Treatment of Menorrhagia

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Menorrhagia is defined as excessive uterine bleeding occurring at regular intervals or prolonged uterine bleeding lasting more than seven days. The classic definition of menorrhagia (i.e., greater than 80 mL of blood loss per cycle) is rarely used clinically. Women describe the loss or reduction of daily activities as more important than the actual volume of bleeding. Routine testing of all women with menorrhagia for inherited coagulation disorders is unnecessary. Saline infusion sonohysteroscopy detects intracavitary abnormalities such as endometrial polyps or uterine leiomyoma and is less expensive and invasive than hysteroscopy. Endometrial biopsy is effective for diagnosing precancerous lesions and adenocarcinoma but not for intracavitary lesions. Except for continuous progestin, medical therapies are limited. The levonorgestrel-releasing intrauterine device is an effective therapy for women who want to preserve fertility and avoid surgery. Surgical therapies include endometrial ablation methods that preserve the uterus; and hysterectomy, which results in high satisfaction rates but with potential surgical morbidity. Overall, hysterectomy and endometrial ablation result in the greatest satisfaction rates if future childbearing is not desired. Treatment of menorrhagia results in substantial improvement in quality of life. (Am Fam Physician 2007;75:1813-9,1820. Copyright © 2007 American Academy of Family Physicians.)

▶ **Patient information:** A handout on menorrhagia, written by the authors of this article, is provided on page 1820.

The term "abnormal uterine bleeding" encompasses noncyclic and cyclic bleeding. Anovulatory bleeding is the most common type of noncyclic uterine bleeding. Menorrhagia is defined as excessive cyclic uterine bleeding that occurs at regular intervals over several cycles, or prolonged bleeding that lasts for more than seven days.[1] Anovulatory bleeding and menorrhagia, although often grouped together in discussions of treatment, do not have the same etiology or require the same diagnostic testing.

Average menstrual blood loss is between 30 and 40 mL per cycle.[2] An early population-based study concluded that the upper limit of normal menstrual blood loss was between 60 and 80 mL, with the upper limit subsequently adopted as the classic definition of menorrhagia.[3,4] A greater prevalence of impaired iron status was noted with a loss of more than 60 mL.[3] There are shortcomings to this volume definition because actual blood loss is largely subjective and difficult to quantify objectively.

In 34 percent of women, the subjective complaint of "heavy periods" appears to correlate with a significantly higher quantified average blood loss.[5] Some women, however, do not consider heavy menstrual flow to be abnormal. Of women who rated their flow as very heavy, 25 percent had losses of less than 35 mL per cycle, and 25 percent of those who rated their periods as heavy had losses of more than 82 mL.[6] Physicians may be unable to judge volume from patient history or may consider measurements unimportant in deciding treatment.[5] Pictorial blood loss assessment charts may not accurately reflect the hygiene products used.[5] Additionally, women change hygiene products at a varied frequency whether saturation has occurred or not. Therefore, the criterion of loss of more than 80 mL is of doubtful clinical significance.[4]

The clinical features associated most strongly with blood loss volume include the rate of change of sanitary protection during full flow, and the total number of pads and tampons used.[6] Other associations include the size of clots and the number of clots greater than about 1 inch in diameter. A low ferritin level correctly predicts 60 percent of women with periods with measured losses of more than 80 mL; therefore, a loss of more than 80 mL can be predicted moderately well by a model that includes ferritin levels, clot size, and the rate of pad change during full flow.[6]

Dysmenorrhea, mood change, and a perceived increase in the volume of menstrual bleeding are reported more often as severe

