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A Review On The Evaluation And Management Of Menorrhagia.

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ABSTRACT

Menorrhagia is a common gynecological disorder. Menstruation is a normal process in puberty, but when there is increased uterine bleeding it is associated with significant morbidity. It may pose a threat for the well-being of the individual. Menorrhagia may be induced by thyroid dysfunction, coagulation defects, and endometrial polyps, and sub mucosal fibroids, heritable bleeding disorders, surgical and genital trauma. This review article discusses about the various methods for diagnosis and accurate management of menorrhagia. The review concluded the following: Intrauterine device was the most acceptable by the patients and showed positive results in decreasing the excessive blood flow; treatment with tranexamic acid and combined oral contraceptive pills (OCPs) was found to be the most preferred second line choice; norethisterone was identified to be the third line of choice of treatment.

Keywords: menorrhagia; evaluation; management; surgical interventions

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INTRODUCTION

Menarche is a trademark in adolescence. It is the transformation from childhood to puberty. Menorrhagia is a one of the frequently occurring symptoms in gynecology which adversely affect the quality of life in women. It is defined as a regular cycle that occurs in menstruation with excessive blood flow, which is characterized by prolonged bleeding time occurring at regular intervals or prolonged uterine bleeding lasting more than seven days[1].National Institute for Health and Care Excellence (NICE) identifies menorrhagia as excessive blood loss that hampers with a woman's physical, social, emotional and/or quality of life[2].It is a condition that affects 20–30% of women of a reproductive age[3]. Even though it does not endanger life it has effect on the various personal, social and work related essence of life[4].About 53 in 1000 women are affected by menorrhagia. Less than 1% of cases had underlying bleeding disorders. Women hospitalized with the diagnosis of menorrhagia 79 underwent hysterectomy during their hospitalizations. Current gynecological surveys report that 30% of all premenopausal women perceive their menses to be excessive. The World Health Organization recently reported that 18 million women aged 30-35 years perceive their menstrual bleeding to be exorbitant[5]. Reports show that only 10% of these women experience blood loss severe enough to be termed menorrhagia. Patients those who lose about 80ml of blood repetitively are at risk of medical squeal. Most patients are found to be aged above 30, as heavy menses in younger females are an ovulatory in nature. Iron deficiency and anemia are results of menorrhagia which has negative effects on women[6]and no underlying cause is identified in 40-60% of heavy bleeding. There are many causes which lead to menorrhagia and are classified under mainly endocrinology, hematologic, pregnancy complications, sexually transmitted diseases, certain medications, trauma, and systemicillness. Menorrhagia occurring due to fibroids or endometrial polyps is not observed until the women reaches her; mid-thirties[7].

DIAGNOSIS

Physical examination

Initial method of evaluation should include the physical examination of the patient who represents menorrhagia.

History of menstrual bleeding

One should focus on signs such as hypovolemia and anemia. It should also be evaluated that she was a definite case of menorrhagia and was not bleeding from other parts of the genital tract. During the assessment of history of menstrual bleeding and determination of the cycle length, it is necessary to ask the time duration from the first day of the given period to the first day of the next. Vital signs such as tachycardia and hypotension may signify a case of acute hemodynamic instability that is in need of urgent medical intervention. Presence of tachycardia, pallor or heart murmur signifies anemia[8].

A detailed family history of birth, gynecologic bleeding and non-gynecologic bleeding is important to determine any case of heritable bleeding disorder. It was also necessary to collect history of the various medication used including hormonal contraceptives. For those patients reporting heavy menstrual bleeding, a questionnaire which consists of the following should be included:

1) Are you soaking through pads/tampons in 1 hour for 2-3 hours in a row?
2) Is there any presence of blood clots ≥1 inch in diameter?
3) Are you using the double protection method?
4) Do you constantly have a feeling of flooding or gushing of blood?
5) Do you leak through the protection?
6) Were you ever diagnosed with anemia?

Pelvic Examination

Pelvic examination of sexually active patients should be obtained if there is any case of pain or changes in the bleeding patterns as compared to the previous pattern.

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Laboratorial Investigations

Complete blood count

Laboratorial investigation is done to authenticate about the patient severity and its complication. Evaluation is done by complete blood count including white blood cells and platelet count to determine heavy menstrual bleeding and anemia. However due to continuous lose of blood in menorrhagia there will be a rapid decline in WBC count and platelet count. About one third of women with menstrual blood loss greater than 80 ml per cycle have evidence of anemia[9].

