Dysmenorrhea in adolescents

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Studies show that between 41% and 91.5% of young women, school-aged and university-aged, are affected by dysmenorrhea. Primary dysmenorrhea, which is caused by the production of prostaglandins, is defined as cramping pain in the lower abdomen and/or pelvis occurring just before or during menstruation, in the absence of other diseases such as endometriosis, and typically lasting 1-3 days and with a negative physical examination. Secondary dysmenorrhea presents with similar signs and symptoms but is a result of underlying pelvic pathology, for example endometriosis or uterine fibroids. Dysmenorrhea most typically presents as abdominal cramping; however, it can also present with headaches, nausea, vomiting or other generalized symptoms. The diagnosis is mainly clinical, but other tests such as a pelvic examination, a pregnancy test and STI screening may be helpful in ruling out other sources of pain. Although the mainstay of treatment for dysmenorrhea is NSAIDs and hormonal therapy, lifestyle changes and complementary/alternative medicine can also be helpful approaches. Lifestyle changes include aerobic exercise and stretching, while complementary alternative medicine include peppermint, cinnamon, ginger and other herbs and supplements. Finally, endometriosis must be considered as a potential cause for secondary dysmenorrhea and would warrant a prompt referral to gynecology.

Curr Probl Pediatr Adolesc Health Care 2022; 52:101186

Introduction

Dysmenorrhea is an important topic in adolescent medicine due to the large impact it has on the quality of life of teenage and young adult women. Studies have shown that dysmenorrhea is the leading cause of recurrent short term school absence in adolescent girls[1] and that the prevalence of primary dysmenorrhea in this group varies from 16% to possibly as high as 93%.[2] This paper aims to review the topic by discussing its most recent definitions, pathophysiology, epidemiology, clinical presentation and management, as well as to offer a most current view on endometriosis in adolescents.

Definitions

Primary dysmenorrhea can be defined as cramping pain in the lower abdomen and/or pelvis occurring just before or during menstruation, in the absence of other diseases such as endometriosis, and typically lasting 1-3 days and with a negative physical examination.[1,3] Although the etiology of primary dysmenorrhea is not completely understood, it is thought to be caused in large part by the production of uterine prostaglandins, which generate uterine contractions that result in ischemia and nerve sensitivity throughout the uterus.[3,4]

Primary dysmenorrhea can be defined as cramping pain in the lower abdomen and/or pelvis occurring just before or during menstruation, in the absence of other diseases such as endometriosis, and typically lasting 1-3 days and with a negative physical examination.[1,3]

This is in contrast to secondary dysmenorrhea, which presents with similar signs and symptoms but is a result of underlying pelvic pathology, for example endometriosis, fibroids, and/or ovarian cysts.[5] Secondary dysmenorrhea accounts for about 10% of cases of dysmenorrhea.[4] The most common etiology of secondary dysmenorrhea is endometriosis, which is defined as the presence of endometrial tissue outside the uterus.[6] It is estimated that up to two thirds of adolescent girls with persistent dysmenorrhea refractory to non-steroid anti-inflammatory drugs (NSAIDs) or hormonal therapy have endometriosis. Endometriosis

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Curr Probl Pediatr Adolesc Health Care 2022;52:101186
1538-5442/$ - see front matter
Published by Elsevier Inc.
https://doi.org/10.1016/j.cppeds.2022.101186

should therefore be considered in any patient with persistent and clinically significant dysmenorrhea, particularly in patients who do not respond to typical treatments. Other causes of secondary dysmenorrhea include fibroids, cysts and reproductive tract abnormalities such as hymenal obstruction or mullerian anomaly.[5] Although it can be similar in presentation, chronic pelvic pain is a diagnosis of its own and differs from both primary and secondary dysmenorrhea. Whereas dysmenorrhea is associated with the menstrual cycle, chronic pelvic pain refers to pain in the pelvic area lasting longer than 6 months and the timing can be cyclic, acyclic, intermittent or constant.[5]