SORT: KEY RECOMMENDATIONS FOR PRACTICE

Clinical recommendation	*Evidence rating*	*References*	*Comments*
Physicians should prescribe oral progestin therapy for 21 continuous days (days 5 to 26 of the menstrual cycle) to reduce menstrual blood loss.	A	26	21-day continuous progestin therapy is the most effective short-term medical treatment of menorrhagia, but patient satisfaction is higher with the levonorgestrel-releasing intrauterine device.
The levonorgestrel-releasing intrauterine device is an effective long-term option for menorrhagia if future childbearing is desired.	A	31	—
Physicians should prescribe hysterectomy for patients in whom no further childbearing is desired.	A	37	This is for patients who are willing to assume the risk of major surgery.
For patients who wish to avoid major surgery and in whom childbearing is completed, endometrial ablation is a reasonable and effective alternative to hysterectomy.	A	37	—

A = consistent, good-quality patient-oriented evidence; B = inconsistent or limited-quality patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, see page 1754 or http://www.aafp.org/afpsort.xml.

problems by women with menorrhagia than is absolute blood loss.[4] Patient distress may be related more to disruptions in work, sexual activity, or quality of life than menstrual volume alone. These perceptions are important, because the amount of blood loss alone is not linked to a decision to proceed with hysterectomy. A woman's perception of blood loss and the disruption that it causes are the key determinants of subsequent treatment.[7]

Risk Factors

Established risk factors for menorrhagia include increased age,[8] premenopausal leiomyomata,[9] and endometrial polyps.[10] Parity, body mass index, and smoking are not risk factors.[8] For some women, a cause of menorrhagia is not identified.

Abnormalities of platelet function, such as von Willebrand's disease, appear to be more prevalent in women with menorrhagia than in the general population.[1,11] The prevalence of von Willebrand's disease in women with menorrhagia varies from 5 to 24 percent.[12] There are no data suggesting that a lower quality of life occurs more commonly in women with menorrhagia and von Willebrand's disease than in those with menorrhagia alone.[13]

Diagnostic Testing

The American College of Obstetricians and Gynecologists (ACOG) recommends testing for von Willebrand's disease in adolescents with severe menorrhagia, in adult women with menorrhagia, and in women undergoing hysterectomy for the sole indication of menorrhagia.[14] A more stringent meta-analysis concluded that there are inadequate data to justify routine testing for all women with menorrhagia.[13] Generally, if the patient has von Willebrand's disease, it is already known at the time of evaluation.

ACOG does not recommend a complete blood count, thyroid function test, or prolactin test for women with menorrhagia.[1] Evidence-based guidelines from the Royal College of Obstetricians and Gynaecologists, however, recommend these tests, although thyroid function and bleeding disorders should be evaluated only if other historical or clinical features suggest specific conditions.[15]

ACOG lists menstrual irregularity as a risk factor for endometrial cancer,[16] and it is reasonable to exclude cancer in adult women with persistent menorrhagia.[15] This is particularly true in cases where it is difficult to determine whether the menorrhagia is caused by anatomic causes, such as fibroids or polyps, or is a function of abnormal uterine bleeding. An exception is in adolescents, in whom endometrial cancer is rare and in whom most abnormal uterine bleeding is a result of physiologic anovulation. Invasive diagnostic modalities include endometrial biopsy, transvaginal ultrasonography, saline infusion sonohysteroscopy, and hysteroscopy[1] *(Table 1[17-21])*. Although abnormal uterine bleeding in adolescents is usually physiologic, reproductive-age women with menorrhagia require evaluation for a specific cause.[1]

The detection rate of endometrial cancer using endometrial biopsy is 91 percent, with a 2 percent false-positive rate in premenopausal women,[17] making it an accurate diagnostic test for women with abnormal uterine bleeding.[18] Greater sensitivity (97 percent) and negative predictive value (94 percent) can be achieved by combining endometrial biopsy with saline infusion sonohysteroscopy.[19] Saline infusion sonohysteroscopy incorporates real-time ultrasonography with static images during infusion of sterile saline into the uterus.[22] If bleeding persists despite a negative endometrial biopsy or saline infusion sonohysteroscopy, hysteroscopy (sensitivity 86 percent, specificity 99 percent) should be considered despite the cost and invasive nature of the procedure.[23]

