

MANAGEMENT OF MENORRHAGIA IN ADOLESCENTS

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Abstract : Menorrhagia is common in adolescents and young women. In most cases, it is consequent to anovulation due to immaturity of the hypothalamic-pituitary-ovarian feedback mechanism, but in many cases it may be the presenting sign of an underlying illness requiring further evaluation and long term treatment and follow up. The second most common cause of menorrhagia in adolescents and young women is bleeding disorders the main etiology being idiopathic thrombocytopenic purpura and von Willibrand disease. However it is essential to rule out pregnancy in all adolescents who present with unexplained heavy bleeding especially in those who previously had regular cycles. Management of menorrhagia in adolescents is a challenging condition. Management depends on its cause and severity. The primary treatment even in severe cases of bleeding is medical and surgical intervention is rarely warranted. The various principles of management of menorrhagia in adolescents are: control of acute episode, maintenance of normal flow during subsequent cycles, treatment of underlying cause, treatment and prevention of anaemia and allay anxiety.

INTRODUCTION

Menorrhagia is common in adolescents and young women. In most cases, it is consequent to anovulation due to immaturity of the hypothalamic-pituitary-ovarian feedback mechanism, but in many cases it may be the presenting sign of an underlying illness requiring further evaluation and long term treatment and follow up. Besides interfering with daily activities of adolescents and young women, it is associated with the problem of delayed diagnosis and management due to hesitancy on the part of them to seek help.

ETIOLOGY

The aetiology of menorrhagia can be broadly classified into four categories- hormonal, haematological abnormalities, pregnancy related complications and genital organ or genital tract related pathology. However, the contribution of each of these four etiological factors in causing menorrhagia varies with the age of patient. The commonest cause in an adolescent girl is hormonal imbalance compared to pregnancy related complications in young adult women and premalignant and malignant lesions in premenopausal and postmenopausal women respectively.

Focussing on aetiology of menorrhagia in adolescents and young women it was observed in a study that 74% were secondary to hormonal imbalance, 19% due to haemostatic disorders, and remaining 7% were due to pregnancy related complication and local pathology¹. In another study on 106 teenagers presenting with heavy period to a paediatric hospital 85% were found to have evidence of anovulation while 23% had a bleeding disorder².

D) Hormonal

The basic problem is anovulation which may be secondary to immature hypothalamic-pituitary-ovarian axis, hypo or hyperthyroidism, adrenal disease, polycystic ovarian syndrome, pituitary tumours, drug abuse, eating disorders and significant level of sporting activities³. As anovulatory bleeding is unrelated to anatomic lesions of the uterus, some authors refer to this as dysfunctional uterine bleeding (DUB)⁴. It can be irregular, excessive or prolonged bleeding from uterine endometrium. Adolescents presenting with menorrhagia often represent a subset of these anovulatory patients. In majority, etiologic factor centres around slow

maturation of the hypothalamic-pituitary-ovarian axis in female adolescents, leading to unopposed secretion of estrogen resulting in an unstable endometrium. The establishment of orderly ovulatory bleeding may take up to 5 years, however it usually establishes within fifteen months after menarche⁵. This is the most common cause of adolescent menorrhagia and contributes to about 74% to 85% of all cases^{1,2}.

II) Haematological disorder

The second most common cause of menorrhagia in adolescents and young women is bleeding disorders. It can be congenital or acquired. The prevalence as reported in literature ranges from 8.2% to 48%^{2,6}. Claesens and Cowell found bleeding diathesis to be the cause of menorrhagia in 19% of their cases over a period of 9 years in a paediatric clinic¹, the main etiology being idiopathic thrombocytopenic purpura and von Willibrand disease^{1,2,3,7}.

*Idiopathic Thrombocytopenic Purpura (ITP)*⁸

ITP is defined as isolated thrombocytopenia with normal bone marrow and the absence of other causes of thrombocytopenia. It is primarily a disease of increased peripheral platelet destruction, with approximately 60% of patients having antibodies to specific platelet membrane glycoprotein. It is also known as immune thrombocytopenic purpura. The diagnosis of ITP is one of exclusion. Despite the destruction of platelets by splenic macrophages, the spleen is normally not enlarged. In fact, in the presence of enlarged spleen, investigations to rule out other possible causes of thrombocytopenia are indicated.

