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Menstrual Suppression in Special Circumstances

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Abstract

Objective: To provide a Canadian consensus document for health care providers with recommendations for menstrual suppression in patients with physical and/or cognitive challenges or those who are undergoing cancer treatment in whom menstruation may have a deleterious effect on their health.

Options: This document reviews the options available for menstrual suppression, its specific indications, contraindications, and side effects, both immediate and long-term, and the investigations and monitoring necessary throughout suppression.

Outcomes: Clinicians will be better informed about the options and indications for menstrual suppression in patients with cognitive and/or physical disabilities and patients undergoing chemotherapy, radiation, or other treatments for cancer.

Evidence: Published literature was retrieved through searches of Medline, EMBASE, OVID, and the Cochrane Library using appropriate controlled vocabulary and key words (heavy menstrual bleeding, menstrual suppression, chemotherapy/radiation, cognitive disability, physical disability, learning disability). Results were restricted to systematic reviews, randomized controlled trials, observation studies, and pilot studies. There were no language or date restrictions. Searches were updated on a regular basis and new material was incorporated into the guideline until September 2013. Grey (unpublished) literature was identified through searching websites of health technology assessment and health technology-related agencies, clinical practice guideline collections, clinical trial registries, and national and international medical specialty societies.

Values: The quality of evidence was rated using the criteria described in the Report of the Canadian Task Force on Preventive Health Care (Table 1).

Benefits, harms, and costs: There is a need for specific guidelines on menstrual suppression in at-risk populations for health care providers.

Recommendations

1. Menstrual suppression and therapeutic amenorrhea should be considered safe and viable options for women who need or want to have fewer or no menses. (II-2A)

2. Menstrual suppression should not be initiated in young women with developmental disabilities until after the onset of menses. (II-2B)

3. Combined hormonal or progesterone-only products can be used in an extended or continuous manner to obtain menstrual suppression. (I-A)

4. Gynaecologic consultation should be considered prior to the initiation of treatment in all premenopausal women at risk for abnormal uterine bleeding from chemotherapy. (II-1A)

5. Leuprolide acetate or combined hormonal contraception should be considered highly effective in preventing abnormal uterine bleeding when initiated prior to cancer treatment in premenopausal women at risk for thrombocytopenia. (II-2A)

Table 1. Key to evidence statements and grading of recommendations, using the ranking of the Canadian Task Force on Preventive Health Care

Quality of evidence assessment*	Classification of recommendations†
I: Evidence obtained from at least one properly randomized controlled trial	A. There is good evidence to recommend the clinical preventive action
II-1: Evidence from well-designed controlled trials without randomization	B. There is fair evidence to recommend the clinical preventive action
II-2: Evidence from well-designed cohort (prospective or retrospective) or case–control studies, preferably from more than one centre or research group	C. The existing evidence is conflicting and does not allow to make a recommendation for or against use of the clinical preventive action; however, other factors may influence decision-making
II-3: Evidence obtained from comparisons between times or places with or without the intervention. Dramatic results in uncontrolled experiments (such as the results of treatment with penicillin in the 1940s) could also be included in this category	D. There is fair evidence to recommend against the clinical preventive action
	E. There is good evidence to recommend against the clinical preventive action
III: Opinions of respected authorities, based on clinical experience, descriptive studies, or reports of expert committees	L. There is insufficient evidence (in quantity or quality) to make a recommendation; however, other factors may influence decision-making

*The quality of evidence reported in these guidelines has been adapted from The Evaluation of Evidence criteria described in the Canadian Task Force on Preventive Health Care.[62]

†Recommendations included in these guidelines have been adapted from the Classification of Recommendations criteria described in the Canadian Task Force on Preventive Health Care.[62]

