

MENSTRUAL DISTURBANCES

Abnormal uterine bleeding may either be excessively heavy regular menstrual periods or irregular bleeding.



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THE MENSTRUAL CYCLE

An understanding of the sequence of events that occur in a normal menstrual cycle is necessary for the management of menstrual disturbances. The hypothalamus secretes gonadotropin-releasing hormone (GnRH) in a pulsatile manner that stimulates the pituitary to release follicle-stimulating hormone (FSH) and luteinising hormone (LH). The co-ordination of these trophic hormones stimulates the ovary to develop a cohort of follicles, selects the dominant Graafian follicle which secretes oestrogen in the follicular phase, releases an oocyte in response to the LH/FSH surge (ovulation) and then forms the corpus luteum that secretes progesterone. The lifespan of the corpus luteum is about 14 days if implantation does not occur. The ovarian steroid hormones (oestradiol and progesterone) provide feedback to the hypothalamus and pituitary to prepare for the next menstrual cycle. Changes in any portion of the hypothalamic-pituitary-ovarian (HPO) axis can lead to menstrual cycle disturbances.

CAUSES OF ABNORMAL UTERINE BLEEDING

The causes of abnormal vaginal bleeding include gynaecological pathology (30%), endocrine disorders (5%), haematological causes (5%), and in the majority of cases (60%) there is no organic disease, and the bleeding is termed dysfunctional. Menorrhagia is usually due to ovulatory dysfunctional uterine bleeding (DUB), whereas oligomenorrhoea is due to anovulatory DUB which often occurs at the extremes of reproductive age.

Following clinical evaluation, the approach to management of menstrual disturbances depends on, among others, the age, reproductive wishes (fertility or contraception), and if the bleeding is secondary to contraceptive or hormonal therapy. In sexually active women presenting with menstrual aberrations, pregnancy complications must be excluded.

I shall approach the management of these women in the context of their clinical presentation:

- the adolescent presenting with irregular menses
- abnormal bleeding on hormonal contraception
- bleeding in the perimenopausal years
- postmenopausal bleeding.

ABNORMAL UTERINE BLEEDING DURING ADOLESCENCE

Adolescents with menstrual problems usually present with irregular cycles and heavy periods. Although a few patients do have an organic lesion that causes abnormal bleeding, most suffer from DUB, which is defined as abnormal bleeding for which no cause is found. In 95% of cases of DUB, the slow maturation of the HPO axis leads to anovulatory cycles. The physiological abnormality is the lack of a positive feedback mechanism necessary to initiate a LH surge and subsequent ovulation. Anovulation results in continuous oestrogen production without progesterone, producing a thick, unstable and fragile endometrium that outgrows its blood supply; sloughing occurs in a disordered fashion and produces breakthrough bleeding, resulting in excessive blood loss leading to anaemia. A minority of adolescents will present with regular, heavy periods (ovulatory DUB) due to a prostaglandin imbalance and excessive fibrinolytic activity in the endometrium.

In the sexually active adolescent, pregnancy and its complications, and bleeding resulting from hormonal contraception, must be excluded. Those who present at menarche or soon after with an acute bleeding episode resulting in anaemia (haemoglobin < 10 g/dl) must be evaluated for a bleeding disorder, endocrine disorders and systemic illnesses. In the non-sexually active adolescent, pelvic examination should be replaced by abdominal palpation, vulval inspection and non-invasive pelvic ultrasound examination.

Once a diagnosis of DUB is made, a simple explanation of the physiology of menses should be given together with reassurance regarding functional and anatomical normality of the genital tract. Many cases of DUB resolve spontaneously and no specific treatment is required.

Assessing menstrual flow objectively is difficult and is best assessed by measuring haemoglobin (Hb) levels. If the Hb level is > 12 g/dl, reassurance and explanation are necessary with a review at 6-monthly intervals. The use of a menstrual calendar will help in assessing improvement. The majority of cases will resolve within 1 - 2 years with the onset of spontaneous ovulation.

A patient with an Hb value of < 12 g/dl should be offered iron supplementation and hormonal treatment to regulate the menses. Cyclical progestogen therapy (Provera or Primolut N) for 10 days a month or the low-dose combined oral contraceptive (COC) pill will help regularise her menstrual cycle. Many parents of younger adolescents are reluctant to encourage the use of the COC; in these cases it is advisable to use progestogens. If there is associated dysmenorrhoea (ovulatory DUB), prostaglandin synthetase inhibitors (mefenamic acid) are prescribed during menses.