Prothrombin time and activated partial thromboplastin factor VII

It is also necessary to find out prothrombin time and activated partial thromboplastin time in order to find out mild bleeding disorder, it is also reasonable to find out factor VIII, Von Willebrand factor antigen, and ristocetin co-factor activities[10,11]. Due to certain difficulties in achieving some of the coagulation test the health care professionals may refrain from further evaluations: this may affect in providing optimal patient care[7,10,12].

Transvaginal ultrasonography

Transvaginal ultrasonography is a method to evaluate the ovaries, uterus, and endometrium. This test can detect small ovarian cysts, leiomyoma, endometrial carcinoma, as well as evaluation of the endometrium with respect to thickness, which would indirectly reflect the endometrial histology, and hormonal status of patients. However saline infusion sonohysterography is also done by infusion of saline during transvaginal ultrasonography that provides an amplified view of the endometrium[13,14].If the underlying causes are not obtained through ultrasonography another method for evaluating the endometrium is by visualizing with hysteroscopy[15].

Hysteroscopy

Hysteroscopy allows for the examination of the whole endometrial cavity, lower segment and cervical canal.It is used to detect small polyps or sub-mucous fibroids that have been missed by ultrasonography, endometrial biopsy or blind curettage. In women with irregular bleeding, polyps are present in about 25 % of cases and sub mucous fibroids are present in 15 – 18 % of cases[16,17].Hysteroscopy with biopsy is the best diagnostic test for intrauterine pathology with high specificity and sensitivity. For those women who are over the age of 45 and those younger than 45 with a history of unopposed estrogen exposure such as in patients with obesity or polycystic ovary syndrome, endometrial sampling should be done as a first line test[18].

MANAGEMENT

The choice of treatment depends on clinical stability, underlying cause of bleeding, need for future fertility and other underlying medical problems. The missions for management are 1) to keep the current heavy bleeding under control 2) to reduce the menstrual blood loss in the forthcoming cycles[19].Hormonal, non-hormonal therapies and as a final option surgical intervention is also available for menorrhagia in order to reduce blood flow. The treatment is summarized in Table 1.

Table 1: Treatment for heavy menstrual bleeding

Medication	Dose	Adverse Drug Reaction
Anovulatory bleeding		
Combination oral contraceptive[4]	≤ 35 mcg of ethinyl estradiol monophasic or triphasic pills.	Breast tenderness, Elevated blood pressure, headaches, nausea.
Medroxyprogesterone acetate (Provera)[9]	10 mg per day for 10 to 14 days per month.	Vaginal itching or discharge, Breast tenderness or discharge, skin rash, increased acne.
Endometrial hyperplasia without atypia		

Medroxyprogesterone acetate[14]	10 mg per day for 14 days per month.	Vaginal itching or discharge, Breast tenderness or discharge, skin rash, increased acne, hives.
Megestrol (Megace)[11]	40 mg per day.	Hyperglycemia, nausea, vomiting, insomnia.
Levonorgestrel-releasing intrauterine system (Mirena)[31]	Releases 20 mcg per 24 hours.	Back pain, nervousness, bloating, and breast tenderness.
Ovulatory bleeding		
Levonorgestrel-releasing intrauterine system[34,35]	Releases 20 mcg per 24 hours.	Back pain, nervousness, bloating, and breast tenderness.
Medroxyprogesterone acetate[34]	10 mg per day for 21 days per month.	Vaginal itching or discharge, Breast tenderness or discharge, skin rash, increased acne.
***NSAIDs*[36,37]**		
Ibuprofen	600 to 1,200 mg per day, five days per month.	Upset stomach, mild heartburn, nausea, bloating, ringing in ears.
Naproxen sodium (Anaprox)	550 to 1,100 mg per day, five days per month.	Indigestion, stomach pain, swelling in hands and feet, bruising .
Mefenamic acid (Ponstel)	1,500 mg per day, five days per month.	Dizziness, stomach pain, constipation, diarrhea.
Tranexamic acid (Lysteda)[38,39]	650 mg; two tablets three times per day, five days per month.	Allergic reactions, blood clot and vision changes, nausea, vomiting.

