2004, both administered every 12 weeks. Since ovulation is inhibited for as many as 7 to 9 months after a single DMPA intramuscular injection,[71] it may be used for alleviating dysmenorrhea symptoms. While the subcutaneous formulation of DMPA delivers a 30% lower total dose of DMPA than the intramuscular formulation, it was also found to suppress ovulation for more than 13 weeks,[72] and thus may improve dysmenorrhea symptoms as well. About two thirds (64%) of adolescents reported less dysmenorrhea symptoms while using DMPA (Depo-Provera®) as a contraceptive method.[73] Since the use of this progestin-only contraceptive may lead to relative estrogen deficiency, there is a concern regarding its effect on bone mineral density (BMD), particularly when used during adolescence, a critical period for BMD accrual. On November 17, 2004, the FDA issued a "Black Box Warning" for DMPA, stating that prolonged use of the method may result in significant loss of BMD, that the loss is greater the longer the drug is administered, and that BMD loss may not be completely reversible after discontinuation of DMPA.[74] A once-a-month combined medroxyprogesterone acetate and estradiol

cypionate injectable contraceptive (Lunelle®) was approved by the US FDA in October 2000 (currently withdrawn from the US market because of manufacturing difficulties), but there are no data yet about its effect on dysmenorrhea in adolescents.

Other Long-acting Hormonal Contraceptives

Women (age 25−47 years) who used the levonorgestrel releasing intrauterine system (Mirena®) considered the absence or reduced intensity of menstruation and the amelioration of menstrual pain as the main advantages of this method.[75] The combined estrogen and progestin transdermal patch (Ortho Evra®) also has the potential to alleviate dysmenorrhea. However, in one study of adolescent girls using Ortho Evra®, only 39% of participants reported decrease in dysmenorrhea symptoms, while 11% actually reported worsening of symptoms.[76] It remains to be determined in further studies whether Ortho Evra® may be less beneficial than OCP in the management of dysmenorrhea. To date, no study has evaluated the effect of the combined estrogen and progestin vaginal ring (Nuvaring®) on dysmenorrhea in adolescents and young adults.

Approach to Adolescents and Young Adults with Dysmenorrhea

Evaluation of the adolescent or young adult with dysmenorrhea starts with a history that is obtained privately and confidentially. The patient should be asked about age at menarche, menstrual pattern, onset and character of menstrual cramps and other menstruation associated symptoms, response to analgesic medication, sexual activity, sexual abuse history, contraception, condom use, history of sexually transmitted diseases, vaginal discharge, school performance and school/work absenteeism, and family history of menstrual disorders. The Cox Menstrual Symptoms Scale can be used to assess frequency and severity of dysmenorrhea symptoms.[77]

Pelvic examination is not necessary if the patient has never been sexually active, and if the history suggests primary dysmenorrhea. Because of the risk of pelvic inflammatory disease in a sexually active adolescent, an interim pelvic examination should be performed if the patient develops new-onset or more severe dysmenorrhea. Pelvic and rectal examinations should be performed in adolescents with a history suggestive of secondary dysmenorrhea. Endometriosis is associated with adnexal, uterine, or rectovaginal tenderness on pelvic examination. Palpable nodularity may be found on rectal examination.[78]

Adolescent care providers should explain about the menstrual cycle, menstruation associated symptoms, and physiologic etiology of dysmenorrhea to every girl who suffers from menstrual cramps and/or other

Table 1. NSAIDs Used During Menstruation in the Treatment of Primary Dysmenorrhea in Adolescents and Young Adults

Drug	Dosage
Ibuprofen	200−600 mg every 6 h as needed
Naproxen sodium	440−550 mg initially, followed by 220−275 mg every 8 h as needed
Mefenamic acid	500 mg initially, followed by 250 mg every 6 h as needed
Celecoxib[a,b]	400 mg initially, followed by 200 mg every 12 h as needed

NSAIDs = nonsteroidal anti-inflammatory drugs; h = hours
[a]For girls ≥ 18 years
[b]Cyclooxygenase-2 specific inhibitor

menstruation associated symptoms. During counseling, an effort should be made to encourage girls who smoke to quit smoking, since smoking may be associated with prolonged dysmenorrhea symptoms.[13] In addition, girls should be encouraged to increase consumption of fish such as salmon, tuna, mackerel, and herring, which are rich in very long chain omega-3 polyunsaturated fatty acids. A review of effective treatment options for primary dysmenorrhea should be provided.

