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Management of contraceptives and menstrual complaints in patients with Down syndrome

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ABSTRACT

Enhanced health care for patients with Down syndrome (DS) results in improved overall quality of life and longer life expectancy. The main gynecologic complaints of patients with DS and their caregivers relate to menstrual cycles, hygiene and reproductive issues. Certain aspects, such as age of menarche, menstrual cycles, internal genitalia, and hormone profile are similar to those observed in the general population. However, individuals with DS may have a higher incidence of other disorders related to menstruation, such as hypothyroidism, epilepsy and use of anticonvulsants. Contraceptive measures for individuals with DS can be used for both contraception and control of menstrual symptoms. The physician must be to make an individualized recommendation aimed at offering the most efficient and least invasive method with the fewest side effects. Among medical options are oral contraceptives, quarterly injectable medroxyprogesterone acetate, oral progesterone, a levonorgestrel-releasing intrauterine system, transdermal patch and vaginal rings. Surgical methods, including hysterectomy, endometrial ablation, or tubal ligation, are rarely considered because they raise ethical and legal questions. This article reviews the literature and basic guidelines to assist physicians who attend adolescent girls and women with DS to provide guidance on the appropriate management of the main gynecologic complaints of this population.

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Introduction

Down syndrome (DS) is the most common chromosomal abnormality (occurring in 1:800 to 1000 live births). It is the main cause of mild to moderate intellectual disability [1]. In recent decades, the birth rate of children with DS has increased in Western countries because of increasing maternal age [2]. Adolescent girls and young women with intellectual disability are increasingly integrated into society and have a longer life expectancy. These patients and their caregivers increasingly present with questions about gynecologic issues, including about menstrual cycles and contraception, for which physicians need to develop the requisite knowledge and specific management skills [3–5].

Certain issues are no different from those seen in the general population, such as the age of menarche, menstrual cycles, internal and external genitalia, and sex hormone profiles. However, for those with DS who have intellectual disabilities, issues of menstrual hygiene, premenstrual disorders, and contraception are more challenging to address [4].

Women with DS can become pregnant and are vulnerable to sexual abuse, which are common concerns for parents and caregivers [4,6]. Risk of abuse may be reduced by instructing DS patient about protective behaviors and providing adequate social and personal support [7,8]. Contraception, which can prevent unwanted pregnancies and help control menstrual cycles, is therefore an important topic for physicians caring for patients with DS [4].

Barriers to good gynecologic guidance for individuals with DS include the lack of appropriate sex education and the fact that they may be regarded as asexual, particularly by caregivers. However, health professionals may also receive inadequate training about gynecologic issues specific to patients with DS [9–12].

The objective of this review is to update knowledge and promote better understanding of particular aspects of contraceptive use and menstrual complaints that may be raised by girls and women with DS.

Social inclusion and contraception

Youngsters with DS may have an active social life, including school and perhaps dating; some will even marry when they are older [10]. As adolescents develop, they begin to create a self-identity as functional sexual beings, which is also true of girls with an intellectual disability [13]. However, those with DS are less likely to be allowed to express sexual feelings or to have consensual relationships if they wish to do so [11]. Historically, their fertility has been suppressed in order to avoid pregnancy, not least because they are at greater risk of sexual abuse than is the general population [11,13].

Current medical and social models centering on cultural and sexual norms may make adaptation to adult life harder for individuals with DS because of a communication gap between health professionals and the patients' caregivers [13]. The increasing social inclusion of adolescents and young adults with DS involves

Table 1. Main studies about contraceptive methods available for people with Down syndrome.

