Dysfunctional uterine bleeding

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BACKGROUND

Dysfunctional uterine bleeding (DUB) is the major cause of heavy menstrual bleeding and impacts on women's health both medically and socially.

OBJECTIVE

This article reviews the management of DUB.

DISCUSSION

Dysfunctional uterine bleeding is defined as heavy menstrual uterine bleeding not due to any recognisable cause and is therefore a diagnosis of exclusion. Other conditions such as uterine fibroids, endometrial polyps and systemic diseases should be excluded by appropriate investigations. In the adolescent, investigations for a coagulopathy should be performed. The pathophysiology of DUB is largely unknown but occurs in both ovulatory and anovulatory menstrual cycles. Medical treatments include nonsteroidal anti-inflammatory drugs or antiprostaglandins, tranexamic acid, the progestogen releasing intrauterine device, combined oral contraceptive pills, and other hormonal therapies. As no medical treatment is superior to another, each woman should be individually assessed as to appropriate management. Surgical treatments include endometrial ablation and hysterectomy.

Dysfunctional uterine bleeding (DUB) is defined as excessively heavy, prolonged or frequent bleeding of uterine origin that is not due to pregnancy or any recognisable pelvic or systemic disease. It is, therefore, a diagnosis of exclusion. The mechanisms for the abnormal bleeding and the site from which it arises are largely unknown. Menstruation is a very complex process involving oestrogen and progesterone and their receptors, endometrial vasculature, endometrial vasoactive substances, processes of tissue breakdown and remodelling, and endometrial repair and regeneration.

Dysfunctional uterine bleeding is the diagnosis in 40–60% of women with excessive menstrual bleeding which is defined as greater than 80 mL blood loss (normal menstrual loss <80 mL). Heavy menstrual bleeding may affect a woman's health both medically and socially, causing problems such as iron deficiency anaemia and social phobia respectively. Dysfunctional uterine bleeding is the commonest cause of iron deficiency in the developed world and of chronic illness in the developing world.[1]

In the reproductive years, one in five women in Australasia are affected by DUB.[2] It is estimated that the United Kingdom spends £800 million per year to treat women with menorrhagia, and in a Swedish study 10% of working women were absent from work because of excessive bleeding.[1]

There are two types of DUB: ovulatory and anovulatory. Ovulatory DUB accounts for about 80% of cases. In ovulatory DUB the menstruation is regular, preceded by ovulation and heavy but of normal duration. It is most common in women in their 30s. Anovulatory DUB is more likely to occur at the beginning and end of the reproductive years. The menstrual cycle is irregular and the bleeding is heavy and may be prolonged. Polycystic ovary syndrome may be associated with chronic anovulation.

Differential diagnosis

In women with abnormal uterine bleeding both uterine (endometrial and myometrial) and systemic causes need to be excluded before DUB can be diagnosed.

Uterine causes

Endometrial polyps, hyperplasia, and rarely endometrial carcinoma, may cause heavy menstrual bleeding but also may present with intermenstrual bleeding. Uterine fibroids, in particular submucous fibroids, may have increased vascularity with large vessels on the uterine surface that rupture during the menses. Adenomyosis, which simplistically is endometriosis in the

myometrium, can cause heavy painful periods and dyspareunia. It is difficult to diagnose but features may be seen on ultrasound and directly at hysteroscopy and laparoscopy. Heavy bleeding can occur in the presence of an intrauterine device (IUD), usually a nonhormonal releasing IUD.

Systemic causes

Heavy menstrual bleeding has been reported with hypothyroidism. Coagulopathy is considered to be a rare cause, but studies have shown an increase in the prevalence of Von Willebrand disease. A systemic review of 11 studies from Europe and the USA showed an overall prevalence of 13% with the range from 5–24%.[3] In adolescents, investigation for a coagulopathy may be more relevant. In chronic renal disease, heavy menstrual bleeding may occur but is not likely to be an initial presentation.

Assessment

Clinical assessment is most important in determining the cause of heavy menstrual bleeding. A careful history and examination should be performed to exclude organic disease and to determine the extent of lifestyle impairment, what previous treatments have been used, and the woman's expectations from treatment.

The assessment of heavy menstrual bleeding is quite subjective and women may over or underestimate their menstrual loss. The symptoms and signs that may signify heavy menstrual bleeding include:

- an unusual increase in blood loss
- more than 7 days of bleeding
- bleeding or flooding not contained within pads or tampons (particularly if wearing the largest size)
- clots greater than 3 cm, and
- the presence of signs of anaemia or iron deficiency on blood testing.

Investigations

Clinical examination should include a routine Pap test. A full blood examination should be performed if anaemia is suspected or a serum ferritin to detect iron deficiency. As a coagulopathy such as Von Willebrand disease is a possible cause in the adolescent woman, a coagulation screen or platelet function tests should be performed when appropriate. Other tests such as thyroid function tests, renal investigations or autoantibodies such as lupus coagulant should be performed if organic disease is suspected. A transvaginal ultrasound (except in the adolescent woman) will aid in excluding pelvic causes of heavy bleeding. Hysteroscopy with dilation and curettage or endometrial biopsy, or laparoscopy if there is associated pain, will be diagnostic but not curative for DUB.