INTRODUCTION

Menstrual suppression involves the use of various hormonal regimens prescribed in an extended or continuous fashion to achieve therapeutic amenorrhea. This can involve decreasing the blood loss and the number of menstrual cycles per year or eliminating menses altogether. The goal may also include management of associated menstrual side effects, such as bloating, nausea and vomiting, headaches, mood and behavioural changes, and cyclic exacerbation of seizures or migraines. The ultimate goals of menstrual suppression are to reduce morbidity and improve quality of life for women and/ or their caregivers.[1,2] Menstrual suppression is often medically indicated. The Canadian Consensus Guideline on Continuous and Extended Hormonal Contraception describes many indications for suppression.[2] These include social choice, severe dysmenorrhea associated with endometriosis, abnormal uterine bleeding, hemorrhagic diatheses, hormone withdrawal symptoms, and premenstrual dysphoric disorders. This guideline focuses on the needs of women with developmental disabilities and women undergoing cancer treatment and at risk for iatrogenic thrombocytopenia. Both of these conditions present commonly in adolescence. For management of women with inherited bleeding disorders, please refer to SOGC Clinical Practice Guideline No. 163.[3] The following guideline will address each indication for menstrual suppression (disabilities and cancer treatment) separately.

ABBREVIATIONS

AUB	abnormal uterine bleeding
BMD	bone mineral density
CHC	combined hormonal contraception
DEXA	dual X-ray absorptiometry
DMPA	depot medroxyprogesterone acetate
GnRH	gonadotropin releasing hormone
IM	intramuscular
IUD	intrauterine device
IV	intravenous
LA	leuprolide acetate
LNG-IUS	levonorgestrel intrauterine system
OCP	oral contraceptive pill
POP	progestin-only pill

CONSIDERATIONS AND OPTIONS FOR MENSTRUAL SUPPRESSION IN WOMEN WITH DISABILITIES

Women with developmental challenges and disabilities are a varied group. Patients may have cognitive and/or physical impairments, various levels of communication and independence in activities of daily living, numerous comorbidities, polypharmacy, and differences in their abilities to participate in informed consent. Families of adolescents with disabilities often present for counselling before or after menarche, which usually occurs at the same age as in the general population.[4,5] There is some indication that women with cerebral palsy undergo puberty earlier, but reach menarche slightly later, than the general

population,[5,6] people with neurologic impairment have a higher risk of precocious puberty,[7] and neuroleptic drugs can lead to hyperprolactinemia and amenorrhea.[5,7] While menstrual irregularities are common in the first 2 to 3 years post menarche because of anovulatory cycles, AUB and dysmenorrhea in women with disabilities require the same investigations as those undertaken in the general population. In a retrospective study of 300 adolescents with developmental disabilities, 30% experienced heavy, painful, or irregular menstrual bleeding, and rates of behavioural or mood symptoms approached 22%.[8]

In 2 retrospective studies, 32% to 43% of caregivers approached physicians for information on menstrual suppression prior to the young woman's menarche because of their anxiety and concerns about coping with hygiene and possible behavioural changes.[4,8] Behavioural concerns can include mood changes, aggression, and self-mutilation,[6] which may also reflect pain.[9] Defining the reasons for intervention can assist in the formation of treatment goals.[1] Table 2 outlines the pertinent points to elicit from history prior to initiation of therapy when considering menstrual suppression. There is a general consensus that menstrual suppression therapy should not commence until menarche.[4] Often, education and support of the normal progression through puberty and menarche are all that is required.[4,8,9] Awaiting menarche also confirms normal hormonal function and the absence of an obstructive anomaly. Once a decision is made to pursue treatment, medical interventions that are the least intrusive, are reversible, and have the lowest side effect profile are desirable. Surgical or permanent interventions are rarely required and are fraught with ethical and legal issues if the individual is unable to participate fully in consent.[1,5,7,9,10] All of the available options for reversible contraception are acceptable for menstrual suppression (Table 3) and satisfaction can be achieved in most disabled adolescents and their families with 1 or 2 hormonal methods.[8]

Recommendations

1. Menstrual suppression and therapeutic amenorrhea should be considered safe and viable options for women who need or want to have fewer or no menses. (II-2A)
2. Menstrual suppression should not be initiated in young women with developmental disabilities until after the onset of menses. (II-2B)

Combined Hormonal Options

Decreased number of periods or complete menstrual suppression, with control of menstrual-related side effects, can be achieved with extended or continuous use of CHC. There have been several studies in the general population that examine the different routes for delivering extended or continuous CHC, and no single regimen has been recognized as superior to the others.[11–13] Unscheduled bleeding generally decreases over time.[1,2]