Pathophysiology

The pathophysiology of dysmenorrhea starts with the secretion of prostanoids via the cyclooxygenase pathway. Prostanoids are a class of lipid mediators which include prostaglandins, thromboxanes and prostacyclins. At the end of the luteal phase of menstruation, as progesterone levels decline, lysosomes break down and release phospholipase A2. Thus, primary dysmenorrhea can only occur in the case of ovulation, which explains why it presents most frequently within 2 years after menarche-once the patient has regular ovulatory cycles. The major prostaglandins involved in dysmenorrhea are PGF2α and PGE2. PGF2α is directly involved in constriction of the arcuate vessel, and also causes direct uterine contractions. Both of these actions cause hypoxia in the uterus, which can lead to ischemic changes and can also cause the accumulation of anaerobic metabolites that stimulate pain receptors. At the same time, PGF2α sensitizes nerve receptors, thereby lowering the pain threshold and causing pain to be experienced more severely and more frequently. PGE2 acts on the myometrium and can cause contraction. As the amount of prostaglandin increases during menstruation, the signs and symptoms associated with dysmenorrhea increase. Prostaglandins are also responsible for gastrointestinal pain −including cramping, exacerbation of hemorrhoids and changes in stooling−seen in dysmenorrhea.[7] Although less studied than prostaglandins, Leukotrienes C4 and D4 are also thought to mediate the uterine contractions that cause dysmenorrhea. These leukotrienes have been reported to be found in higher concentrations in the menstrual fluid of patients with dysmenorrhea, suggesting their role in the pathophysiology.[7] Additionally, patients with dysmenorrhea have been found to have higher levels of serum vasopressin. In other countries, Atosiban, which blocks vasopressin receptors, has been used to alleviate dysmenorrhea. Studies on this have not shown consistent results, and thus there is not a full understanding of the role of vasopressin in dysmenorrhea.[7]

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Another contributing factor to the pathophysiology of dysmenorrhea is basal uterine tone. When comparing the baseline uterine tone in patients with dysmenorrhea versus patients with painless periods, patients with dysmenorrhea demonstrate an increased basal tone and increased pressure in the uterus during menstruation, which explains why they are at a higher risk for pain with uterine contraction.[7] It is also possible that patients with primary dysmenorrhea have a general central sensitization syndrome. Central sensitization syndrome refers to overall increased responsiveness to pain stimulation; it can manifest in the form of dysmenorrhea, as well as irritable bowel syndrome, low back pain and headache.[7]

Epidemiology

Although there is a paucity of data in recent years to determine general prevalence rates of dysmenorrhea, studies have suggested that in various subgroups the prevalence of dysmenorrhea in young women, school-aged and university-aged, ranges from 41-91.5%. [8-13] Severe pain affects up to 29% of affected girls with dysmenorrhea.[2,14] Dysmenorrhea has been reported to contribute to up to 140 million hours lost in school annually,[8] and up to one third of girls with primary dysmenorrhea report missing at least one day of school.[2,15] The most

recent literature reveals that risk factors for primary dysmenorrhea include earlier age at menarche, longer menstrual periods, heavier menstrual periods and a family history of dysmenorrhea. Additionally, cigarette smoking and high emotional stress play a role in the risk of dysmenorrhea, [2,14,16-17] as do poor mental health and poor social support.[1] Parity and the use of oral contraceptives have been found to be inverse risk factors for dysmenorrhea.[14,16] Some studies have shown a positive correlation between socioeconomic status and dysmenorrhea, but studies have generally shown very little correlation between race and dysmenorrhea.[8] Furthermore, studies that have been done throughout different countries tend to show similar rates of dysmenorrhea. Obesity may be a risk factor for dysmenorrhea, although the data is inconsistent, and another study demonstrated that attempts to lose weight could also contribute to dysmenorrhea.[3,14] Studies have repeatedly shown that many patients with dysmenorrhea do not seek medical advice, even in those for whom school absenteeism has become a major manifestation of dysmenorrhea.[2,15]

