Menstrual dysfunction

Gail Busby

Abstract

Menstrual dysfunction is common, with approximately 9–30% of reproductive-aged women presenting with menstrual irregularities requiring medical evaluation. The causes are diverse and with multiple treatment options are available. Appropriate management relies on relevant investigation and accurate diagnosis. This article reviews the most common causes of menstrual dysfunction using case histories for illustration. The conditions covered in this review include menstrual dysfunction around the time of menarche, ovulatory and anovulatory dysfunctional uterine bleeding, polycystic ovarian syndrome, uterine fibroids and dysfunctional bleeding around the perimenopause. Appropriate investigations and current management strategies are also discussed.

Keywords abnormal uterine bleeding; dysfunctional uterine bleeding; endometrial hyperplasia; menstrual dysfunction; perimenopausal bleeding; polycystic ovarian syndrome; uterine fibroids

Introduction

The majority of menstrual cycles are between 24 and 32 days and a normal cycle is considered to be 28 days. The menstrual cycle varies during the reproductive years, and is most regular between the ages of 20 and 40. The mean blood loss per cycle is between 37 and 43 ml, and the upper limit for menstrual loss is taken as 80 ml per menses. Menstrual dysfunction, or disruption in the flow or timing of this cycle is a very common cause for presentation to a gynaecologist. The causes are myriad, but several common causes are reviewed here and treatment options discussed.

The normal menstrual cycle

The first day of the menstrual cycle is the first day of menstruation, when oestrogen and progesterone are low. Ovulation occurs mid-cycle in response of high oestrogen and luteinising hormone (LH) levels. The remaining granulosa cells then become the corpus luteum which produces progesterone. If fertilization does not occur, the corpus luteum degenerates and progesterone and oestrogen levels fall.

In the uterus, endometrial cells proliferate in response to rising oestrogen levels in the follicular (preovulatory) phase of the ovary, glands enlarge, and the endometrium becomes richly supplied with blood vessels. The secretory phase after ovulation is characterized by progesterone secretion by the corpus luteum, which makes the endometrium receptive to a fertilized embryo. In absence of pregnancy, the decrease in oestrogen and progesterone result in involution of the endometrium and menstrual loss.

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Menstrual dysfunction or abnormal uterine bleeding generally can be categorised as anovulatory or ovulatory abnormal uterine bleeding (AUB). Anovulatory AUB is caused by failure of the corpus luteum to sustain the developing endometrium. Ovulatory cycles are predictable and patients often have an imbalance of prostaglandin levels and increased fibrinolytic activity. Both ovulatory and anovulatory AUB may coexist with intracavitary lesions, including polyps or fibroids, which may cause heavy or erratic bleeding. In all cases of dysfunctional uterine bleeding, pregnancy, and the complications thereof should be ruled out as a cause.

Table 1 summarizes the differential diagnosis of menstrual dysfunction.

This review gives five scenarios which are common presentations of menstrual dysfunction.

Case 1: Abnormal uterine bleeding around the menarche

A 15 year old presents with a history of heavy, irregular periods. Her periods started nine months before and although initially average in flow, they increasingly became heavier and more frequent.

Anovulation looms large in the pathogenesis of heavy, irregular bleeding around menarche. Within the first 2 years after menarche, lack of ovulation is common due to the immaturity of the hypothalamic–pituitary–ovarian axis. The result of this is prolonged stimulation of the endometrium by oestrogen until the thickened endometrium is unable to be supported and sheds.

The adolescent with irregular and heavy periods should be investigated for clotting abnormalities as the reported prevalence of bleeding disorders in adolescents with menorrhagia varies between 10.4% and 48%. Specifically, von Willebrand's disease and platelet disorders may present for the first time at menarche. Pregnancy should not be forgotten as a possible cause of irregular bleeding in this age group. Appropriate investigations include a pregnancy test, full blood count with platelets, bleeding time, prothrombin time and partial thromboplastin time and von Willebrand's factor.

Women with clotting abnormalities should be co-managed with a haematologist. Successful medical options for treatment of von Willebrand's disease include the combined oral contraceptive pill (COCP), desmopressin acetate, antifibrinolytic agents and plasma-derived concentrates rich in the high-molecular-weight multimers of von Willbrand's factor (vWF).

If there are no haematological abnormalities, irregular cycles can be regulated by the use of cyclical progestogens or the COCP. These should both make the periods regular and decrease menstrual flow. If flow remains a problem, the addition of Tranexamic acid and/or Mefenamic acid during withdrawal bleeds is frequently adequate.

This treatment can be continued indefinitely, or stopped after 1 year or so to determine if ovulatory cycles have commenced, which should result in regular cycles of normal flow.