For patients without contraindications to estrogen, the OCP, contraceptive patch, or vaginal ring can be used to prevent cyclical or abnormal menstrual bleeding. The safety, efficacy, and acceptability of extended or continuous use have been studied in randomized controlled studies[14,15] and are similar to rates for contraceptives used cyclically. The extended use of hormones for menstrual suppression for dysmenorrhea, endometriosis, heavy menstrual bleeding, and menstrual-related symptoms is also well established. For specific details, please refer to SOGC Clinical Practice Guideline no. 195.[2] There are no data on the long-term safety of CHC in patients with cognitive or physical impairments.

The prescription of extended use of CHC has been shown to be acceptable in adolescents[16] and patients with disabilities.[4,8] CHC also suppresses ovulation, which improves menstrual-related mood symptoms or behaviours. These are common presenting complaints in adolescents with Down syndrome, autism, and cerebral palsy.[6] Adjustment to a higher dose estrogen-containing formulation or to an alternate antiepileptic may be required because enzyme-inducing anti-epileptic drugs can interfere with the cytochrome p450 system and metabolism of CHC.[17] The need for frequent courses of antibiotics may affect the efficacy of hormonal therapy. Malnutrition or gastric feeding tubes can affect the route of drug administration and absorption.[5] Immobile and wheelchair-bound individuals may be at increased risk of venous thromboembolism.[6,18] In a recent cohort study of adolescents with disabilities, none of the permanent wheelchair users who used an OCP or the patch developed thromboembolisms during the study period.[8]

The choice of a monophasic or triphasic combined contraception pill is often at the discretion of the prescriber. Similarly, the dose of the pill should depend on the side effects experienced or the comorbidities and polypharmacy of the patient. There is some concern regarding a decrease in the expected gain in BMD in adolescents who use 20 mcg ethinyl estradiol formulations.[19] For adolescents with heavy or irregular menstrual bleeding, it may be appropriate to consider starting with cyclic use prior to extended or continuous use to minimize breakthrough spotting and discontinuation.[16] In a recent retrospective study, OCP was the most commonly selected initial and second-choice method for menstrual suppression in adolescents with disabilities.[8]

Table 2. Considerations for menstrual suppression in girls and women with developmental disabilities

Menarchal status
    Premenarchal: counselling and education
    Postmenarchal: menstrual suppression options

Quality of life
    Hygiene
    Degree of anxiety
    Activity restrictions
    Caregiver concerns

Treatment goals
    Degree of suppression or amenorrhea desired
    Contraceptive needs

Type of disability or risk
    Cognitive
    Physical
    Communicative
    Abuse

Degree of required support
    Ambulatory vs. wheelchair user
    Support required with activities of daily living
    Access to support (home, school, and respite care)

Menstrual symptoms
    Menstrual bleeding patterns
    Dysmenorrhea
    Behavioural, mood, and/or premenstrual symptoms

Medical history and comorbidities
    Cerebrovascular disease
    Complicated valvular heart disease
    Diabetes with end-organ disease
    Decreased BMD
    Liver disease
    Malnutrition or feeding tube
    Migraines with neurological symptoms
    Obesity
    Seizure disorder
    Thromboembolic risk or history
    Thyroid dysfunction
    Uncontrolled hypertension

Medications
    Antiepileptics
    Antibiotics
    Neuroleptics
    Steroids

The contraceptive patch delivers 35 mcg of ethinyl estradiol and 150 mcg of norelgestromin daily and requires weekly replacement. The patch may be considered in patients with gastrointestinal issues (difficulty swallowing or malabsorption) or in those with poor compliance using daily oral contraceptives.[1] In a randomized controlled trial evaluating continuous use of the patch in the general population, menstrual bleeding was delayed to 54 days and amenorrhea rates of 28% and 12% were achieved through extended use to 8 and 12 weeks, respectively.[11] The side effect profile is similar to that of OCP,[20,21] with spotting as a common initial side effect. Based on data analyzed for pregnancy outcome, the efficacy of the patch appears to be reduced in patients who weigh 90 kg or more.[22] In a cohort study of adolescents with disabilities, 20% of patients and their families elected to use the patch as their first choice for menstrual suppression.[8] Disadvantages of the transdermal patch included skin irritation, behavioural or mood concerns, breast tenderness, and attempted removal of the patch by the disabled adolescent.