The most common anatomic causes of menstrual disorders in premenopausal women are uterine polyps and submucous fibroids.[20] Transvaginal ultrasonography (sensitivity 60 percent, specificity 93 percent) and endometrial biopsy are less effective than saline infusion sonohysteroscopy for diagnosing intracavitary abnormalities. Saline infusion sonohysteroscopy is more accurate for detecting uterine fibroids (sensitivity 87 percent, specificity 92 percent) than for endometrial polyps (sensitivity 86 percent, specificity 81 percent); therefore, a negative test does not rule out intracavitary abnormalities.[23] It is unknown if structural lesions missed on saline infusion sonohysteroscopy are diagnosed more efficiently with hysteroscopy.[21] Saline infusion sonohysteroscopy is a more effective initial diagnostic test for intracavitary abnormalities in premenopausal women than transvaginal ultrasonography if the goal is to avoid expensive and invasive hysteroscopy.[20,21,24]

Treatment of Menorrhagia

Menorrhagia can result in severe anemia. Of 115 women with physician-diagnosed menorrhagia, 58 percent reported a history of anemia, for which 89 percent received treatment.[11] Additionally, 4 percent had received transfusion. Treatment of menorrhagia results in substantial improvement in quality of life.[25]

MEDICAL THERAPIES

The treatment of choice for anovulatory bleeding is medical therapy with oral contraceptive pills or progestogens.[1] High-quality comparative evidence on which to base therapy for menorrhagia, however, is limited.

Oral progestogens are the most commonly prescribed therapy for menorrhagia.[26] When administered solely in the luteal phase, they are significantly less effective than the levonorgestrel-releasing intrauterine device (IUD; Mirena).[26] Oral progestin therapy for 21 continuous days (days 5 to 26 of the menstrual cycle) effectively reduces menstrual blood loss, but patient satisfaction is higher with the levonorgestrel-releasing IUD. This regimen has the strongest role in the short-term treatment of menorrhagia.[26]

There is insufficient evidence to assess the effectiveness of monthly oral contraceptive pills for reducing

Table 1. Endometrial Evaluation for Women with Menorrhagia

Evaluation type	*Reliability*	*Comment*
Endometrial biopsy	Sensitivity, 91 percent; false-positive rate in premenopausal women, 2 percent	To rule out neoplasia in adult women; office procedure, well tolerated, anesthesia and cervical dilation usually not required; limitations include cervical stenosis and insufficient samples if endometrial atrophy present
Transvaginal ultrasonography	Sensitivity, 60 percent; specificity, 93 percent	Less effective than saline infusion sonohysteroscopy for identification of intracavitary abnormalities
Saline infusion sonohysteroscopy	For fibroids, sensitivity, 87 percent; specificity, 92 percent For polyps, sensitivity, 86 percent; specificity, 81 percent Negative predictive value, 94 percent when combined with endometrial biopsy	Sterile isotonic fluid is infused into the uterus under continuous visualization of the endometrial surface with transvaginal ultrasonography
Hysteroscopy	Sensitivity, 86 percent; specificity, 99 percent	Highest cost; may require cervical dilation; does not reduce hysterectomy rate despite absence of intracavitary pathology; used as the preferred method over other procedures

Information from references 17 through 21.

Table 2. Endometrial Ablation Methods

First-generation methods* (amenorrhea rate)
Rollerball ablation (25 to 60 percent)
Transcervical resection of endometrium (26 to 40 percent)
Laser ablation (37 percent)
Second-generation methods (amenorrhea rate)
Laser intrauterine thermotherapy (71 percent)
Microwave ablation† (Microsulis‡; 61 percent)
Thermal balloon ablation§
Cavaterm (58 percent)
Thermachoice‡ (14 to 26 percent)
Cryoablation (Her Option‡; 53 percent)
Radiofrequency ablation (Novasure‡; 41 percent)

**—Satisfaction rates with first-generation methods are 80 percent or greater; subsequent hysterectomies are performed on 2 to 21 percent of patients.*

†—Can be used for patients with uterine polyps, irregularly-shaped uterus, or moderate fibroids.

‡—Approved by the U.S. Food and Drug Administration.