Von Willibrand disease

With the initiation of menstruation following sloughing of the endometrial lining, the primary stage of haemostasis takes part in controlling the amount of blood loss during menses. vWF mediates platelet adhesion to damaged subendothelium, which leads to platelet activation, secretion of granule contents and aggregation to form the platelet plug. Qualitative and quantitative defects in either vWF or platelets lead to defective haemostasis and thus, patients with these defects are more likely to experience menorrhagia. vWF is required for normal platelet adhesion and also acts as a carrier of factor VIII in the plasma. When vWF is deficient or aberrant, factor VIII

deficiency and abnormalities in the early steps of primary haemostasis result. Majority (95%) of young women who have von Willibrand disease experience menorrhagia. Classically, menorrhagia may be the presenting symptom of von Willibrand disease, with a history of heavy bleeding from the very first menstrual cycle. Typically a family history of menorrhagia can be elicited. vWF levels are under the influence of hormones, which complicate the disease expression, and diagnosis of vWF deficiency. The level of vWF is lowest in early follicular phase rising to as much as 20% by midcycle. The level increases with age approximately 15% for each decade of life⁹. In the classic case, the results of screening tests reveal a normal platelet count and a prolonged aPPTK. In many cases, the aPPTK may be normal. Criteria for the laboratory diagnosis of vWD are imperfect and no test by itself is sensitive and specific enough to diagnose all patients. The vWF and factor VIII are acute phase reactants. Their levels increase with stress, trauma, estrogen therapy and pregnancy. Thus fluctuating level of vWF from time to time make the diagnosis of vW disease difficult. A battery of tests should be considered to conclusively evaluate a patient.

III) OTHER CAUSES OF MENORRHAGIA

It is essential to rule out pregnancy in all adolescents who present with unexplained heavy bleeding especially in those who previously had regular cycles. Also pelvic inflammatory disease particularly chlamydia endometritis and tubercular endometritis should be excluded. Tumours and polyps as causative factors are very rare but are usually detected on ultrasonography and/or pelvic examination. These diagnoses need to be kept in mind especially in patients where management is proving difficult.

MANAGEMENT

Management of menorrhagia in adolescents is a challenging condition. Management depends on its cause and severity. The primary treatment even in severe cases of bleeding is medical and surgical intervention is rarely warranted. There are no studies available to support any specific treatment plan or any particular hormone regime for the management of menorrhagia in adolescents; choice is based on clinical experience¹⁰.

Principles of management:

- 1) Control of acute episode
- 2) Maintenance of normal flow during subsequent cycles
- 3) Treatment of underlying cause
- 4) Treatment and prevention of anaemia
- 5) Allay anxiety.

Management of acute episode of bleeding and maintenance of normal flow during subsequent cycle

All patients with acute episode of severe bleeding need hospitalisation. Arrest of acute episode of bleeding can be achieved in most patients with high dose oral contraceptives pills (OCP) or progestin alone preparations. Progestin alone preparations (medroxyprogesterone acetate or 19 nortestosterone derivatives) are administered in the dose of 15 – 30 mg daily in 3 - 4 divided doses till 1 -2 days after the bleeding stops and then gradually tapered to 5 mg once or twice a day for a total of 21 days from the initiation of therapy. This is followed by withdrawal bleeding and maintenance therapy in the dose of 5 -10 mg daily from 5th to 25th day of the menstrual cycle for 3 -6 cycles. Nortestosterone derivatives have a better haemostatic effect than medroxyprogesterone derivatives. As regards combined oral contraceptive pills one tablet is given every 4 hours till 1-2 days after the bleeding stops and then gradually tapered to 1-2 tablets daily for a total of 21 days from the start of therapy.

This is followed by withdrawal bleeding and 3-6 cycles of combined pills starting from day 2 of the menstrual cycle. Antiemetics have to be given to reduce the nausea and vomiting associated with intake of oral pills. In severely anemic girls the withdrawal bleeding can be postponed by continuously administering the hormonal pills for 2-3 months to gain time to build them up. It is essential to counsel the patient to maintain a regular interval between pills e.g. if a pill has to be administered 8 hourly, she should be advised to take it at 6am, 2pm and 10pm.

Occasionally conjugated equine estrogens (Premarin) 25mg 6 hourly intravenously for a maximum of 6 doses is used to arrest severe acute haemorrhage. It is to be followed by combined oral contraceptive pills 6 to 8 hourly for 3 to 4 days and tapered slowly to once daily for a total of 21 days from initiation of therapy.

Acute episode of bleeding in adolescents and young girls with history of haemostatic disorders

Adolescents and young girls with vWD¹¹:

In patients with von Willibrand disease, acute bleeding episode can be controlled by either increasing endogenous vWF levels with desmopressin (DDAVP) or replacing vWF using an intermediate-purity Factor VIII product or cryoprecipitate, which contains vWF.

i) Desmopressin (DDAVP)

The dose is 0.3 to 0.4 µg/kg body weight intravenously. It avoids the need to use plasma products. The dose can be repeated every 24 hours, but the effect is reduced after some days of treatment.

ii) Factor VIII products

Reserved for patients unresponsive to desmopressin, it is essential to use a virally inactivated product that contains vWF. These products are called intermediate purity Factor VIII concentrates. Recommended dose schedule for Factor VIII is 14-20 iu/kg body weight. It is available as Factor VIII concentrate (500 iu/bottle).

iii) Cryoprecipitate

It is effective, but is not available in virally inactivated form in most countries. Cryoprecipitate containing 80-100 iu of Factor VIII is usually obtained from 250 ml of fresh frozen plasma and is administered in the dose of 1 pack/ 4 kg body weight.