Case 2: Ovulatory abnormal uterine bleeding

A 28 year old nullipara is referred to the gynaecology clinic due to heavy regular periods. She is in a stable relationship, but not wishing to conceive at the moment. She uses barrier

Differential diagnosis of abnormal uterine bleeding

Category	Differential diagnosis
Anovulatory	Adolescence
	Diabetes mellitus uncontrolled
	Eating disorder
	Hyper-/hypothyroidism
	Hyperprolactinaemia
	Anticonvulsants
	Antipsychotics
	Perimenopause
	Polycystic ovarian syndrome
Ovulatory	Bleeding disorders (Haemophilia carriers)
	Factor deficiency (FVII, FXI, FV + FVIII, FXIII, FV, FX, Fibrinogen deficiency)
	Leukaemia
	Platelet disorders (Bernard-Soulier Syndrome, Dense granule deficiency, Glanzmann's thrombasthenia, Alpha granule deficiency)
	von Willebrand's disease
	Liver disease, advanced
	Structural lesions- fibroids, polyps

Table 1

contraception. Clinical examination and pelvic ultrasound scans are normal.

The diagnosis here is AUB due to endometrial causes. This is defined as abnormal bleeding in the absence of intracavitary or uterine pathology, such as endometrial polyps or uterine fibroids. The history of regular periods suggests that this is a case of ovulatory AUB.

The need to preserve fertility in this case limits treatment options to non-surgical, hormonal and medical non-hormonal treatment modalities. The need for reliable contraception should be taken into consideration in deciding upon treatment options.

Antifibrinolytics

Antifibrinolytics such as Tranexamic acid may reduce menstrual loss by 29–58%. Tranexamic acid acts to reduce the breakdown of fibrin in pre-formed clot. Menstrual bleeding involves the liquefaction of clotted blood in spiral arteries within the endometrium, and tranexamic appears to work by retarding this process. Tranexamic acid is not contraceptive. The contraindications are thromboembolic disease, fibrinolytic conditions following disseminated intravascular coagulation and a history of convulsions.

Non-steroidal anti-inflammatory agents

Non-steroidal anti-inflammatory agents (NSAIDS) such as Mefenamic acid and Naproxen have been shown to reduce menstrual loss by 20–49%. They work by decreasing prostaglandin synthesis by the inhibition of cyclooxygenase. Prostaglandins are implicated in uterine bleeding and uterine cramps. They also therefore have a positive effect on dysmenorrhoea. They should not be used in heavy menstrual bleeding associated with clotting abnormalities. NSAIDS are not contraceptive.

COCPs

COCPs contain oestrogen and progestogen in combination. They work on the hypothalamic–pituitary axis to inhibit ovulation and decrease fertility. They may reduce menstrual loss by 43%, and also provide reliable contraception in the compliant patient.

Progestogens

Oral progestogens taken solely in the luteal phase of the menstrual cycle have not been shown to be effective in reducing heavy menstrual bleeding. Cyclical progestogens taken for 21 days of the cycle (day 5–day 26) have been shown in a small study to reduce menstrual loss by 83%. The mechanism of action of oral progestogens in reducing menstrual loss is unclear.

The progesterone only pill (POP) can be used to provide reliable contraception, but has a varied effect on menstrual flow. Twenty percent patients will be amenorrhoeic, 40% bleed regularly and 40% have erratic bleeding. This inconsistent effect on menstruation this is not generally first-line treatment. Indeed, altered bleeding patterns is the most common reason given by women for stopping POPs. Injected progestogens such as Depot Medroxyprogesterone Acetate (DMPA) provide reliable contraception and are injected every 12 weeks. Although this is not licensed for the treatment of heavy menstrual bleeding, it is associated with amenorrhoea rates of 12–47% after one year of use.

The levonorgestrel-releasing intrauterine system (Mirena) provides an effective treatment option for AUB in the patient who is also desirous of reliable contraception. This device produces a dramatic decline in menstrual blood loss (65–98%) within 12 months of use. The device, imbedded with 52 mg of levonorgestrel, releases 20 μg of levonorgestrel per day, causes pseudodecidualization of the endometrium with very little systemic absorption of progesterone. It is licensed for contraception, treatment of idiopathic menorrhagia, and as the progestogenic arm of HRT. Its contraceptive effect lasts for 5 years.

In cases of ovulatory AUB where the patient has no further reproductive ambitions, surgical options can be entertained such as endometrial ablation and hysterectomy.

Endometrial ablation

Endometrial ablation refers to a host of techniques designed to destroy the endometrium, and thereby reduce menstrual bleeding. Initially, rollerball ablation, transcervical resection and laser ablation were the predominant endometrial destruction techniques performed under direct hysteroscopic vision. Over the past decade, a second generation of techniques, which do not require hysteroscopy have been developed which are safer, easier to perform, involve shorter hospital stays or are performed in the outpatient setting under local anaesthesia.

These techniques employ devices which are sited within the uterine cavity and are activated in order to produce global destruction of the endometrium. Various methods of destruction are used, including high-temperature fluids within a balloon (Thermachoice and Cavaterm), Microwave energy (Microsulis), and Bipolar radiofrequency electrical energy (Novasure). Less commonly used ablative techniques include free fluid at high temperature (Hydrothermablator), endometrial laser intrauterine thermotherapy (ELITT) and cryoablation