§—Contraindications include previous cesarean delivery and uterine wall thickness of less than 8 mm.

Information from references 7, 35, and 36.

menorrhagia.[2] Although continuous-use oral contraceptive pills and injectable progestins reduce bleeding episodes over an extended period,[27] there have been no specific studies done for menorrhagia.

No recommendations can be made about the effectiveness of nonsteroidal anti-inflammatory drugs,[28] danazol,[29] or the antifibrinolytic agent tranexamic acid (Cyklokapron)[30] in reducing menorrhagia, because the studies are small and underpowered to detect a difference.

Although used as a contraceptive, the levonorgestrel-releasing IUD produces significant reductions in menstrual blood loss. This IUD has not been compared with placebo or no treatment.[31] One small trial compared it with oral progestin administered on days 5 to 26 of the menstrual cycle and showed the IUD to be significantly more effective in reducing menstrual blood loss.[31] There were more short-term adverse effects in the IUD group, but a significantly greater number of

Table 3. Comparison of Medical and Surgical Therapies for Menorrhagia

*Therapy**	*Effectiveness*	*Advantages*	*Disadvantages*
Nonsteroidal anti-inflammatory drugs	Insufficient evidence	Low cost, cyclic use	Adverse gastrointestinal effects
Danazol	Insufficient evidence	—	Adverse androgen effects; low compliance with daily use
Continuous oral contraceptives	Insufficient evidence	Convenience	Common adverse effects and known contraindications
Oral progestogens	Luteal only, ineffective; 21-day regimen reduces menorrhagia	Low cost, noninvasive progestin therapy	Irregular bleeding, breast tenderness, lower satisfaction than levonorgestrel-releasing IUD
Levonorgestrel-releasing IUD	More effective than continuous progestin in reducing menorrhagia but significantly less effective than endometrial transcervical resection or balloon ablation	Office procedure, ease of use improves patient satisfaction and compliance	Possible contraindications to IUD, possible irregular bleeding
Endometrial ablation	Up to 60 percent amenorrhea for hysteroscopic procedures such as rollerball ablation	Some nonhysteroscopic ablations may be done as outpatient under local anesthesia	Equipment failure, technical skill requirement higher for hysteroscopic methods
Hysterectomy	100 percent amenorrhea	Definitive procedure	One out of 30 women with major adverse event; anesthesia risks; longer recovery time

$ = least expensive; $$$$ = most expensive; IUD = intrauterine device.

**—No medical therapy, including the levonorgestrel IUD, is U.S. Food and Drug Administration approved for treatment of menorrhagia.*

Information from references 2, 7, 25, 27 through 31, and 37.

women were satisfied and willing to continue with the IUD compared with the progestin (77 versus 22 percent, respectively).[31]

Ablation methods (transcervical resection and balloon ablation) resulted in greater reductions of mean menstrual blood loss and higher amenorrhea rates than the levonorgestrel-releasing IUD,[30] but the satisfaction rates were similar despite more adverse effects with the IUD.[29]

When the levonorgestrel-releasing IUD and hysterectomy were compared, there was no difference in quality of life or satisfaction rates, but the surgery was more expensive at one and five years after surgery.[31] About 70 percent of women continued with the IUD at 12 months.[32] More than 64 percent of women using the levonorgestrel-releasing IUD as a bridge to a previously scheduled hysterectomy for menorrhagia cancelled their surgery.[33]

SURGICAL THERAPIES

Minimally invasive methods of endometrial destruction have been evaluated as alternatives to hysterectomy in women with menorrhagia. The procedures are divided into first- and second-generation methods depending on whether a hysteroscope is used. Preoperative endometrial thinning with gonadotropin-releasing hormone analogues or danazol improves technical performance and results in higher rates of postoperative amenorrhea.[34]

Clearly, selection of women is important. Women must have completed childbearing and have a benign cause for their menorrhagia.[35] First- and second-generation methods are effective in reducing average blood loss. Complication rates for both are low, and satisfaction is high.[7,15] Studies evaluating the effectiveness of endometrial ablation have been performed primarily on women with menorrhagia, not on anovulatory women.[1]