Signs and symptoms

The most common presenting symptom of dysmenorrhea is abdominal cramping. However, many adolescent patients also suffer from other symptoms associated with menstruation. These can include headaches, nausea and vomiting. Typically, symptoms will occur around the start of the menstrual flow and they will be most severe for 24-48 hours.[4] Other associated symptoms may be sweating or tremors.[2] Patient history will reveal a cyclic nature to these symptoms relating to the menstrual cycle. Although most patients recognize that their symptoms are in relation to the menstrual cycle, some may not, and may describe these symptoms on a more random basis. A skilled clinician can ask questions to identify that these symptoms occur in conjunction with the menstrual cycle, and therefore interpret these as signs and symptoms of dysmenorrhea.

Diagnosis

The diagnosis of primary dysmenorrhea is mainly clinical. A thorough history will reveal the signs and symptoms most commonly associated with dysmenorrhea, such as abdominal cramping, pelvic pain (sometimes with radiation to the legs), low back pain, headache, nausea, vomiting or fatigue. These symptoms can begin to occur within 6-12 months post menarche, and will be found to occur around the time of menstrual bleeding, sometimes a few hours before the onset of the menstrual cycle. Pain often is most severe at the time of the heaviest blood flow.[17-18] Primary dysmenorrhea will classically present with pain in the midline, whereas unilateral pain may suggest secondary dysmenorrhea.[18] Pain will be cyclic and predictable in association with the menstrual cycle, distinguishing it from other conditions of pelvic pain.[18] A urine test should be done to rule out pregnancy and/or infection.[17] Although a pelvic examination is not required for diagnosis, a normal pelvic examination will guide the clinician to diagnose primary dysmenorrhea. A normal pelvic examination can also help rule out sexually transmitted infections or uterine and reproductive tract anomalies associated with secondary dysmenorrhea.[18] For patients with first-time pelvic pain later than 12 months post menarche, a pelvic examination may be more strongly considered as there is a higher likelihood of secondary causes.[18] However, in adolescent patients, particularly pre-coitarche, pelvic examinations are generally not indicated.

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The diagnosis of secondary dysmenorrhea is also clinical. Given that secondary dysmenorrhea suggests that something else is causing the patient's symptoms, further diagnostic tests may be required to fully evaluate the patient. For the diagnosis of endometriosis, pelvic examination has a 76% sensitivity, 74% specificity, 67% positive predictive value and 81% negative predictive value.[17] Pelvic examination may reveal a fixed uterus or uterine hypomobility, adnexal mass or uterocervical nodularity.[17] A diagnosis of endometriosis will require transvaginal and pelvic ultrasonography to identify endometriomas. Magnetic resonance imaging (MRI) may also be required, as well as biopsies.[17]

Differential diagnoses

Ultimately, a large differential diagnosis exists for both primary and secondary dysmenorrhea. Among the possible diagnoses are sexually transmitted infections (including pelvic inflammatory disease), chronic pelvic pain, urinary tract infections, and pregnancy or ectopic pregnancy. Pelvic inflammatory disease will present in sexually active patients with lower abdominal and pelvic pain. The pelvic examination will reveal cervical motion tenderness and possibly adnexal tenderness. The patient may also present with fever and cervical/vaginal mucopurulent discharge. Laboratory tests may show an elevated erythrocyte sedimentation rate (ESR), an elevated C-reactive protein (CRP) and an elevated white blood cell count consistent with infection. Microscopy of the vaginal fluid may show the offending organism and cervical fluid samples and/or urine may test positive for *Neisseria Gonorrhoeae* and/or *Chlamydia Trachomatis*.[17] Urinary tract infections will present with acute dysuria, increased urinary frequency and urgency, and foul-smelling urine. A urinalysis will be positive for leukocyte esterase and leukocytes, and possibly nitrites. A urine culture will grow greater than or equal to 10^3 colony-forming units per mL of a uropathogen.[19] A patient with chronic pelvic pain will endorse pelvic pain that is present for at least six months, and which is not cyclical in its timing. Pain will radiate toward the vagina or the rectum and may be exacerbated by anxiety. Pelvic examination findings will be normal, although rectal palpation may yield pain which would indicate pudendal nerve entrapment.[17] Pregnancy or ectopic pregnancy will present with missed periods, nausea and vomiting and fatigue, and a urine HCG or serum HCG will be positive. Although less common in adolescents, other sources of pelvic pain that could be considered in the differential diagnosis for dysmenorrhea are leiomyomata, adenomyosis and interstitial cystitis.[17]