Method	Limitations	Benefits	Author, year
OCPs	Increased risk of thromboembolism	Contraception Reduced bleeding	Burkman, 2004 Cromer, 2004
	Drug interactions with antiepileptic medication Daily dosing Reduced bone mass gain in adolescents	Amenorrhea within 1 year (continuous regimen) Improved hygiene	Quint, 2008 Gold, 2009 Albanese, 2007
POP	Spotting	Reduced bleeding	Kirkham, 2013 ACOG, 2009 Committee on Practice Bulletins - Gynecology, 2013 Albanese, 2007
MPA	Weight gain Reduced BMD Spotting (49%)	Simple dosing (150 mg intramuscularly every 12 weeks) Amenorrhea	ACOG, 2009 Albanese, 2007 Dizon, 2005
Transdermal patch	Skin irritation Reduced effect in patients weighing >90 kg	Weekly dosing Reduced hormone fluctuation	Kirkham, 2013 Paransky, 2003
Subcutaneous progesterone implant	Low rate of amenorrhea Poorly tolerated	Contraception	Hubacher, 2009 Zacharin, 2009
Vaginal ring	Vaginal manipulation required	Reduced bleeding Reduced hormone fluctuation	ACOG, 2009 Sulak, 2008
LNG-IUS	High cost Insertion requires general anesthesia	Amenorrhea Contraception	Kirkham, 2013 Hillard, 2012 Atkinson 2003 Albanese 2007 Pillai 2010
	No improvement of hormone fluctuation Irregular bleeding		Paterson 2009 Paransky 2003 Hidalgo, 2002 ACOG, 2009
Surgical sterilization	Legal and ethical issues Violation of patient's rights Unreliable production of amenorrhea (endometrial ablation)	Contraception Amenorrhea (hysterectomy)	BRASIL, 1996 ACOG, 2009

ACOG: The American College of Obstetricians and Gynecologists.

challenges to health professionals regarding reproductive issues, particularly as they talk with parents or other caregivers who may deny the sexual maturation taking place or who are opposed to sex education for those they care for [13]. This is problematic because sexual feeling and relationships, along with accompanying questions about contraception and pregnancy, are part of a safe. Healthy transition into young adulthood, regardless of intellectual ability [13].

Use of contraceptives

The sexual behavior of intellectually disabled women may be similar to that of those with normal cognitive ability [14]. Cognitively impaired adolescents may be slower in understanding their sexual development. However, those with mild to moderate intellectual disability have sexual desires and interests similar to those of their peers with normal cognition [14]. Adolescents who are able to have consensual intercourse may require contraception [14].

They should be given guidance depending on their level of comprehension, taking into account the elevated risk of sexual abuse among this population. The use of barrier methods to prevent sexually transmitted infections should particularly be encouraged [4,12,15–17]. Cheng and Udry reported a correlation between low cognitive ability and higher rates of such infections, supporting the use of barrier methods but also indicating the need to be alert for signs of a sexually transmitted disease [18].

Hormonal contraceptive methods may be less effective for someone using medications that interact with them, such as anti-convulsants [12].

Menstruation

Irregular bleeding, menstrual hygiene, and hormone-related behavioral changes are the main complaints of adolescents with DS and their caregivers [11,12,19–21].

The primary reason for the prescription of contraceptives is in fact to suppress menstruation and its symptoms. Gynecologists are often asked to control menstruation or induce amenorrhea, so they must be prepared to advise patients and their caregivers in this regard [16].

Prescription of agents to control the menstrual cycle requires careful investigation of who is asking for it – the patient or the caregiver – and the reasons for the request. Depending on the patient's ability to communicate, this can be discussed directly between the physician and patient. If the caregiver initiates the request, the reason should be clearly identified, such as convenience, vulnerability to sexual abuse, risk of unwanted pregnancy, or a concern that menses are significantly affecting the patient's daily activities [16].

When breast development begins, some caregivers may request that menarche be delayed. In such cases, it is important to explain the need for physiologic menarche and the fact that exposure to endogenous estrogen is essential to promote good skeletal and cardiovascular development [17,20].

Most women with DS have regular menstrual cycles. Reports in the literature describe cycles of 22–33 days, with the most common intervals being 25–30 days. One group compared menses in adolescents with and without DS, finding a mean interval of 28.3 versus 28.6 days and length of bleeding of 5.5 versus 5.4 days [6,22].

Although it is not unusual for adolescents to have menstrual irregularity for 2–5 years after menarche, those with DS are more likely to have menstrual irregularity [23].

