TOOLBOX

Medical management of menorrhagia

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Excessive menstrual loss, or menorrhagia, is a significant health care problem in the developed world. In the United Kingdom, 5% of women of reproductive age seek help for this symptom annually¹; by the end of reproductive life, the risk of hysterectomy (primarily for menstrual disorders) is 20%.² This is also the situation in New Zealand.³ Objectively, menorrhagia is defined as a menstrual blood loss of 80 mL per month. Population studies have shown that this amount of blood loss occurs in 10% of the population⁴; yet nearly a third of all women consider their menstruation to be excessive.⁵ This symptom thus creates a substantial workload for health services.

In clinical medicine, the paradigm of evidence-based medicine currently holds sway. Evidence-based medicine implies not only the application of effective treatments but also their rational use within a rational overall management framework. In the management of excessive menstrual loss, many physicians do not necessarily prescribe the most effective treatments. In the United Kingdom, for example, more than a third of general practitioners prescribe norethisterone [norethindrone]—arguably the least effective option—as first-line treatment, whereas only 1 in 20 prescribe tranexamic acid, probably the most effective first-line treatment.⁶ The problem is not confined to primary care. In New Zealand, where the use of tranexamic acid is restricted to secondary care, 50% of gynecologists still use luteal-phase progestogens, and less than 10% use tranexamic acid.⁷

In this review, I provide a rational overview of the diagnostic and therapeutic management of menorrhagia, relying on the systematic reviews presented in three articles—two guidelines for the management of excessive menstrual loss published in 1998^{8,9} and a consensus view published in 1995¹⁰—and the Cochrane Library for the source literature.

Summary points

- Menorrhagia is an important healthcare issue
- Despite widely available evidence inappropriate treatments are being prescribed
- Guidelines exist for the appropriate management of menorrhagia
- Appropriate treatments enhance patient choice and may increase patient satisfaction
- Medical treatments may be an effective alternative to surgery

CAUSE AND DISORDER OF MENORRHAGIA

Menorrhagia can be associated with both ovulatory and anovulatory ovarian cycles. It is important to distinguish the menstrual consequences of each cycle. Ovulatory ovarian cycles give rise to regular menstrual cycles whereas anovulatory cycles result in irregular menstruation or, extremely, amenorrhea. This distinction is critical in management. Both ovulatory and anovulatory cycles can give rise to excessive menstrual loss in the absence of any other abnormality—so-called dysfunctional uterine bleeding. Other disorders may be associated with excessive loss, for example, fibroids and adenomyosis, but the association may not always be causal. Endocrine disorders do not cause excessive menstrual loss, with the exception of the endocrine consequences of anovulation. Equally, except in selected populations, hemostatic disorders are rare causes of menorrhagia, despite suggestions to the contrary.¹¹

Excessive menstrual loss in regular menstrual cycles is the most common clinical presentation. Patients with this complaint ovulate regularly. Laboratory-based research has shown that several abnormalities can occur in

the endometrium of these women—for example, increased fibrinolytic activity¹² and increased production of prostaglandins.¹³ These observations provide the rational basis for treatment.

One consequence of excessive menstrual blood loss is iron deficiency anemia. In the western world, menorrhagia is the commonest cause of iron deficiency anemia, and low hemoglobin concentrations may predict objectively heavy menstrual blood loss.¹⁴

INVESTIGATIONS

Numerous investigations are undertaken for menorrhagia. The purpose of investigation is threefold: to assess the morbidity associated with excessive menstrual loss, to exclude major intrauterine disease, and to assess the importance or otherwise of coexistent disorders. The utility of commonly performed investigations is detailed on p 254.