Ultimately, a large differential diagnosis exists for both primary and secondary dysmenorrhea. Among the possible diagnoses are sexually transmitted infections (including pelvic inflammatory disease), chronic pelvic pain, urinary tract infections, and pregnancy or ectopic pregnancy.

Consistently, the most well-established treatment for primary dysmenorrhea is the use of NSAIDs. NSAIDs induce analgesia through the inhibition of prostaglandin synthesis, which is the known cause of pain in dysmenorrhea.

Treatment and management of primary dysmenorrhea

Fortunately, the management of dysmenorrhea has myriad options. Treatment can be classified by pharmacologic (NSAID analgesics and hormonal pills), complementary/alternative medicine, and lifestyle modification categories.

Pharmacologic - NSAIDs

Consistently, the most well-established treatment for primary dysmenorrhea is the use of NSAIDs. NSAIDs induce analgesia through the inhibition of prostaglandin synthesis, which is the known cause of pain in dysmenorrhea. Thus, NSAIDs have been particularly effective at relieving the cramping associated with dysmenorrhea.[20] Importantly, it has been demonstrated that NSAIDs are most effective if used at the start of menstruation but before the onset of pain.[20,21] NSAIDs work by interrupting cyclooxygenase 2 (cox2) activity, thereby reducing prostaglandin production and in turn decreasing uterine contractions. They also work by having a direct analgesic effect on the central nervous system. Most studies seem to conclude that the side effects of NSAIDs are minimal in healthy young women, particularly when limited to 72 hours at a time.[21-22] Studies have not consistently found that any one NSAID is superior to another in the treatment of dysmenorrhea.[21] However, many studies have used mefenamic acid to compare NSAIDs to other alternative medications, suggesting that this may be a good option when available. Other practices prefer naproxen as it can be dosed every 12 hours, as opposed to the more conventional ibuprofen which is dosed more frequently throughout the day (every 6 hours) and thus can result in less adherence.

While NSAIDs are the only well-established pharmacologic nonhormonal treatment for dysmenorrhea, other medications have been noted to be of use off label. Nitric oxide can produce smooth muscle relaxation and thus can relieve the cramping associated with dysmenorrhea. However, up to 25% of patients experience headaches as an adverse effect.[21] Magnesium has been documented to reduce PGF2alpha and thus induce muscle relaxation. It also can cause vasodilation, which decreases ischemia in the uterus. Despite this, its use in dysmenorrhea does not have clear evidence.[21] Calcium channel blockers (such as nifedipine, 20-40 mg) are also known to induce smooth muscle relaxation, which reduces uterine contractions. Nifedipine could also inhibit prostaglandin production. Nifedipine, however, has also been associated with the side effect of headache.[21]

Pharmacologic-hormonal

After NSAIDs, the use of hormonal contraceptives is another highly established treatment regimen for dysmenorrhea. Combined hormonal contraception works by inhibiting ovulation and thus preventing endometrial proliferation, which in turn decreases prostaglandin, progesterone and vasopressin production and secretion.[21] Studies have found these to be effective in up to 90% of women, with many studies demonstrating these findings.[21] The most concerning side effect of combined hormonal contraceptives is blood clots, most commonly deep vein thrombosis.[21]Thus, these cannot be used on any patient in whom estrogen is contraindicated. Progesterone-only methods of contraception also have been shown to be effective in the amelioration of dysmenorrhea. Progesterone can induce endometrial atrophy and therefore lead to pain relief [21,22] but this has not been studied as extensively as combined hormonal contraceptives.