Adolescents and young girls with idiopathic thrombocytopenic purpura¹²:

Platelet infusion is required in the presence of excessive bleeding. Dosage required is 6 to 8 unit of platelet concentrate or 1unit/10kg body weight. One unit of platelet concentrate increases the platelet count by 5,000 to 10,000/cu mm. It is obtained from a single donor unit of blood. Platelets are also available as platelet concentrate, which is collected by plateletpheresis from a single donor and is equivalent to 3-10 units of platelet concentrates. Acute bleeding can be controlled with glucocorticoids and intravenous immunoglobulins. Emergency splenectomy may be indicated in cases not responding to medical measures.

Some other occasionally utilized techniques for control of acute haemorrhage are the use of an inflated balloon of a Foley's catheter as a tamponade to control uterine bleeding and rarely the use of uterine artery embolization has been reported for life threatening bleeding at menarche¹³.

Need for blood transfusion is individualized on the basis of amount of bleeding and general condition of patient. It is indicated in the presence of rapid blood loss of >15% of total blood volume

manifested by orthostatic symptoms, irrespective of level of haemoglobin or hematocrit.

Alternative modalities available for managing subsequent cycles These are extended OCP regime, long acting depo-medroxyprogesterone acetate (DMPA), Levonorgestral releasing IUD, non steroidal anti-inflammatory drugs, antifibrinolytic agents, danazol and GnRH analogues.

OCPs have been reported to reduce menstrual loss by 43%¹³. Over the last few years, use of extended regime is becoming more common. Numerous clinical trials on women with menorrhagia have shown that extended regimen without hormone free interval, is a safe and effective method to relieve these symptoms and ultimately induce amenorrhoea in 80% to 100% of women by 10 to 12 months use till such time their haemoglobin is restored to normal¹⁴.

Intramuscular injection of a long acting progestational agent such as depo- medroxyprogesterone acetate (DMPA) has been used over the last decade to achieve therapeutic amenorrhea in the management of menorrhagia. However, some patients experience breakthrough and irregular bleeding. Such irregular bleeding pattern may further complicate the tendency for uncontrolled bleeding in patients with haematological abnormalities.

Non steroidal anti-inflammatory drugs like mefenamic acid (500mg 8 hourly) and antifibrinolytic drug like tranaxaemic acid (1gm 6-8 hourly) are indicated as an alternative to OCPs during menstruation in those patients who are hemodynamically stable and have moderate to heavy flow. NSAIDS and antifibrinolytic drugs reduce menstrual loss by an average of 30% and 50% respectively.^{15,16}

Danazol¹⁷ is an isoxazol derivative of 17 α ethinyl- testosterone and has a pure progestogenic action. It inhibit release of pituitary gonadotropin thereby suppresses the endometrium. However, its use is limited due to its cost and side effects like androgenic features, weight gain, muscle cramps, skin rashes etc.

GnRH agonists¹⁸ causes pituitary down regulation and subsequent inhibition of cyclical ovarian activity. It is effective in reducing mean blood loss (MBL), however its use is limited to short term because of its cost and significant side effect like osteoporosis etc.

TREATMENT AND PREVENTION OF ANAEMIA

All adolescents with anaemia (haemoglobin less than 12 gm%) are treated with 180-200mg of elemental iron in divided doses whereas those with haemoglobin more than 12gm% should be prescribed prophylactic dose of 100 mg of elemental iron daily.

REASSURANCE

Reassurance is needed for all adolescents with menorrhagia to allay anxiety both related to disease and treatment. Parents and guardians are often reluctant for use of hormonal therapy in the form OCP etc. for their children. Proper counselling needs to be done.

PROGNOSIS AND FOLLOW UP^{19, 20}

Adolescents with menorrhagia constitute a high risk group as there is an increased incidence of anaemia, need for transfusion, subsequent infertility, spontaneous abortion, and impaired reproductive potential. Chronic anovulation in PCOS also predisposes patients to endometrial hyperplasia and frank carcinoma in later life.

The importance of continued follow up in these girls is reinforced by the results of a 25 year prospective evaluation of adolescents' menstrual abnormalities. In 291 patients, 2 years after onset of the presenting episode, bleeding problem continued in 60% at 4 years, in 50% at 10 years and in 30 to 40% after more than 10 years. The worst prognosis was found in those with menorrhagia at the time of menarche.

The girls with underlying coagulation disorder remain a therapeutic challenge, best managed by the combined effort of both a haematologist and gynaecologist.

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