The transvaginal ring is a preparation with daily delivery of 15 mcg ethinyl estradiol and 120 mcg etonogestrel.[22] One randomized controlled trial in the general population evaluated continuous use of the ring versus extended use with a 4-day ring-free interval, with the latter resolving breakthrough bleeding or spotting.[23] Continuous or extended use had high continuation rates and reduced menstrual flow and pelvic pain. An advantage of the ring is that it can be used for one month before requiring replacement. Although the use of the transvaginal ring has not been studied in the developmentally delayed population, this option can be presented to patients with minor cognitive delay and familiarity with tampon use or no physical impairment to ring insertion.

Progestin-only Options

Progestin-only options for menstrual suppression offer alternatives to estrogen-containing contraceptives and can be administered by intramuscular, oral, or intrauterine routes. The progestin implant is not available in Canada.

Oral progestins (0.35 mg norethindrone tablets) are prescribed daily without a pill-free interval. The POP does not confer the same degree of amenorrhea (10% of patients),[24] but it is effective contraception with a failure rate of only 0.5% with perfect use.[22] Side effects are much less common with POP than with OCP, but may include breakthrough bleeding, emotional disturbances, acne, and breast tenderness. POP treatment has not been studied exclusively in patients with disabilities.

Table 3. Reversible therapeutic hormonal options for menstrual suppression

Type of contraception	Benefits	Difficulties	Risks
OCP	Oral or feeding tube administration Extended or continuous regimen Reduced menstrual flow and dysmenorrhea Reduction in ovarian, endometrial, colorectal cancer	Compliance with daily administration Breakthrough bleeding	Venous thromboembolism Gallbladder disease Contraindicated in patients with hepatic disease or hormone-dependent cancers on chemotherapy
Contraceptive patch	Weekly transdermal application Avoids first pass metabolism Same as OCP	Skin irritation Removal (inadvertent or deliberate) Reduced efficacy in patients ≥ 90kg	Same as OCP
Vaginal ring	Administration every 3 weeks Avoids first pass metabolism Same as OCP	Insertion by woman or caregiver Not studied in disabled population	Same as OCP
DMPA injection	Administration every 10–12 weeks Amenorrhea within 1 year in 50% of patients Safe for patients with contraindications to estrogen	Injection Breakthrough bleeding Weight gain Requires dietary calcium and vitamin D supplementation	Reduced BMD during treatment (reversible)
Oral progesterone	Oral or feeding tube administration Safe for patients with contraindications to estrogen	Compliance with daily administration Breakthrough bleeding Weight gain	Minimal
LNG-IUS	5-year effectiveness Minimal systemic effects Progressive reduction in menstrual flow and pain Amenorrhea within 1 year in 50% of patients	Insertion may require general anaesthesia Initial irregular bleeding Minimal uterine length of 5–6 cm Post-operative ultrasound for placement in patients with disabilities	Perforation Expulsion Infection (first 21 days)
GnRH analogue leuprolide	Administration every 4 (3.75 mg im) or 12 weeks (11.25 mg im) Amenorrhea rates of 73–96% Effective for prevention of heavy menstrual bleeding with iatrogenic thrombocytopenia	Cost Intramuscular injection Ideal administration 3–4 weeks prior to chemotherapy in luteal phase Long-term use requires add-back therapy* to prevent hypoestrogenic symptoms of endometriosis	Reduced BMD during treatment; add-back therapy or adequate dietary calcium and vitamin D supplementation are recommended

None of these methods protect against sexually transmitted infections.

*Various add-back therapy regimens (estrogen and/or progestin) are available.