Management

Before any treatment other pathology must be excluded. Where there is systemic disease, treat accordingly or refer on to the appropriate specialist. Iron therapy, usually oral, is prescribed if iron deficiency anaemia is diagnosed.

Medical treatment

Nonsteroidal anti-inflammatory drugs (NSAIDs) or antiprostaglandins reduce prostaglandin levels which are excessive in heavy menstrual bleeding, but the mechanism of action is not fully understood. Blood flow is reduced by about 30% and menstrual pain is also reduced. All the major NSAIDs available have been shown to be effective. Mefenamic acid is prescribed for the heavy days of the menses in a dose of 1 g three times per day. Side effects of NSAIDs include headaches and gastrointestinal symptoms such as nausea, vomiting, diarrhoea and dyspepsia. Contraindications include acute gastrointestinal disorders such as ulcers, intolerance to NSAIDs, or asthma.

Tranexamic acid

Tranexamic acid (cyklokapron) is an antifibrinolytic agent that reduces the endometrial fibrinolytic enzymes that are increased in DUB. Menstrual blood loss is reduced by 45–60%. Tranexamic acid is prescribed on only the heavy days of the menses, usually during the first 5 days. The dose prescribed is 1 g 3–4 times per day. Side effects are infrequent but include nausea and leg cramps. Thrombosis is a rare risk. Tranexamic acid is the appropriate first line therapy for ovulatory DUB.[2]

Progestogen releasing intrauterine device

The levonorgestrel (LNG) releasing intrauterine device (IUD) releases LNG at a low dose of 20 µg per day leading to endometrial atrophy and thickened cervical mucus. There is a major reduction in blood loss up to 97% after 12 months of use. The IUD is suitable in both ovulatory and anovulatory DUB. Irregular light bleeding can be a troublesome side effect particularly in the first 3 months but decreases with time in most cases. The IUD is also contraceptive and its duration of action is 5 years.[2] The LNG releasing IUD is available on the Pharmaceutical Benefits Scheme for contraception, but not for treatment of DUB specifically.

Combined oral contraceptive pill

In small studies, both the 30 µg and 50 µg combined oral contraceptive pills (COCP) have reduced menstrual blood loss significantly by up to 50%. The COCP probably acts by inducing a thin endometrial layer and has the added advantages of reducing dysmenorrhoea and providing contraception.

Progestogens

The progestogens, or progestins, are usually used cyclically but can be used continuously. They are the first line treatment in anovulatory DUB and are prescribed in the luteal phase from about day 15 to day 25. In ovulatory DUB, the progestogen is prescribed from day 5 to day 25.

For emergency suppression of heavy menstrual bleeding noresthisterone 15 mg per day or greater, or medroxyprogesterone acetate 30 mg per day or greater, is prescribed until bleeding ceases; a maintenance dose should be continued until the woman has 3–4 weeks free of bleeding. Ceasing the progestogen will result in a withdrawal bleed.

Other therapies

Danazol has been found to effectively reduce heavy menstrual bleeding but its use has been limited because of its recommended short term use and side effects including headaches,

acne, depression, weight gain, oily hair and voice changes. Danazol is also used as a 6 week treatment before endometrial ablation.

Gestrinone is similar to danazol but is a twice per week dose. Gonadotropin releasing hormone (GnRH) agonists have a very limited role in the treatment of DUB but are used as pretreatment for endometrial ablation, and fibroid or endometriosis surgery. Treatment the GNRH agonists is limited to 6 months because of bone demineralisation due to the temporary 'chemical menopause' induced.

Surgical treatment

The decision to perform surgery for the treatment of DUB will depend on a number of factors including:

- failure of medical therapies
- other associated symptoms such as pain, and
- the woman's request for surgery and what she expects the outcome of the procedure will be.

In deciding on the appropriate form of surgical treatment, outcomes need to be taken into account such as whether the relief of symptoms will be temporary or permanent, potential complications of the surgery, recovery time with loss of work, total cost of the procedure, and patient satisfaction. Dilation and curettage with hysteroscopy is a diagnostic investigation not a treatment for DUB.

Endometrial ablation or resection is a procedure to destroy the endometrium by either a form of diathermy or removal. First generation techniques (including laser ablation, roller ball diathermy or resection) and second generation techniques including microwave ablation are all very effective when performed by the appropriately trained specialist. Although the procedure is not contraceptive, it should not be performed if a woman wishes to have further pregnancies.

Hysterectomy leads to guaranteed amenorrhoea but does have a significant morbidity rate. However, the complication rate may be less with an experienced operator. There are three types of hysterectomy: laparoscopically assisted, vaginal, and abdominal. The laparoscopically assisted hysterectomy by a competent and experienced operator is the most appropriate technique with less morbidity.

Conclusion

Dysfunctional uterine bleeding is a common problem in women in the 30–50 years age group. The pathophysiology is not fully understood and it is complex. Dysfunctional uterine bleeding is a diagnosis of exclusion. Uterine and systemic causes must be excluded before the diagnosis is made. Ovulation occurs in about 80% of women with DUB. Dysfunctional uterine bleeding also occurs at the extremes of the reproductive years; in the adolescent, coagulopathies should be excluded. Management is initially with medical treatments. Surgical procedures are performed only if other treatments prove ineffective.[4]

Conflict of interest: Dr Farrell is a current investigator of a menopause related pharmaceutical company funded research project.

References

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