Patients presenting with acute profuse bleeding and/or hypotension require emergency management. Fluid resuscitation and blood transfusion may be required. Immediate management with hormone therapy is also indicated. Haemorrhage may be arrested by large oral doses of progestogen or high doses of oestrogen followed by a progestogen-dominant COC (Ovral). Patients unable to take oral medications may be given intravenous Premarin 25 mg every 4 - 6 hours for a maximum of 6 doses. Progestogens, either oral or intramuscular Depo Provera, must follow intravenous oestrogen to stabilise the endometrium. Once bleeding is under control, Ovral should be given 3 times a day for 2 - 3 days and then a single pill daily to complete 21 days of therapy. Large doses of oestrogen may cause vomiting and an anti-emetic may also be required. A withdrawal bleed will then occur and Ovral or a lower-dose monophasic pill (Nordette) may be continued for at least 6 months or until iron stores return to normal. Any relapse may be treated with progestogen as described above. Dilatation and curettage (D & C) should be utilised as a last resort in a small group of patients.

ABNORMAL UTERINE BLEEDING ON HORMONAL CONTRACEPTION

Bleeding problems are among the most common reasons for unsuccessful use and discontinuation of hormonal contraception. Inter-menstrual or breakthrough bleeding and spotting occur in approximately 25% of women during the first 3 months of the COC, but become less common with ongoing use. Bleeding on contraceptives rarely signifies major pathology in premenopausal women, although it may alarm women. Nevertheless it is still important to take a detailed history and examination to exclude other causes of abnormal bleeding.

Combined oral contraceptives (COC)

The management of intermenstrual bleeding on COCs begins with counselling prior to prescription of the COC. Ensure that the woman is not smoking and that compliance is good. Cigarette smoking is associated with anti-oestrogenic effects and may lower oestrogen levels. If bleeding occurs in the first 3 months, reassurance and encouragement is all that is needed. If bleeding occurs after 3 months and if other causes including pregnancy are excluded, treatment with supplemental oestrogen and/or a non-steroidal anti-inflammatory drug (NSAID) will stop the bleeding. Supplemental oestrogen (Premarin 0.625 mg or Estinyl 20 µg daily for 1 week) will increase endometrial thickness and stabilise the endometrium and blood vessels. If the bleeding persists, try another COC containing a different progestogen.

Progestogen-only pill (POP)

Menstrual aberrations may occur in more than 50% of women. As POP are short-acting (up to 20 hours) timely ingestion is important. The POP should be taken at the same time every day as a variability of 2 - 3 hours can cause menstrual disturbances. In women having prolonged bleeding, 1 POP taken twice daily for 7 - 10 days should control the bleeding. Repeat the course once if bleeding continues. Discontinue this method if bleeding still persists and switch to a COC pill if this is not contraindicated. Supplemental oestrogen must not be used as this may impair the cervical mucus effect and reduce the effect of the POP. If there has been amenorrhoea followed by bleeding, an ectopic pregnancy or miscarriage must be excluded.

Injectable progestogens

Unpredictable bleeding occurs in 70% of women using injectable contraception. Regular cycles may disappear and are replaced by the occurrence of erratic spotting, intermittent bleeding

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or a brown discharge following the first one or two injections. With continued use, this decreases and oligomenorrhoea or amenorrhoea develops.

Counselling prepares women for both initial irregular spotting and the latter development of amenorrhoea. In the treatment of prolonged spotting which occurs in the first 6 weeks after the first or second injection, it is important to reassure the woman that her bleeding is not due to cancer but to endometrial atrophy and she will soon become amenorrhoeic. Antiprostaglandins and tranexamic acid may be prescribed. A course of oestrogen (1 - 3 weeks) and iron supplements may be given to women who insist on a therapeutic intervention. If the bleeding is heavy and prolonged, examination must exclude pregnancy complications, fibroids, infection and polyps. In the absence of pathology, high-dose oestrogen (Premarin 1.25 -2.5 mg or Ovral) for up to 21 days may be used for heavy bleeding. A withdrawal bleed will occur after cessation of either of these regimens. The course

may be repeated if this withdrawal bleed lasts for more than a week.

If bleeding occurs in the latter half of the injection cycle, the subsequent injection may be administered. Bleeding should stop within a week and the next routine injection can follow. Bleeding after the third injection can be treated with oestrogen, as already described. If bleeding persists, the regimen may be repeated once and if it still persists another method of contraception must be recommended.

BLEEDING IN THE PERIMENOPAUSE

Endometrial cancer is predominantly a disease of postmenopausal women; however 5% of patients present with irregular menses before the menopause. This together with endometrial hyperplasia are the two most important conditions that need to be excluded in women > 40 years old with abnormal uterine bleeding. Intermenstrual and postcoital bleeding may be of common aetiology. A cervical ectropion, cervical cancer, cervicitis, submucous fibroids and endometrial/cervical polyps may cause bleeding and therefore warrant exclusion. Dysfunctional bleeding is also common towards the menopausal years.