DMPA is an injectable progesterone of 150 mg administered intramuscularly every 12 weeks. Despite American and Canadian advisories in 2004 and 2005, respectively, regarding concerns over loss of BMD, the advantages of DMPA have led to its continued use. Prior to evidence of the association between DMPA and bone loss, DMPA was the most commonly prescribed method of menstrual suppression (59%) in adolescents with developmental delay.[4] Recent Canadian data have shown a shift in prescribing methods to the extended combined oral contraceptive, although DMPA remains a popular initial choice in 12% of adolescent patients with disabilities.[8]

The dosing schedule of DMPA, administered every 12 weeks or sometimes every 10 weeks in patients on anti-epileptic medications,[25,26] confers a possible advantage in patients with disabilities. DMPA also minimizes concerns over compliance and is acceptable in patients who are unable to swallow pills or tolerate a vaginal ring or transdermal patch. DMPA may also be considered for the quick initial induction of amenorrhea, to be followed by the use of alternative longer-term methods of menstrual suppression. Rates of amenorrhea at 12 to 24 months reach 55% to 70% in the general population,[25,27] with irregular bleeding as a common initial side effect that diminishes over time. It is an extremely effective contraceptive with a failure rate of 0.3%.[24] Additional advantages include a relative lack of drug interactions and reductions in seizures[28] and sickle cell crises.[29]

The reduction in estrogen levels from the use of DMPA during adolescence is associated with bone loss of 3.1% at the lumbar spine and 6.1% at the hip.[19,30] Fortunately, studies suggest that loss of BMD is transient and its recovery has been demonstrated in adult and adolescent patients with cessation of the injection.[30–33] Modifiable factors such as dietary calcium intake, even at levels lower than the daily recommended intake of 1300 mg per day, contribute to BMD gain in the femoral neck and lumbar regions in adolescents.[34] The DEXA scan can be used to quantify bone mass during DMPA treatment. Age appropriate norms should be used. However, whether this surrogate marker for bone strength translates into a measure of fracture risk has yet to be elucidated. Considerations of bone density are particularly important in wheelchair-bound and immobile patients or those on systemic steroids, who are already at risk for lower BMD. Regular appointments to readdress the need for continued DMPA, to consider alternatives, and to encourage adequate dietary calcium with vitamin D supplementation and weight-bearing exercise are strongly encouraged.[35]

Weight gain of 1 to 2 kg per year of use is also a possible side effect of DMPA through appetite stimulation.[36] Obese young women are more susceptible to increased weight gain on DMPA,[36] and weight gain may be an important issue in individuals who require assistance with transfers.[6]

Levonorgestrel Intrauterine System

The LNG-IUS is indicated for control of heavy menstrual bleeding and long-acting reversible contraception. Through daily delivery of 20 mcg of levonorgestrel, the local effects of the device lead to inhibition of endometrial proliferation, thickening of cervical mucus, and impaired sperm mobility.[37] In the general population, menstrual blood loss is reduced by 85% in 3 months,[38] and rates of amenorrhea reach nearly 50% in 6 months[39] and continue to increase over time, while irregular spotting, particularly in the months following insertion, diminishes. In a randomized controlled trial, LNG-IUS was shown to be more effective in reducing menstrual bleeding than a 10-day regimen of 10 mg oral medroxyprogesterone acetate per month.[40] In adolescents, the most common indication for use of the LNG-IUS was heavy menstrual bleeding, which occurred in 17% of patients.[41]

A significant benefit of the LNG-IUS is its length of treatment (5 years), after which it can be removed and alternatives can be re-evaluated or a new IUS can be reinserted. Side effects are few and complications such as perforation, expulsion, and infection are rare in adult and adolescent populations,[18,40–42] with high rates of continuation in adolescents of 75% to 85%.[41,43] In one study of 14 young women with disabilities,[44] 50% achieved amenorrhea with LNG-IUS and there was 1 expulsion, which is in keeping with the low rates of expulsion (7 to 8%) of IUDs in young women with or without disabilities.[41,43] In another study of adolescents with cognitive and physical challenges,[8] the LNG-IUS was a popular second-line option for menstrual suppression in 19% of patients who switched from alternate methods. Ovulation is not suppressed by the LNG-IUS, and thus hormonal cycling and associated mood symptoms or behaviours may not be ameliorated.