CHOOSING AN APPROPRIATE TREATMENT

In most patients, no specific abnormality will have been identified from the history, examination, and investigation, a hallmark of dysfunctional uterine bleeding. The choice of treatment must, therefore, be considered in relation to several factors (see box). An element of choice for the patient is important. It has been suggested that involving patients in

Factors influencing treatment choices

- Presence of ovulatory or anovulatory cycles
- Need for contraception
- Patient preference (particularly desire to avoid hormonal therapy)
- Contraindications to treatment

Utility of commonly performed investigations for menorrhagia

Full blood count

- Hemoglobin concentration is a surrogate assessment for excessive menstrual loss.¹⁴ Other indices within the full blood count may more accurately assess iron state.⁹ Full blood count should be undertaken in all women presenting with menorrhagia

Coagulation screen

- Tests for coagulopathies such as von Willebrand's disease should only be undertaken when specifically indicated by the history

Thyroid function tests

- There is little evidence to link hypothyroidism with excessive menstrual loss¹⁵ and no evidence for hyperthyroidism to be a cause.¹⁶ Thyroid function tests should not be routinely undertaken

Other endocrine investigations

- No significant endocrine abnormality has been detected in menorrhagia.^{17,18} There is no indication for any endocrine investigation

Pelvic ultrasound

- Routine pelvic ultrasound has little place in evaluating the primary complaint of excessive menstrual loss.⁸ It is of value in evaluating other pelvic disorders discovered during clinical examination

Endometrial sampling

- As part of initial assessment there is no place for endometrial sampling.⁹ Sampling should be combined with further assessment of the endometrial cavity, for example, hysteroscopy, in selected cases only. Selected cases would include women over 40, women complaining of intermenstrual bleeding, and after a failed trial of medical treatment

The two main first-line treatments for menorrhagia associated with ovulatory cycles are nonhormonal: the antifibrinolytic tranexamic acid and nonsteroidal anti-inflammatory drugs (see box). The effectiveness of these treatments has been shown in randomized trials²⁰⁻²² and reported in systematic reviews of treatment.^{8,9,23,24}

Tranexamic acid reduces menstrual blood loss by about half, and nonsteroidal anti-inflammatory drugs reduce it by about a third. Both have the advantage of being taken only during menstruation itself—an aid to compliance—and are particularly useful in women who either do not require contraception or do not wish to use hormonal therapy. They are also of value in treating excessive menstrual blood loss associated with the use of nonhormonal intrauterine contraceptive devices.

Traditionally, hormonal therapy for menorrhagia has been progestogens given during the luteal phase of the cycle. Such treatments are ineffective.²⁵ Despite this, they remain the first choice of many general practitioners and gynecologists.^{6,7} Progestogens are effective when given for 21 days in each cycle,^{25,26} but the side effects may be such that patients choose not to continue with treatment.²⁶ Although progestogens have a contraceptive effect, their use in this way may not be the best choice when contraception is required by the patient.

The combined contraceptive pill is both an effective contraceptive and treatment of menorrhagia compared with other medical treatment.²⁷ This statement, however, cannot be expanded upon because good-quality data are lacking,²⁷ and the use of the contraceptive pill in this area has been insufficiently studied. Nevertheless, like cyclical progestogens, combined oral contraceptives are useful for anovulatory bleeding because they impose a cycle.

More fully evaluated is the recently licensed levonorgestrel-releasing intrauterine system. This system consists of a T-shaped intrauterine device sheathed with a reservoir of levonorgestrel that is released at the rate of 20 µg daily. This low level of hormone minimizes the systemic progestogenic effects, and patients are more likely to continue with this therapy than with cyclical progestogen therapy.²⁶ The levonorgestrel-releasing intra-

Effective treatments for menorrhagia

Tranexamic acid

Non-steroidal anti-inflammatory drugs

Combined oral contraceptives

Cyclical (21 days) progestogens

The levonorgestrel releasing intrauterine system

uterine system is not yet licensed for use in the treatment of menorrhagia, but when contraception is also required, its use is legitimate. It exerts its clinical effect by preventing endometrial proliferation and consequently reduces both the duration of bleeding and the amount of menstrual blood loss.²⁷ For up to 6 months, patients may have irregular bleeding or spotting, especially in the first 3 months, but after 12 months of therapy, most women have only light bleeding, and a major proportion have amenorrhea.⁹ Many of the potential problems of bleeding and spotting can be overcome by thorough pretreatment counseling.