First-line therapy for the treatment of heavy menstrual bleeding

It is a levonorgestrel-releasing intrauterine system (IUS) – Mirena which is long-term treatment which should be left inside the uterine cavity for at least 12 months[2].It improved the women's quality of life and also by increased the patient compliance[20].The termination rate of Mirena® was established to be high in 12 months by 16% and 2 years by 28%[21].

Second-line therapy for the treatment of heavy menstrual bleeding

This includes tranexamic acid, mefenamic acid or the combined oral contraceptive pill (COCP):Mefenamic acid acts by blocking prostaglandin synthesis. It decreases menstrual loss by around 25% in three quarters of women and is better accepted than tranexamicacid. Tranexamic acid is a plasminogen-activator inhibitor. It inhibits the dissolution of thrombosis that leads to menstrual flow. It can reduce flow by up to 50%[22].It has proven to decrease menstrual loss connected with IUCDs, fibroids and bleeding diathesis.

Third-line therapy for the treatment of heavy menstrual bleeding

This is with norethisterone. A decrease in menstrual loss was seen when a dose of 15 mg daily, from day 5 to 26 (or injected long-acting progestogens) was provided. It was used for the short term treatment of menorrhagia[23].

Hormonal Therapy

Oral contraceptive pills

In patient with heavy menstrual bleeding, oral contraceptive pills are the appropriate treatments. It include esnorgestrel 0.3mg which is a first line therapy consisting of 30µg-35µg of estrogen [24].Mood changes, breast tenderness and headaches are a common side effects of this treatment.

Levonorgestrel

Levonorgestrel intrauterine device (LNG-IUD), is a steroid-releasing system, is used worldwide as a successful contraceptive method. It is a T-shaped device which releases LNG, a potent 19-nortestosterone derivative progestin, directly into the uterine cavity at initial rate of 20 mcg/day[25,26].Effects on the

endometrium are related to endometrial thinning, glandular atrophy and inflammation[27-29].They are independent of the phase of the menstrual cycle and appear as early as 1 month after LNG-IUD insertion, which thereby makes this system an effective nonsurgical treatment for menorrhagia in women[27].For extending the medication, administration oflevonorgestrel 0.15mg which is a combination hormone pills which is for 84 days which is followed by 7 days of low dose estrogen. Combined oral contraceptives and oral progestin are taken in multi dose regimens. If the goal is to achieve amenorrhea, then the OCP can be given continuously, but is usually withdrawn every 3 to 4 months to allow endometrial shedding and avoid irregular bleeding. When used continuously oral contraceptives reduce menstrual flow volume[30].Progestin can decrease excessive menstrual bleeding it is given for 21 days per month to be effective[31].

Progestin

Continuous progestins may be indicated if the goal is to achieve amenorrhea (e.g., busy professional or athlete, intractable menstrual migraine, seizures, severe mental retardation). Maintaining amenorrhea is often more difficult than cycling a progestin (i.e., there may be unpredictable spotting). Options include: Oral progestin: medroxyprogesterone(Provera) 10 to 20 mg daily (Minipill) (e.g., 0.35 mg of norethindrone daily) Depo-medroxyprogesterone (Depo-Provera) 150 mg IM every 13 weeks are often used in adolescents to improve compliance and less often used in ages 40 years due to risk of osteoporosis[32].Patient with poor estrogen tolerance, progesterone are use such as medroxyprogesterone 10mg which is to be taken orally in a cyclic manor 10-12 days monthly. Norethindrone acetate 5-10mg daily of oral progesterone should be taken[33].Once the bleeding has been controlled a number of options are available for the long term treatment of menorrhagia that include levonorgestrel intrauterine system which is better tolerated than the 21 day oral regimen[31,33,34].Bloating, Breast tenderness etc. are known adverse drug effects of progestin's.

Non-Hormonal Therapy

Non-hormonal therapy include non-steroidal anti-inflammatory drugs [NSAIDs] and anti fibrinolytic drugs [tranexamic acid].

NSAIDs

NSAIDS can decrease prostroglandin levels there by reducing menstrual bleeding[35].Patients with bleeding disorders or platelet function abnormalities should avoid NSAIDs due to their effect on platelet aggregation and their interaction with other drug which may affect liver function and production of clotting factors[36]. Mefenamic acid 500mg thrice daily should be given during menses. When heavy menstrual bleeding co exists with dysmenorrhea NSAIDS are more preferred. NSAIDS are known for their adverse drug effects such as peptic ulcer and indigestion.