In the evaluation, a complete history and examination is mandatory and should include a Papanicolaou smear and a pelvic ultrasound, if necessary.

Women with regular, heavy menses and a normal general and pelvic examination may be empirically managed as DUB. Medical interventions include the use of antifibrinolytics, antiprostaglandins and COCs. In most situations, if there is failure of medical therapy, inpatient hysteroscopy and surgery is performed. The only therapeutic role for D & C is in cases of continuous profuse bleeding not responding to other therapeutic modalities (this is very uncommon). Histological examination of an endometrial biopsy obtained either with the pipelle or at the time of hys-

teroscopy and curettage is the method of choice to exclude endometrial hyperplasia or malignancy.

Medical therapy

Tranexamic acid (Cyclokapron) reduces menstrual loss by 35 - 55% by its antifibrinolytic action. NSAIDs reduce endometrial prostaglandins, thereby reducing pain and blood loss by approximately 25%.

The COC pill induces regular shedding of a suppressed endometrium and may reduce menstrual blood loss by 50%. In normotensive women who do not smoke and do not have risk factors for thrombosis, the low-dose COC (< 35 µg) can be used until menopause. In perimenopausal women with anovulatory cycles, COCs not only reduce blood loss and the need for surgical intervention, but also alleviate vasomotor symptoms. Cyclical progestogen therapy may also co-ordinate regular shedding of the endometrium in anovulatory women. It is ineffective in ovulatory women unless used in high doses for prolonged periods. This is however not a viable strategy as the side-effects of nausea, weight gain, fatigue, mood changes, headaches, depression and loss of libido are unacceptable to women.

The levonorgestrel intrauterine system (Mirena) reduces menstrual blood loss by 86% after 3 months and 97% after 12 months of use. Thirty-five per cent of women who use Mirena become amenorrhoeic after 1 year. This method is an alternative to hysterectomy and should be offered before any surgical option.

Surgical treatment

Conservative surgery (retaining the uterus) by ablating the endometrium is offered following failed medical therapy and in women who have completed their families. Ablation techniques include laser ablation, resection, cryosurgery and microwaves. The use of Mirena and endometrial ablation is likely to dramatically reduce the need for hysterectomy in cases of DUB.

POSTMENOPAUSAL BLEEDING (PMB)

The risk of endometrial carcinoma in PMB increases with age from about 1% at 50 years to 25% at 80 years of age. In developing countries, carcinoma of the cervix is the leading malignant cause of PMB. The majority of women with PMB have a benign cause for their bleeding, the commonest being genital tract atrophy. Polyps and endometrial hyperplasia are other possible causes. Following history, examination and a cervical smear, the traditional management was a D & C. This procedure sampled less than 50% of the endometrium and missed up to

10% of endometrial pathology and 15% of endometrial cancers. Recent advances using transvaginal ultrasound, outpatient endometrial biopsy (Pipelle) and hysteroscopy either alone or in combination have become the methods of choice in the assessment of PMB. Cervical visualisation and cytology must be performed in all PMB cases, irrespective of when last performed.

Atrophic endometritis may be treated with a short course of vaginal or systemic oestrogen as long as its use is not contraindicated. Progestogen therapy may be used in women with sim-

ple hyperplasia who are not fit for surgery. Basically, treatment is that of the underlying pathology.

CONCLUSION

Menstrual disturbances are among the commonest reasons for women visiting their general practitioners. An understanding of the endocrinology of the menstrual cycle and the influence of exogenous hormones is crucial in the counselling and management strategies of the various clinical presentations.

IN A NUTSHELL

The major cause of abnormal uterine bleeding is dysfunctional uterine bleeding (DUB).

In sexually active women presenting with menstrual aberrations, pregnancy complications must be excluded.

Simple explanation and reassurance should be given to adolescents with DUB regarding the functional and anatomical normality of the genital tract.

Breakthrough bleeding and spotting occur in 25% of women during the first 3 months of the oral contraceptive pill, but improves with ongoing use.

The progestogen-only pill should be taken at the same time every day as a variability of 2 - 3 hours can cause menstrual disturbances.

Endometrial cancer and hyperplasia are the two most important conditions that need to be excluded in perimenopausal women with abnormal uterine bleeding and a normal cervical smear.

Tranexamic acid and prostaglandin synthetase inhibitors reduce menstrual loss by 35 - 55%.

Hysteroscopy and biopsy is preferable to dilatation and curettage (D & C) as the latter is a blind procedure that samples less than 50% of the endometrium in 60% of patients and misses up to 10% of endometrial pathology and 15% of endometrial cancers.

Further reading

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