Comorbidities common in those with DS, such as thyroid disorders – with a prevalence of 25–30% – may lead to menstrual irregularity, amenorrhea, or abnormal uterine bleeding [23].

Epilepsy, which affects up to 13% of people with DS, may also be associated with menstrual irregularities because serum levels of sex hormones are affected by antiepileptic drugs [23].

Valproate may increase the incidence of polycystic ovary syndrome, which may be more frequent in women with seizure disorders, aggravating menstrual irregularity [24,25]. Metoclopramide and neuroleptics may lead to oligomenorrhea or even amenorrhea by increasing serum prolactin levels [12,16,24,25]. Other causes of menstrual irregularity are obesity and the use of mood stabilizers [20,26,27].

The most appropriate measure to suppress menstruation are reversible, noninvasive, efficient, and carry few side effects so that the treatment improves the patient's quality of life and relieves the caregiver's workload [3,16,28,29]. Prior to 'suppressing menses' a non-hormonal therapeutic approach to menorrhagia causing iron deficiency and dysmenorrhea limiting normal daily activities should be the first-line approach in these circumstances.

Suppression of menstruation in intellectually impaired adolescents should be individualized. Behavioral changes caused by low tolerance to seeing blood or difficulties with menstrual hygiene are other indications for menstrual suppression [12].

The age at menarche in DS is similar to that of the general population. Menarche suppression is not recommended except in cases of precocious puberty [10]. The physician's role in this matter is to guide caregivers and the patients themselves on managing menses, reducing the need for intervention [17].

Health care for women with DS

There are barriers to gynecologic care of women with DS, mainly because gynecologists lack training and adequate knowledge [9,13]. Provision of good medical care often requires longer, well-structured consultations [30,31].

Women with DS usually seek gynecologic care for the same reasons as other women. The gynecologist needs to engage these patients in discussion of their complaints and distress, which is facilitated by understanding the unique gynecologic, reproductive, and sexual aspects of this population [12].

Menstruation control and suppression, contraception, and sexuality are the main issues in the care of patients with DS [9]. Parents and caregivers must be aware of physical and psychosocial changes of puberty and sexuality, as well as aspects of menstruation such as irregular bleeding in the first years after menarche [13].

During this period, the use of non-steroidal anti-inflammatory drugs (NSAIDs) may help treat painful cycles [17]. Careful management allows assessment of the menstrual profile, examination of the genital tract, and avoidance of exogenous hormones that might suppress long bone growth [17].

Non-hormonal drugs such as NSAIDs and tranexamic acid should be the first-line approach for blood loss reduce and menstruation management. NSAIDs may reduce blood loss 30%, mainly with mefenamic acid and ibuprofen. NSAIDs have no amenorrhea effect and may cause gastrointestinal upset. Tranexamic acid may reduce about 50% blood loss have some impact on pain and can be used with OCPs (is no prothrombotic). None of them have contraceptive effects [29,32].

Contraceptive methods

The main benefits and limitations of each contraceptive method are summarized in Table 1.

Contraception in DS requires clinical and cognitive assessment of the patient as well as of the caregiver's capacity to manage medical recommendations, including the cost of care. Noninvasive contraceptive methods should be considered as the first option for patients with DS. Training should be provided to help the patient do as much as she can to handle contraception, menses, and self-hygiene. Sex education aimed at preventing sexual abuse is also advisable [16].

Two cohort studies (with 41 and 215 patients) found that oral contraceptives were used more commonly than quarterly injections of medroxyprogesterone acetate (MPA). Management of bleeding was primarily with a levonorgestrel-releasing intrauterine system (LNG-IUS) device or a transdermal patch [17].

In a small study, the intrauterine device expulsion rate was higher in intellectually disabled patients [17,33].

Oral contraceptive pills (OCPs)

The use of oral contraceptive regimens combining estrogen and a progestin may result in regular cycles and decreased blood loss. These agents may be prescribed to be taken continuously use or cyclically, with scheduled breaks at longer intervals to reduce days of bleeding [12,20,34]. Amenorrhea is possible for up to 1 year, and approximately 26% of patients may experience spotting [34]. The main concern in the daily use of OCPs in women with DS is whether they can remember to take the pill every day [13].