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Nonpharmacologic: alternative/ complementary medicine

Myriad options in the category of complementary and alternative medicine have been evaluated for their effectiveness in ameliorating the symptoms of dysmenorrhea. The most commonly studied have been zinc, mint, lemon balm, cinnamon, fennel and ginger.

Some studies have demonstrated that zinc (doses and timing vary, but generally 14-60 mg in the morning and evening, starting 4-5 days prior to menses) can be effective in preventing cramping and bloating.[23] This has been determined through observational studies and thus the evidence is not clearly established. No clear mechanism of action for zinc has been established; however several studies have suggested that zinc may affect cyclooxygenase-2 (cox-2), thus having an effect on the production of prostaglandins.[23]

Peppermint has been studied sparsely as a treatment for dysmenorrhea. In a randomized crossover study, Masoumi et al found that peppermint was effective in decreasing symptoms of dysmenorrhea when compared to a placebo, but was less effective compared to NSAIDs. However, peppermint had far fewer side effects (if any) than NSAIDs and could thus be a possible starting choice to consider for treatment.[24] Peppermint contains menthol, which acts as a muscle relaxant of smooth muscle, including in the uterus.[24]

Lemon balm (*Melissa Officianlis*, an herb from the Labiate family) is another herbal treatment that has been used for dysmenorrhea. *Melissa* is thought to inhibit smooth muscle contractions and has also been thought to decrease prostaglandins.[25] Therefore, it would be expected that *Melissa* could decrease the cramping associated with dysmenorrhea. Studies have shown varied results on this. One study found a significant decrease in the systemic symptoms of "lack of energy," "mood swings" and "feeling faint" when *Melissa* was given to patients during their menstrual cycles, as compared to a placeo, but with no effect on the menstrual cramping, headache or diarrhea seen in dysmenorrhea.[25] Another study found a decrease in severity of menstrual cramping after the administration of *Melissa*, with a significant difference when compared to placebo. [26] *Melissa* is safe to administer and patients have been receptive to trying it.[25-26]

Cinnamon (*Cinnamomum*) has been used as an antioxidant, antibacterial, antifungal and anti-

inflammatory agent in some settings for years. Cinnamon contains the essential oil cinnamaldehyde, which has an antispasmodic effect. Cinnamon also contains eugenol, which can inhibit prostaglandin formation. Furthermore, cinnamon has been noted to have a tocolytic effect, thus inhibiting uterine contractions regardless of prostaglandin production.[27] Several studies have shown that cinnamon can in fact be used as treatment for dysmenorrhea. In one randomized controlled trial, it was found that 3 g cinnamon daily significantly reduced the severity of menstrual pain as compared to placebo.[28] Another study found that when 420 mg cinnamon was administered three times per day for the first 72 hours of menstruation, there was a significant decrease in pain severity, nausea and vomiting, and in bleeding amount, as compared to placebo.[29] When compared to both ibuprofen and placebo, cinnamon was found to again reduce the duration and severity of pain, but to a lesser degree than ibuprofen.[30] Overall, cinnamon appears to be an effective way to treat symptoms associated with dysmenorrhea, but not to the extent that NSAIDs do. Still, with zero adverse effects, [27-30] it can be an option to consider for those that wish to avoid NSAIDs.

Fennel (*Foeniculum vulgare)* has also been suggested as a possible treatment for dysmenorrhea. Fennel has been shown to have an antispasmodic effect when the spasms are induced by oxytocin and PGE2, as confirmed in the uteri of mice.[27] A meta-analysis done in 2021 reviewed several studies and ultimately found that F. vulgare was consistently effective in reducing the severity of dysmenorrhea, although generally not more effectively than NSAIDs.[31] However, when looking at each of the studies, outcomes have been mixed – one study showed a significant decrease in the amount of bleeding, but no changes in pain intensity.[32] Another study showed significant changes in pain intensity with the administration of fennel, but to a lesser degree than mefenamic acid.[33] Another study showed that in young women aged 18-23, there was no significant effect on nausea, but there was a significant effect on pain and stress/worry during menses.[34] Many studies reported malodor and an unpleasant taste as an adverse effect of fennel, as a reason for noncompliance.[32-33]