Insertion in virginal or young women with disabilities may require general anaesthesia or conscious sedation. Pre-insertion considerations include vaginal and cervical swabs in patients at risk for infection, screening for pregnancy, ultrasound for vertical length of the uterine cavity (5 to 6 cm is recommended), and administration of oral or vaginal misoprostol.[44,45] Long-term menstrual suppression with LNG-IUS offers effective reduction in menstrual blood loss, high rates of amenorrhea, and low rates of complications.[8,41,44]

Recommendation

3. Combined hormonal or progesterone-only products can be used in an extended or continuous manner to obtain menstrual suppression. (I-A)

MENSTRUAL SUPPRESSION FOR ONCOLOGY PATIENTS

Each year in Canada there are approximately 600 new cancer cases and 80 deaths from cancer in girls and women aged 0 to 19 years and 12 450 new cases and 4800 deaths in women aged 20 to 49 years.[46] This constitutes a substantial number of women of reproductive age who will develop cancer and require treatment, such as chemotherapy, radiation, or hematopoietic stem cell or bone marrow transplantation. Ablative therapy may induce pancytopenia with thrombocytopenia and result in moderate to severe uterine bleeding in nearly 40% of oncology patients.[47]

AUB in premenopausal women with malignancy is caused by thrombocytopenia from the cancer itself and can be further exacerbated by cancer treatment. The resulting bleeding worsens thrombocytopenia through increased platelet consumption. Heavy bleeding may result in the need for transfusion and delay or interrupt their treatment regime.[47,48] These immunosuppressed women are also at increased risk of infection from both neutropenia and prolonged bleeding. Iatrogenic thrombocytopenia necessitates prevention of heavy menstrual bleeding through menstrual suppression.

Recommendation

4. Gynaecologic consultation should be considered prior to the initiation of treatment in all premenopausal women at risk for abnormal uterine bleeding from chemotherapy. (II-1A)

GnRH Analogues

Most of the data on menstrual suppression in women with malignancies focus on the use of the GnRH agonist LA. Heavy menstrual bleeding can be mitigated through induced hypo-estrogenism and gonadal suppression. The first reported study by Ghalie et al. (1993) compared LA administered 1 mg IV daily or 7.5 mg IM monthly prior to bone marrow transplant at different times during the menstrual cycle in 34 patients.[48] No adverse effects were observed and menstruation was prevented in 73% of patients. When LA was started at least 2 weeks prior to the onset of thrombocytopenia, the failure rate was 6%; when it was initiated at a later time, the failure rate was 33%.[48] Prospective studies with different doses or routes of administration of LA, such as 3.75 mg IM prior to chemotherapy,[49–51] showed similar relations between the success of therapeutic amenorrhea and the timing of the treatment. The efficacy of GnRH analogues in preventing bleeding has been shown in 85% to 100% of patients when initiated at least 1 month prior to chemotherapy.[49,50] Duration of therapy is usually directed by the risk or presence of thrombocytopenia or is dependent on the duration of myelosuppressive therapy.

Recommendation

5. Leuprolide acetate or combined hormonal contraception should be considered highly effective in preventing abnormal uterine bleeding when initiated prior to cancer treatment in premenopausal women at risk for thrombocytopenia. (II-2A)

In 2007, Quaas and Ginsburg published a systematic review on the prevention and treatment of uterine bleeding in premenopausal patients with malignancies. They concluded that GnRH agonists are very effective for the prevention of uterine bleeding in these patients. The prevention of bleeding was recommended over the acute treatment of bleeding and a consultation with a gynaecologist prior to starting any treatments was encouraged.[52] Prophylactic management with LA was recommended in a 2011 review.[53] Tranexamic acid, medroxyprogesterone or OCP, or IV estrogen followed by danazol or recombinant factor V11a with desmopressin were recommended as escalated treatment for heavy menstrual bleeding. In a worldwide survey, mainly of oncologists of pediatric bone marrow transplant patients, GnRH agonists were preferentially chosen by 41% of respondents over CHC (29%), progesterone-only oral medication (21%), DMPA (6%), and ethinyl estradiol/norelgestromin patch (3%) for the induction of amenorrhea.[54] There are no studies comparing GnRH agonists directly to OCPs to demonstrate superior effectiveness. Neither GnRH agonists nor OCPs have been shown conclusively to confer protection against ovarian insufficiency.[55,56]