Drug interactions with anticonvulsants have been described, which may reduce the efficacy of the contraceptive, leading to escape bleeding which requires an additional dose of estrogen. Use of OCPs may increase the risk of thromboembolism or breast and cervical cancer. The lowest estrogen dose should be used initially, increasing it only if there is spotting [20,35].

Low-dose estrogens may be associated with reduced gain of bone mass in adolescents, which requires a risk-benefit analysis if they are to be used in patients with DS [20,36].

The safety and efficacy of the cyclic and continuous regimens are similar. A meta-analysis comparing six randomized controlled trials found no difference between the methods [37].

Continuous use of OCPs improves quality of life by reducing symptoms of associated disorders that may be aggravated during menses, such as depression, anemia, bleeding due to coagulopathies, thrombocytopenia, and seizures. Suppression of menstruation by continuous OCPs dosing can benefit patients with DS and their caregivers by attenuating hygiene problems [17].

Progesterone-only pills

When progesterone alone is indicated, and injections are not acceptable, the use of progesterone-only pills is appropriate. Cyclic or continuous use of progesterone reduces blood loss in women with anovulatory cycles, working differently than in ovulating women [16].

These contraceptives contain a low progesterone dose, leading to frequent spotting and making it impossible to control the menstrual cycle. Larger progesterone doses are preferable to suppress menstruation, such as norethisterone 5 mg three times a day continuously. Depression and mood swings have been associated with this medication, although the data in the literature are limited [16,20,38].

MPA

MPA suppresses menstruation and provides contraception simply and effectively with injections of 150 mg every 12 weeks, leading to amenorrhea in most cases. Spotting occurs in 49% of patients, and side effects such as weight gain and reduced bone mineral density (BMD) may be associated with continuous use of MPA [16,19,20,39]. Weight gain may be more pronounced in patients who are overweight before treatment [39]. MPA should not be given without estrogen supplementation. Its powerful suppression of the hypothalamic–pituitary–ovarian axis may cause BMD loss [40].

In 1992, Isart et al. [41] reported on physician surveys, finding that intellectual disability was a frequent indication for the use of MPA. Another study in 2013 found a reduction in the use of MPA from 59% to 11%, compared with an increase in the use of OCPs from 11% to 43% [17]. The decreased use of MPA may be due to new evidence on the adverse effect on BMD associated with continuous use. Recent changes in antiepileptic medications may also have led to greater safety of OCPs [16,32,37].

Transdermal patch

A transdermal patch provides effective and convenient hormonal contraception, releasing estrogen and progesterone transdermally and leading to better acceptance and reduced hormonal fluctuation. The patch is applied once a week for 3 weeks, followed by 1 week off. However, skin irritation may occur, and effectiveness is reduced in patients weighing more than 90 kg [4,17]. Patients with problems picking might not be able to use patch [4].

Subcutaneous progesterone implant

The subcutaneous injection of a progesterone implant is an effective contraceptive method, but it does not perform well in regulating menstrual cycles. Irregular bleeding often occurs (in 7–33% of women), and amenorrhea is achieved only in a minority of cases, 16% in 6 months and 13–22% in 1 year [42]. It may not be tolerated by some patients, because they may feel and try to pick the device [40].

Vaginal ring

A vaginal ring that releases estrogen and progesterone is introduced into the vaginal cavity and left in place for 3 weeks a month. It may also be used continuously, which can lead to less intense bleeding and a longer period of amenorrhea. It may be difficult for patients with DS to insert the ring themselves. Having the caregiver do so may be objectionable because of the intimate physical manipulation required [16].

LNG-IUS

The LNG-IUS is an effective contraceptive method and treats menstrual disorders by inducing amenorrhea. However, it does not suppress hormonal fluctuation symptoms and therefore does not improve behavioral changes [43].