The levonorgestrel-releasing intrauterine system is advocated as an alternative to surgery. Two studies have examined the effect of offering this treatment to women on waiting lists for hysterectomy.^{28,29} In the first of these studies, 50 women on a waiting list were offered this treatment, and 41 of them (82%) were removed from the waiting list as a result.²⁸ In the second study, 56 women on surgical waiting lists were randomly assigned to continue with their current regimen or to use a levonorgestrel-releasing intrauterine system; 18 women (64%) using the system cancelled their surgery compared with 4 women (14%) not using the system.²⁷ When compared with minimally invasive techniques, it seems to be equally effective.³⁰ Whether this treatment will provide a long-term alternative to surgery remains to be evaluated.

Excessive menstrual blood loss is a major health care problem. The publication of guidelines^{8,9} acknowledges that inappropriate management is being applied. Effective medical treatments exist and have a rational basis for their use. Increased use of effective treatments will improve patient choice and provide an alternative to surgery.

the decision-making process may increase the effectiveness of treatment.¹⁹ Patients need to be properly informed, however, to be empowered to make appropriate choices.

Medical treatment can be conveniently divided into nonhormonal and hormonal therapy. Because there is no hormonal defect,^{17,18} the use of hormonal therapy does not correct an underlying disorder but merely imposes an external control of the cycle. For many women, cycle control is as important as the degree of menorrhagia.