Another important complementary treatment for dysmenorrhea is ginger. Ginger contains gingerols, free fatty acids, carbohydrates and proteins, and is known to have analgesic and anti-inflammatory effects. Other studies have shown that ginger can inhibit leukotrienes and the synthesis of prostaglandin by suppressing cox-2.[27,35] One meta-analysis showed that ginger is highly effective for pain relief in dysmenorrhea, and some studies have even shown that ginger produced similar results as analgesic medications.[35] Doses ranged from 750 mg to 2000 mg ginger powder per day. Studies reported minimal adverse effects with ginger.[35]

Several other herbs and dietary supplements have been suggested as possible treatments for primary dysmenorrhea. Examples include black cohosh, chastetree, dong quai, black haw, crampbark, omega-3 fatty acids, vitamin E, thiamine, niacin and magnesium. The studies on each of these are sparse, and there are no randomized control trials to determine true efficacy of these products.[36] However, certain studies on nonhuman subjects have shown that these supplements may produce an effect that could alleviate dysmenorrhea. For example, black cohosh has been shown to produce estrogenic effects via a decrease in leutinizing hormone (LH) in rats, which could provide relief to dysmenorrhea.[37] Certainly, in patients in whom NSAIDs may be contraindicated, or if a patient wishes to avoid NSAIDs, there is an established role for mint, lemon balm, cinnamon, fennel and ginger. Although the other products have less clearly established evidence, it may be worth trying in patients who have exhausted other options.

There are multiple options for nonpharmacologic treatment of dysmenorrhea. Physiotherapy (stretching, muscle relaxation, exercise), transcutaneous electrical nerve stimulation (TENS), acupuncture and heat therapy have all been utilized as possibilities to treat dysmenorrhea.

Nonpharmacologic - lifestyle modifications

There are multiple options for nonpharmacologic treatment of dysmenorrhea. Physiotherapy (stretching, muscle relaxation, exercise), transcutaneous electrical nerve stimulation (TENS), acupuncture and heat therapy have all been utilized as possibilities to treat dysmenorrhea.

Physiotherapy has been studied in various ways as a management option for dysmenorrhea. One study in 2015 designed a physiotherapy program which included stretching, Kegel exercises, jogging and relaxation exercise. In the women studied, patients had a significant reduction in symptoms after 3 menstrual cycles.[38] The symptoms studied were colicky pain in the lower abdomen, bloating, irritability, depression, headache, back pain, breast pain, and leg edema/swelling.[38] The different types of physiotherapy have been studied as isolated activities in other studies. One study found favorable results with only active stretching,[39] another found benefits to only aerobic exercise[40] and another found efficacy of only muscle relaxation.[41-42] Ultimately, there have been a large number of studies on the effect of physiotherapy in dysmenorrhea, and there is almost always some significant difference in pain intensity among patients. Furthermore, all forms of physiotherapy (exercise, stretching, muscle relaxation) have been well established to promote health benefits in other ways. It is thus almost always a positive to recommend aspects of physiotherapy in the management of dysmenorrhea.[21,38,43]

TENS relieves dysmenorrhea in three ways. It works by sending electrical impulses through the nerve root, which raises the threshold for pain reception, and thus makes the pain associated with dysmenorrhea less noticed by the patient. TENS also releases endorphins, which can reduce pain. Finally, it reduces hypoxia and ischemia in the uterine muscles by inducing vasodilation.[21] Several studies have been done to evaluate the utility of TENS for dysmenorrhea. Most studies have found an effectiveness in the use of TENS as compared to no intervention.[44] However, when compared to ibuprofen or other NSAIDs, the results have been mixed in demonstrating its utility.[44] Nonetheless, in a patient averse to the use of pharmacologic treatments, TENS may be a good possibility. It should be noted that to administer TENS, a device is required, so the patient would either have to purchase the device or attend a program which has such a device.