Oral Contraceptive Pills

Although the OCP is often referred to as a standard method for menstrual suppression in women with malignancies, there is little published in this area.[53] Only one small retrospective series of oral contraceptives for prevention of heavy menstrual bleeding in women undergoing stem cell transplantation has been published.[57] Gynaecologic consultation occurred at a median of 12 days after transplantation. Prior to consultation, 21 (64%) of 33 patients had been on OCP; most of the other patients had no hormonal treatments and a small minority were on medroxyprogesterone alone or combined with conjugated estrogens. Heavy menstrual bleeding resolved in 97% of patients, but 21% required more than one form of hormonal therapy and 12% required progressive treatment with higher dose OCP and/or IV conjugated estrogen.[57]

OCP is an important option for patients who cannot tolerate IM injections or who show evidence of osteoporosis. However, oral contraceptives may increase both liver toxicity following stem cell transplant and the frequency of venous thromboembolic events, which are

already increased in patients with malignancy. OCP may also be poorly tolerated or absorbed due to mucositis, vomiting, or diarrhea secondary to radiation enterocolitis or chemotherapy.[57]

In a prospective cohort trial by Sica et al.,[58] 16 premenopausal women with acute leukemia were administered OCP alone (n = 8) or OCP with LA (n = 8) for the prevention of vaginal bleeding during chemotherapy. There were no statistical differences in red blood cell or platelet transfusions or duration of vaginal bleeding, nor were there any flares in either group. Liver toxicity was noted in both groups. However, once the OCP was discontinued, liver damage resolved and menses also resumed in 6 of the 8 patients on OCP versus none in the combined group for whom the OCPs were administered to prevent flares. The authors attributed these findings to the more profound induction of amenorrhea by LA than by OCP alone.

Depot Medroxyprogesterone Acetate

In 2006, Meirow et al. compared D-tryptophan-6-luteinizing hormone-releasing hormone (a GnRH agonist) to DMPA or no treatment in patients prior to myelosuppresive chemotherapy retrospectively in 101 patients.[47] Significantly fewer urgent gynaecologic consultations were required in the patients who were administered GnRHa. In the DMPA group 20% experienced moderate or severe menstrual bleeding. Urgent treatment with conjugated estrogens was required in untreated patients and in patients on DMPA, but not in any of the patients who received GnRH agonists. The authors of this and other studies[52] emphasize the importance of gynaecologic evaluation prior to the initiation of treatment and conclude that GnRH agonist treatment is more effective than DMPA for menstrual suppression and the reduction of heavy menstrual bleeding.

Levonorgestrel Intrauterine System

No studies have been published regarding menstrual management by LNG-IUS in patients undergoing cancer treatment. However, according to the World Health Organization's medical eligibility criteria for contraceptive use, the IUS is acceptable in immunosuppressed patients (such as those with lupus undergoing immunosuppressive treatment and patients with HIV) and patients at risk for venous thromboembolism.[59]

Surgical Options

There are no case reports or trials assessing prophylactic surgical techniques such as uterine artery embolization, endometrial ablation, or hysterectomy to prevent menstrual bleeding in hematologic malignancy. Case reports describe the use of uterine artery embolization to control chemotherapy-induced heavy menstrual bleeding unresponsive to medical management.[60,61]

SUMMARY

Menstrual suppression is often medically indicated. The Canadian Consensus Guideline on Continuous and Extended Hormonal Contraception[2] describes many indications for suppression, including social choice, severe dysmenorrhea associated with endometriosis, abnormal uterine bleeding, hemorrhagic diatheses, hormone withdrawal symptoms, and premenstrual dysphoric disorders. This guideline focuses on 2 groups who often benefit significantly from reduced menstrual bleeding or amenorrhea: women with cognitive and/or physical impairments and women undergoing cancer therapy. While there is a paucity of data from large trials to dictate clinical practice, several options are available to induce therapeutic amenorrhea in women with disabilities or prophylactic menstrual suppression in women with malignancies prone to thrombocytopenia.

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