References

- 1 Vessey MP, Villard-Mackintosh L, McPherson K, et al. The epidemiology of hysterectomy: findings in a large cohort study. *Br J Obstet Gynaecol* 1992;99:402-407.
- 2 Coulter A, McPherson K, Vessey M. Do British women undergo too many or too few hysterectomies? *Soc Sci Med* 1988;27:987-994.
- 3 Paul C, Skegg DC, Smeijers J, et al. Contraceptive practice in New Zealand. *N Z Med J* 1988;101:809-813.
- 4 Hallberg L, Hogdahl AM, Nilsson L, et al. Menstrual blood loss—a population study: variation at different ages and attempts to define normality. *Acta Obstet Gynecol Scand* 1966;45:320-351.
- 5 *Women's health in 1990*. (Research study conducted on behalf of Parke-Davis Research Laboratories.) London: Parke-Davis Laboratories. Market Opinion and Research International; 1990.
- 6 *United Kingdom and Ireland*. Middlesex, England: Intercontinental Medical Statistics; 1994.
- 7 Farquhar CM, Kimble RM. How do New Zealand gynaecologists treat menorrhagia? *Aust N Z J Obstet Gynaecol* 1996;36:444-447.
- 8 *Guidelines for the management of heavy menstrual bleeding*. New Zealand: National Advisory Committee on Health and Disability; 1998.
- 9 *The initial management of menorrhagia: evidence-based clinical guidelines, No. 1*. London: Royal College of Obstetricians and Gynaecologists; 1998.
- 10 National Health Service Dissemination Centre. The management of menorrhagia. *Effect Health Care Bull* 1995;9.
- 11 Kadir RA, Economides DL, Sabin CA, et al. Frequency of inherited bleeding disorders in women with menorrhagia. *Lancet* 1998;351:485-489.
- 12 Dockeray CJ, Sheppard BL, Daly L, et al. The fibrinolytic enzyme system in normal menstruation and excessive uterine bleeding and the effect of tranexamic acid. *Eur J Obstet Gynecol Reprod Biol* 1987;24:309-318.
- 13 Smith SK, Abel MH, Kelly RW, et al. Prostaglandin synthesis in the endometrium of women with ovular dysfunctional uterine bleeding. *Br J Obstet Gynaecol* 1981;88:434-442.
- 14 Janssen CA, Scholten PC, Heintz AP. A simple visual assessment technique to discriminate between menorrhagia and normal menstrual blood loss. *Obstet Gynecol* 1995;85:977-982.
- 15 Scott JC, Mussey E. Menstrual patterns of myxedema. *Am J Obstet Gynecol* 1964;90:161-165.
- 16 Krassas GE, Pontikides N, Kaltsas T, et al. Menstrual disturbances in thyrotoxicosis. *Clin Endocrinol (Oxf)* 1994;40:641-644.
- 17 Haynes PJ, Anderson AB, Turnbull AC. Patterns of menstrual blood loss in menorrhagia. *Res Clin Forums* 1979;1:73-78.
- 18 Eldred JM, Thomas EJ. Pituitary and ovarian hormone levels in unexplained menorrhagia. *Obstet Gynecol* 1994;84:775-778.
- 19 Coulter A, Entwistle V, Gilbert D. Sharing decisions with patients: is the information good enough? *BMJ* 1999;318:318-322.
- 20 Preston JT, Cameron IT, Adams EJ, et al. Comparative study of tranexamic acid and norethisterone in the treatment of ovulatory menorrhagia. *Br J Obstet Gynaecol* 1995;102:401-406.
- 21 Andersch B, Milsom I, Rybo G. An objective evaluation of flurbiprofen and tranexamic acid in the treatment of idiopathic menorrhagia. *Acta Obstet Gynecol Scand* 1988;67:645-648.
- 22 Bonnar J, Sheppard BL. Treatment of menorrhagia during menstruation: randomised controlled trial of ethamsylate, mefenamic acid, and tranexamic acid. *BMJ* 1996;313:579-582.
- 23 Cooke I, Lethaby A, Farquhar C. *Antifibrinolytics for heavy menstrual bleeding*. In: Cochrane Library, Issue 1. Oxford, England: Cochrane Collaboration; 1999. [updated software]
- 24 Lethaby A, Augood C, Duckitt K. *Nonsteroidal anti-inflammatory drugs for heavy menstrual bleeding*. In: Cochrane Library, Issue 1. Oxford, England: Cochrane Collaboration; 1999. [updated software]
- 25 Lethaby A, Irvine G, Cameron I. *Cyclical progestagens for heavy menstrual bleeding*. In: Cochrane Library, Issue 1. Oxford: Cochrane Collaboration; 1999. [updated software]
- 26 Irvine GA, Campbell-Brown MB, Lumsden MA, et al. Randomised comparative trial of the levonorgestrel intrauterine system and norethisterone for the treatment of idiopathic menorrhagia. *Br J Obstet Gynaecol* 1998;105:592-598.
- 27 Silverberg SG, Haukkamaa M, Arko H, et al. Endometrial morphology during long-term use of levonorgestrel-releasing intrauterine devices. *Int J Gynecol Pathol* 1986;5:235-241.
- 28 Barrington JW, Bowen-Simpkins P. The levonorgestrel intrauterine system in the management of menorrhagia. *Br J Obstet Gynaecol* 1997;104:614-616.
- 29 Lähteenmaki P, Haukkamaa M, Puolakka J, et al. Open randomised study of use of levonorgestrel releasing intrauterine system as an alternative to hysterectomy. *BMJ* 1998;316:1122-1126.
- 30 Crosignani PG, Vercellini P, Mosconi P, et al. Levonorgestrel-releasing intrauterine device versus hysteroscopic endometrial resection in the treatment of dysfunctional uterine bleeding. *Obstet Gynecol* 1997;90:257-263.

Keeping it brief

“Sec. 1. Be it enacted by the General Assembly of the State of Ohio, That within thirty days after the passage of this act it shall be the duty of the probate judge in each county in this state to appoint three persons, who shall be reputable, practicing physicians, residents of such county, and no two of whom shall belong to the same school of medicine, whose duty it shall be to consider and pass upon all applications for license to marry, now made to the probate court, and no license to marry shall be granted to persons contemplating marriage unless they shall have received from the persons, so appointed, a certificate setting forth that such applicants are free from the following ailments, any of which shall be deemed sufficient cause for refusing a license: Dipsomania, true insanity, hereditary insanity, or insanity resulting from vice, primary, secondary or tertiary syphilis, hereditary tuberculosis or consumption.”

One sentence—from *Some recent legislation—a bill to regulate the granting of marriage licenses*. In: *Transactions of the Medical Society of the State of California*, 1898.