Tranexamic acid

Tranexamic acid is asynthetic lysine amino acid derivative which is an anti-fibrinolytic drug that prevent activation of plasminogen thereby preventing fibrin degradation is an FDA-approved drug for treatment of menorrhagia two 650 mg tablets are taken three times per day for first five days of the cycle this decrease bleeding significantly than NSAIDs[37,38]. Use of both NSAID and tranexamic acid should be stopped if they do not improve the symptoms within 3 menstrual cycle. It is known to cause adverse drug reaction such as indigestion, diarrhea and headache.

Desmopressin

It is aderivative of the anti-diuretic hormone vasopressin. Desmopressin acts by increasing plasma levels of factor VIII and von Willebrand factor (VWF).For those patients with Von Willebrand disease Desmopressin may be given through intranasal inhalation, intravenously, or subcutaneously[36]. It is provided for patients with von willebrand disease Type 1, hemophilia A and type 2A and also for type 2M von willebrand disease. This should be used with caution as it may cause fluid retention and hyponatremia and should not be given to patients with hemorrhage who are receiving IV fluid resuscitation[32].

Danazol

Danazol is a synthetic steroid that suppressesestrogen and progesterone receptors in the endometrium, leading to endometrial atrophy (thinning of the lining of the uterus) and reduced menstrual loss. It is an effective treatment for heavy menstrual bleeding. However, its side-effect profile, its lack of acceptability to women and the need for continuing treatment limits its use[37,38].

Surgical intervention

When medication therapy fails to respond, the patient may undergo surgical procedure based upon their etiology. The choice which determines the surgical procedure to be undertaken is dictated by suspected etiology and the desire for maintaining fertility succeeding the surgery. Fertility can be sustained through surgical procedures like dilatation and curettage [D&C], hysteroscopy with D &C, hysteroscopy with polypectomy or myomectomy and endometrial balloon tamponade[34].

Endometrial Balloon Tamponade

Endometrial balloon tamponade is an efficient surgical therapy for acute menorrhagia.

In uterus less than 12 weeks size, a Foley catheter with a 30 cc balloon can be interpolated through the cervix and inflated with saline until resistance of myometrium is felt. Ultrasound may be useful to diagnose intra uterine pathology, to confirm the accurate placement and distinction and to exclude any on-going bleeding above the balloon[35].

Uterine Artery Embolization

Uterine artery embolization [UAE] is another successful method to control menorrhagia[37].It is the treatment of choice for those women with fibroids (greater than 3cm) and heavy menstrual bleeding and other symptoms like dysmenorrhea. The aorta is accessed via the femoral artery, a pelvic angiogram is obtained, blood vessels are identified and then occluded; it is considered as second line therapy[38]. Lose of ovarian function is often observed after UAE which may lead to pre mature menopause. Persistent vaginal discharge and post embolization syndrome including: pain, nausea, vomiting, fever are noticed after the Uterine Artery Embolization.

Endometrial Ablation

Endometrial ablation is another effective method that is used to control menorrhagia and is used as an alternative hysterectomy[34].Endometrial ablation should be considered in women with heavy menstrual bleeding who have a normal uterus and also those with small uterine fibroids (less than 3 cm in diameter[2]. Pregnancy is contraindicated in women with endometrial ablation. Vaginal discharge and painful cramps are common after this surgery.

Hysterectomy

Hysterectomy is a definitive surgical treatment for menorrhagia, in patient with acute life threatening hemorrhage[35].It should not be used as a first line treatment solely for the HMB. It is only considered when the patient's wishes for amenorrhea, other options have failed and no longer wishes to retain the uterus and fertility. Hysterectomy should not be delayed in favor of potentially less effective measures, especially if fertility is no longer desired[39].Patients have to take upmost care as infection is common post-surgery. There are improved outcomes with vaginal hysterectomy [40].

CONCLUSION

Menorrhagia is a disorder that can adversely affect the quality of life of women. This can be resolved in the initial stages with effective therapies. However, the definite cause of menorrhagia should be investigated. Proper care should be given to women with menorrhagia along with medical interventions.

Treatment should be provided at initial stages to avoid complications. Intrauterine device was found to be acceptable as it showed more adherence and therefore it is considered the first line treatment of menorrhagia. Combined oral contraceptive pills and tranexamic acid was found to be second line choice of therapy. Third line drug of choice was norethisterone.

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