Acupuncture is another potential treatment option for dysmenorrhea. Acupuncture is a traditional Chinese technique that is well tolerated and without serious adverse effects.[45,46] Acupuncture stimulates the nervous system by creating local counteractive axon reflexes which release opioid proteins and serotonin.[46] Acupuncture often involves fine needles, but could also be done by applying pressure and not using needles, or by using electric impulses at the site of pressure points.[46] Multiple randomized controlled trials have been done to assess the efficacy of acupuncture and they have generally shown that acupuncture is effective in patients with dysmenorrhea. Studies consistently show that acupuncture has a great effect when compared to no intervention. When compared to NSAIDs, electroacupuncture has been found to be more effective, but manual acupuncture has not.[46] A randomized control trial done in 2018 showed that acupuncture significantly decreased the symptoms associated with dysmenorrhea, except for headache, as compared to control groups. Symptoms studied were pain, menstrual cramps, headache, dizziness, diarrhea, feeling faint, mood changes, tiredness, nausea and vomiting.[45] Acupuncture is also used generally to aid against inflammation. It thus can produce a decrease in inflammatory visceral pain. Since cytokines, chemokines and inflammatory cells are implicated in the role of pain in dysmenorrhea, acupuncture may work more generally from this anti-inflammatory perspective.[47]

Finally, heat therapy has been effective in the treatment of dysmenorrhea. Though high-quality trials are lacking, it is known that local heat increases blood flow and improves tissue oxygenation.[21] One recent meta-analysis looked at six randomized controlled trials that studied the effect of heating pads as compared to no intervention and as compared to an analgesic drug. There is a clear benefit of heat therapy for menstrual pain when compared to no intervention.[48] There also appears to be a benefit as compared to acetaminophen, which is an analgesic that does not affect prostaglandin formation (as opposed to NSAIDs). It is less clear if heat therapy is more effective when compared to NSAIDs.[48] Adverse effects of heating pads include burns (which can be prevented by ensuring the heating pad stays below 45 degrees celsius) and pruritus. Another potential downside to heating pads is that they do not work well for a patient who is active and cannot sit still, as the heating pad needs to be constantly applied. Some trials have used heating wraps, which can stay on for longer amounts of time and withstand the patient standing and moving. Heating wraps thus may be a reasonable solution to this issue.[48] Given the lower side effect profile of heating pads and wraps, it may be worth considering using these modalities for therapy in patients suffering from dysmenorrhea.

Endometriosis

Endometriosis is the most common cause of secondary dysmenorrhea in adolescents. The diagnosis should be considered in any adolescent with persistent chronic pelvic pain and providers evaluating these patients should promptly refer to gynecology. Endometriosis is defined as "the presence of endometrial glands and stroma outside the uterine cavity, predominantly in the pelvic compartment" and clinically presents as a chronic inflammatory, estrogen-dependent condition, associated with pelvic pain and infertility.[49] There are several theories regarding the pathophysiology of endometriosis. "Sampson's theory" states that endometriosis arises as the result of retrograde flow of menstrual discharge from the uterus, causing endometrial cells to flow backwards through the fallopian tubes and seed into the peritoneal cavity during menses.[50] While this theory is supported by in-vitro studies, clinical studies show that up to 90% of all women demonstrate some degree of retrograde menstruation, indicating that the development of endometriosis is likely multifactorial.[50] The pain associated with endometriosis is secondary to both an increase in the frequency and amplitude of uterine contractions, as well as the endometriotic lesions themselves, which infiltrate and irritate the surrounding tissue.[51] Additionally, studies have found that the concentration of prostaglandins is higher in the menstrual blood of women diagnosed with endometriosis.[52]

Endometriosis is defined as "the presence of endometrial glands and stroma outside the uterine cavity, predominantly in the pelvic compartment" and clinically presents as a chronic inflammatory, estrogen-dependent condition, associated with pelvic pain and infertility.[49]