Response to treatment is an important component of the evaluation, because dysmenorrhea resulting from endometriosis is less likely to respond to NSAIDs than is primary dysmenorrhea. If the pain does not improve with oral contraceptives, laparoscopy is indicated to evaluate for endometriosis. Pelvic magnetic resonance imaging is indicated to exclude an obstructive pelvic anomaly.

Management of Primary Dysmenorrhea

Treatment with one of the NSAIDs in a therapeutic dose is the preferred initial treatment and should be tried for at least 3 menstrual periods. Treatment with NSAIDs is most effective when it starts 1−2 days before the onset of menses. Adolescents who cannot predict the initiation of their period should be instructed to start NSAIDs as soon as menstrual bleeding begins, or as soon as they have any menstruation-associated symptoms. It is important to provide the adolescent with specific instructions about the dose and maximum daily frequency of the recommended NSAIDs. If one preparation doesn't provide relief, a second NSAID preparation should be tried. The adolescent should be instructed to take NSAIDs with food in order to prevent gastric irritation, and to increase fluid intake in order to prevent renal side effects. Because dysmenorrhea typically resolves by day 2 to 3 of the menstrual period, the short course of treatment limits the development of NSAID side effects. A specific COX-2 inhibitor should be considered in adolescents with a prior history of peptic ulcer,

in adolescents who require high dose of a conventional NSAID during the period, in adolescents with a history of conventional NSAID gastrointestinal adverse effects, and in adolescents with coagulation deficiencies. Table 1 delineates the most common conventional NSAIDs and the available specific COX-2 inhibitor used for treatment of dysmenorrhea in the United States.

If treatment with NSAIDs is not effective, a combination estrogen and progestin pill (OCP) should be offered for at least 3 menstrual cycles. Every OCP containing 20 to 35 mcg of estrogen has the potential of relieving dysmenorrhea. For girls suffering from severe dysmenorrhea symptoms, a pill containing a potent progestin (such as norgestrel or levonorgestrel) should be offered. Dysmenorrhea that does not respond to NSAIDs administered for at least 3 menstrual periods and to combined OCP administered for at least 3 ensuing menstrual cycles should raise suspicion of secondary dysmenorrhea.

Management of Secondary Dysmenorrhea

If dysmenorrhea does not improve within 6 months of treatment with NSAIDs and OCP, a laparoscopy is indicated to look for endometriosis. Due to wide variation in appearance and morphology of endometriosis, a histologic biopsy of the lesions should be considered during laparoscopy in order to confirm the diagnosis. Visible implants may also be obliterated by laser vaporization or resection during this procedure.[79,80]

Initial medical treatment for endometriosis consists of low-dose, monophasic oral contraceptives given in a noncyclic fashion. The goal is to avoid endometrial proliferation, and to prevent endometrial implants from bleeding. It is the endometrial implants that cause the pain, scarring, and infertility associated with endometriosis. Medical management in patients refractory to noncyclic OCP treatment may proceed to gonadotropin-releasing hormone (GnRH) agonists, such as nafarelin or leuprolide, for 6 months. However, the low estrogen state induced by these medications raises concern about bone metabolism, and the treatment may be associated with bothersome side effects such as hot flashes, emotional lability, and headaches.[80] Therefore, ''add back'' sex steroid therapy may be considered if long term treatment with one of the GnRH agonists is planned.[81] Medications such as danazol and methyl testosterone, used in the past for treatment of endometriosis, are seldom utilized anymore because of high rate of adverse effects. Preliminary reports indicate that aromatase inhibitors, which target ovarian as well as extra-ovarian sources of estrogen production, may be useful in the treatment of endometriosis.[82,83] Another novel approach is the use of a selective progesterone receptor modulator,

which has been shown to reduce dysmenorrhea and nonmenstrual pain in patients with endometriosis.[84]

Congenital malformations of the genital tract often require intraoperative hysterosalpingography to elucidate anatomy before reconstruction. Unlike endometriosis that is not associated with an outflow obstruction, endometriosis in patients with reproductive tract anomalies usually resolves after a patent outflow tract is established.

Secondary dysmenorrhea caused by simple ovarian cysts usually resolves spontaneously or with hormonal treatment (i.e., OCP). Cysts that are large or that persist require surgical drainage. Complex cysts with solid components require surgery for biopsy or excision.

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