Disadvantages are the high cost, irregular bleeding, and the requirement for general anesthesia to introduce the device in patients with intellectual disabilities [17]. There are few studies that recommend the use of LNG-IUS as an option to suppress menstruation in such women [3,4,20,44,45].

The LNG-IUS leads to amenorrhea in within 1 year, similar to MAP.

Caregivers should be advised that during the first 3 months after insertion, the LNG-SIU can cause mild irregular bleeds [43].

Compared with MAP, most patients in LNG-IUS trials had significant reduction in bleeding, and 50% achieved amenorrhea in 1 year [46].

The current literature does not specifically address the use of the LNG-IUS in patients with DS. Insertion may require general anesthesia or sedation and can be difficult if the vagina is narrow or the uterus too small [16,43].

Although there is no clear guideline for the use of the LNG-IUS as a contraceptive or menstruation control method, it may be most beneficial in patients with multiple comorbidities [16,43].

Surgical sterilization

Occasionally, parents and caregivers may request hysterectomy, believing that this procedure can improve their daughters' quality of life by abolishing menstrual bleeding and eliminating the risk of unwanted pregnancy [12].

Hysterectomy for the purpose of sterilization is inappropriate and for cessation of normal menses should be considered only after other reasonable alternatives have been attempted [47].

Hysterectomy, however, does not reduce the risk of sexual abuse, nor does it alleviate behavioral changes associated with monthly hormone cycles. It should be performed only for medical reasons after due consideration of the ethical and legal implications [12].

Endometrial ablation, a procedure that selectively destroys the endometrium without removing the uterus, is not recommended for intellectually disabled adolescents. It may not produce amenorrhea and is not a reliable contraceptive procedure. If pregnancy does occur, there is a higher risk of complications [16].

The law on sterilization intellectually disabled patients varies considerably around the world. Some countries have different laws depending on state or region. National legislatures continue to debate the topic. Patient capacity to provide informed consent is the main difficulty.

Brazil has specific legislation about this subject. Law 9,263 promulgated in 1996 provides that surgical sterilization of incapacitated persons can only be carried out with judicial authorization. The same law does allow for assistance with conception or contraception as a basic right for any citizen [48].

However, the law does not establish levels of disability, so that judgments with regard to surgical sterilization in cases of intellectual deficits are difficult. The practice of surgical sterilization does not in principle respect the concepts of autonomy and dignity. It is promoted to reduce social problems, such as difficulties for caregivers and as protection against rape and sexual exploitation.

In this context, the decision made by parents or caregivers often ends up stigmatizing the disabled person, violating their rights, and disrespecting their vulnerability. Therefore, depending on the patient's level of understanding, every effort should be made to include her in the discussion, not allowing family members to automatically override her preference. Sterilization should be considered an option of last resort.

GnRH analogs (GnRHa)

Injectable GnRHa cause effective menstruation suppression through a hypogonadotrophic state. It leads to a profoundly hypo-estrogenic state which causes loss of BMD. Hormone replacement therapy (HRT) should be used to balance the hypo-estrogenic state. Calcium and vitamin D supplementation should be advised in children using GnRHa. Use of GnRHa is not recommended for menstrual management because of markedly negative impact on BMD expect in case of precocious puberty [20,32,49].

Conclusions

There is increasing social inclusion of people with DS. The longer life expectancy and social inclusion of this population mean that medical professionals, especially gynecologists, are increasingly asked to advise on and manage menarche, puberty, menstrual cycles, reproductive health, and sex education for girls and women with DS. Few studies deal with these issues, and there is a shortage of educational material for patients and caregivers and of guidelines and protocols for health-care professionals.

Therefore, there is a need for improved medical knowledge about reproductive health in women with DS.

Proper management of menstruation and contraception is an important component of this population's health care. A personalized approach is necessary, geared to the level of patient's intellectual ability and respecting the family's values. It should include appropriate sex education and proper orientation for caregivers.

Research is needed to create a structured health-care network for women with DS, enabling them as much as possible to exercise their sexual and reproductive rights.

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