The first-generation procedures (endometrial resection and rollerball or laser ablation) are performed through a hysteroscope after uterine infusion of a distension medium to improve visualization.[35,36] Although considered the standard for endometrial ablation, the first-generation procedures take more time to perform, require regional or general anesthesia, and are technically more difficult than second-generation methods.[7] There is a 4 percent risk of fluid overload with first-generation procedures,[37] making them unsuitable for women with cardiac or renal disease.[35]

Second-generation methods are performed "blind" (without a hysteroscope), usually in the outpatient setting under local anesthesia, and require minimal cervical dilation.[35,36] These methods include cryoablation, thermal balloon ablation, radiofrequency ablation, microwave ablation, and diode laser thermotherapy.

A Cochrane review of 13 trials comparing first- and second-generation methods found no differences in satisfaction rates at one, three, and five years.[7] There were also no significant differences for outcomes of inability to work, amenorrhea rates, or requirements for any additional surgery or hysterectomy. All second-generation methods required significantly less operating time and use of general anesthesia than first-generation techniques.[7] There were, however, more reports of equipment failure with the second-generation techniques *(Table 2)*.[7,35,36]

Hysterectomy is a definitive treatment for menorrhagia, but there is risk of surgical morbidity and the economic cost is high.[15,37] Although endometrial resection procedures result in faster return to normal activities than hysterectomy, they are associated with a reintervention rate of up to 22 percent, so the cost difference between hysterectomy and endometrial resection narrows over time.[37] There are no randomized controlled trials comparing various surgical methods with hysterectomy for menorrhagia.

Table 3[2,7,25,27-31,37] compares medical and surgical options for treatment of menorrhagia.

Cost	*Target group*
Generic $, brand $$	Oral therapy, nonhormonal
$$	Oral therapy, nonhormonal
$$	Oral, hormonal contraceptive; preserves fertility
$	Oral hormonal option if estrogen is contraindicated or as a therapeutic bridge to other therapies
$$	Seeking low intervention, contraception, preserves fertility; high patient satisfaction; effective nonsurgical option
$$$	Seeking alternative to hysterectomy; completed childbearing
$$$$	Seeking no further uterine bleeding; completed childbearing

Clinical Decisions About Treatment

It is important to ask women about the amount of menstrual bleeding and level of fertility they will accept before any treatment recommendations are made.[38] When women with menorrhagia were offered an interview and information packet describing treatment options and outcomes, they were more satisfied with their role in decision making and less likely to undergo hysterectomy.[39] Although amenorrhea as a primary end point is easily measured, it is not required for improved quality of life and patient satisfaction.[40] Lifestyle and amenorrhea outcomes correlate poorly and should not be considered interchangeable.[6]

Women who tolerate menstrual bleeding and wish to maintain fertility can try medical therapy with continuous progestin on days 5 to 26 of the menstrual cycle.[15] The levonorgestrel-releasing IUD is an effective long-term option if future childbearing is desired.[33] This IUD is more effective than continuous progestin in reducing menorrhagia but is significantly less effective than endometrial transcervical resection or balloon ablation.[31]

When medical and transcervical resection (ablation) therapy for menorrhagia were compared, women preferred endometrial resection.[41] Women who continued medical therapy had lower quality of life and menstrual outcomes than women undergoing resection. There were significantly fewer secondary treatments in the resection group.[41]

When randomized to continue cyclic progestin for refractory abnormal uterine bleeding or hysterectomy, hysterectomy was shown to be superior for symptom improvement and may be the optimal choice for women who give high priority to resolving bothersome symptoms of menorrhagia and pain.[42]

Hysterectomy is a well-suited option for women who do not desire further childbearing or menstrual bleeding and are willing to assume the risk of surgery.[43] However, if there is a desire to avoid major surgery, and childbearing is completed, endometrial ablation is a reasonable and effective alternative.[44]

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