While chronic pelvic pain is the classic presenting symptom of endometriosis, it is important to note that endometriosis can present with a variety of symptoms-especially in the adolescent age group. Other presenting symptoms can include dysuria, diarrhea, constipation, dyspareunia, and dyschezia. The pelvic pain commonly is menstrual (i.e. dysmenorrhea) but can also progress to non-menstrual pelvic pain, both cyclical and non-cyclical.[51]

Diagnosing endometriosis can be challenging, as no pathognomonic features or biomarkers exist to directly point a clinician toward endometriosis.[53] These challenges often lead to a delay in diagnosis. On average, women ultimately diagnosed with endometriosis see seven physicians prior to their diagnosis.[54] The diagnosis can be even more difficult to make in adolescents since they often do not present with associated symptoms such as dyspareunia or infertility. Up to two-thirds of adolescents with chronic pelvic pain have endometriosis diagnosed on laparoscopy,[55] which supports the idea that not only is this a challenging diagnosis to make, it is also one that is likely often missed; as a procedure such as laparoscopy is usually avoided as long as possible. The gold standard for diagnosis of endometriosis is laparoscopy; however the diagnosis should be strongly considered in any patient with chronic pelvic pain, especially if it is cyclic.

The management and treatment of endometriosis in the adolescent patient should focus on improvement of quality of life, reduction of symptoms, and prevention of disease progression. The ultimate goal is to balance symptom relief without an over-interventional approach, and individualize treatment strategies to the adolescent to decrease unwanted side effects and improve compliance.[50] In addition to surgery, there are several medical options that can be useful in the management of endometriosis.

The management and treatment of endometriosis in the adolescent patient should focus on improvement of quality of life, reduction of symptoms, and prevention of disease progression.

First-line medical treatment options are thought to be safe, effective, and accessible. They can be started in patients with suspected endometriosis who do not yet have laporoscopic confirmation of the diagnosis. These options include NSAIDs and other analgesics, as well as oral contraceptive pills (both combined and progesterone only). The vaginal ring and transdermal patch are alternatives to oral hormonal medications.

Methyltestosterone and danazol are exogenous androgens that can also be useful in the treatment of endometriosis. These medications work by inhibiting

follicular development, which leads to atrophy of endometriosis implants. Due to common undesirable side effects, including hirsutism, deepening of the voice and weight gain, these medications are not first-line agents or commonly prescribed for treatment of endometriosis unless other options have been exhausted or the androgenic side effects are desirable as in the transmale population.[50]

GnRH agonists such as nagrelin or leuprolide have been considered when treatment response has otherwise not been successful. The continuous GnRH stimulation leads to down-regulation of the pituitary gland leading to lower estrogen levels and decreased symptomatology associated with endometriosis.[50] It is important to note that these medications should only be prescribed to adolescents above the age of 16 years due to the adverse effects on bone density.

Surgery is an important option for both diagnosis and treatment of endometriosis in adolescents. Lesions /disease identified on laparoscopy should be assessed and removed/destroyed if possible. Surgical removal of lesions can lead to significant pain relief. Adolescents who are compliant with medical menstrual suppressive treatment after laparoscopy rarely require more than one surgical intervention.[50]

Surgical removal of lesions can lead to significant pain relief. Adolescents who are compliant with medical menstrual suppressive treatment after laparoscopy rarely require more than one surgical intervention.[50]

Conclusions

Dysmenorrhea remains a prominent concern for adolescent and young adult women. Its prevalence is high and it is frequently undertreated. Dysmenorrhea has also been implicated as a major cause of school absenteeism, which is known to be detrimental in a multitude of ways for adolescents. Several types of treatment options exist for dysmenorrhea, and they should be tried as needed. In the case of a patient presenting with cyclic pain associated with menses, both primary and secondary dysmenorrhea should be seriously considered, and treatment options should be discussed immediately with the patient. The clinician, patient and family can then work together to form the best plan possible to alleviate dysmenorrhea, improve quality of life and prevent further manifestations of the condition.

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