REVIEW

Suppression of menstruation in adolescents with severe learning disabilities

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As girls with severe cognitive developmental delay progress into puberty and become young women with learning disabilities, concerns about menstruation are common amongst carers and health care professionals are often consulted for advice. Very little, however, has been published on this area to guide the practitioner and studies are almost exclusively confined to the gynaecological literature. We aim to give an account of the various therapeutic options available and current practice within the paediatric endocrinology unit at our institution.

Girls with learning disabilities or their carers may seek help for a variety of reasons, which vary with the girl's level of ability to self care and understand, and the carers' own perceptions and understandings. Issues may arise concerning inability to cope with menstrual hygiene due to lack of mobility, physical flexibility or understanding. The problem may be of distressing symptoms of pain, heavy flow, irregular bleeding, mood changes or cyclical disturbances in seizure control. Concerns may also arise regarding pregnancy, vulnerability to sexual abuse or sexualised behaviour.

One should be sure to ascertain what is being asked for and what it is hoped can be achieved by any therapeutic intervention. Ongoing dependency can lead to the perception of young adults with learning disabilities as children or asexual; routine requests for suppression of puberty and menstruation without any particular identified problem should be resisted. It is important to establish the views of the girl concerned within the limits of her understanding and communication. Therapeutic intervention should only be considered if the presenting problem is severe enough to cause significant distress to the young woman after all educational and symptomatic approaches have been exhausted.

It is also important to stress the limitations of current treatment options; no long term strategies exist to completely suppress menstruation without the possibility of adverse consequences.

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EDUCATION

Explanation of the natural course of development and menstruation is important. While precocious puberty is more common in girls with neurological abnormalities, overall in most girls with learning disabilities menarche occurs at a similar time to that in controls.[1] Irregular bleeding is common in all girls in the first few years following menarche due to physiological anovulatory cycles, but girls with learning disabilities may have several additional factors which can affect cycling, such as the use of anticonvulsants and neuroleptic drugs or nutritional problems.

Education of the adolescent girl will need to be tailored to her level of understanding and explicit explanation of hygiene issues and acceptable behaviour may be needed. Families may find additional support from other carers in similar situations or health care professionals experienced in the day-to-day care of adolescent girls with learning disabilities helpful.

Help is sometimes sought while the girl is still premenarchal and it is important to emphasise that girls must be allowed to enter puberty normally before any therapeutic intervention can be considered. An explanation of the necessity of oestrogen exposure to promote skeletal and cardiovascular health needs to be given.

THERAPEUTIC OPTIONS

If reduction or abolition of menstruation is the goal, therapeutic options may be medical or surgical. Medical interventions include depot medroxyprogesterone acetate (DMPA, Depo-Provera) injections, continuous combined oral contraceptives, gonadotrophin-releasing hormone (GnRH) analogues and oral progesterones. Surgical options include implantation of a levonorgestrel-releasing intrauterine system (Mirena), endometrial ablation and, rarely, hysterectomy (table 1).

DMPA

DMPA (Depo-Provera) provides a simple and effective way of suppressing menstruation and providing contraception. Given by deep intramuscular injection at a dose of 150 mg every 12 weeks, DMPA is commonly used in those with learning disabilities.[2–4] Amenorrhoea is usually achieved, but spotting or some breakthrough bleeding may occur in up to 49% of patients.[2]

The major concern regarding DMPA use in this population is the well established association between DMPA use and decreased acquisition of bone mineral density (BMD) in adolescent girls. Adolescence is a crucial period of bone mineralisation leading to the achievement of peak bone mass

Abbreviations: BMD, bone mineral density; COC, combined oral contraceptives; DMPA, depot medroxyprogesterone acetate injections; GnRH, gonadotrophin-releasing hormone; LNG-IUS, levonorgestrel intrauterine system; POP, progesterone only contraceptive pill

Table 1 Therapeutic options

	Pros	Cons
DMPA injections	Simple, effective Contraceptive effect	Injection BMD concerns Weight gain Breakthrough bleeding possible
Oral progestogens	Oral route Contraceptive effect	BMD concerns Weight gain Breakthrough bleeding possible
Continuous use of COC pills	Oral route Contraceptive effect	Periods reduced, not eliminated Thromboembolism Concerns about increased breast and cervical cancer risk
GnRH analogues	Highly effective Contraceptive effect Option of add-back oestrogen or tibolone therapy	Injection BMD concerns Expensive Menopausal symptoms Sterile abscesses Polycystic ovary concerns
LNG-IUS	No systemic drugs Contraceptive effect	Invasive Periods reduced, often not eliminated Device expulsion, infection
Endometrial ablation	Less invasive than hysterectomy	Invasive Ethical and legal concerns Poor efficacy, may need repeat procedures No contraceptive effect Potential for permanent sterility
Hysterectomy	Highly effective	Major surgery Permanent sterility Ethical and legal concerns

BMD, bone mineral density; DMPA, depot medroxyprogesterone acetate injections; GnRH, gonadotrophin-releasing hormone; LNG-IUS, levonorgestrel intrauterine system.

in early adulthood.[5 6] Decreased acquisition of BMD during this period could theoretically increase the risk of osteoporosis and fractures later in life.

All studies performed in this area have been confined to adolescents and young adult women who do not have learning disabilities or mobility problems. The data show a net decrease in BMD in adolescent girls receiving DMPA, while controls show a net increase in BMD.[6–9] This has led to a Committee on Safety of Medicines (CSM) warning in the UK advising that ''in adolescents, medroxyprogesterone acetate (Depo-Provera) be used only when other methods of contraception are inappropriate''. A similar warning was issued by the Food and Drug Administration (FDA) in the US suggesting it ''should be used as a long-term birth control method (e.g. longer than 2 years) only if other birth control methods are inadequate''.

It has been shown, however, that adult women regain lost BMD after discontinuation of DMPA,[9] but the 47 younger patients (18–21 years) in this study did not completely regain BMD sufficiently to reach BMD levels seen in controls by the end of the study period. Since the warnings were issued, a more recently published longitudinal study has shown that adolescents gain BMD rapidly after discontinuing DMPA, such that at 12 months after stopping the drug adjusted mean BMD values were as high as those in non-users.[10]

It is not known if these changes in BMD in adolescence translate into any increased fracture risk at any time and it is important to emphasise that no published data exist which are directly relevant to adolescents with learning disabilities. Weight bearing exercise increases BMD in children[11] and osteopaenia is common in individuals with learning disabilities.[12 13] Anticonvulsants can also have a negative effect on BMD and patients with epilepsy are at higher risk of trauma related fractures.[14] Care, therefore, needs to be exercised in the use of DMPA in this population, especially in immobile patients. It is our practice to perform a DEXA scan before starting DMPA in girls with limited mobility and to monitor BMD by repeated scans during treatment. DMPA is not used as a long term solution in this population. Dietary supplementation with calcium and vitamin D is recommended.

DMPA is also commonly associated with weight gain,[15] which may be of particular concern in immobile patients. Weight gain seems to be more pronounced in patients who are overweight before DMPA treatment.[6]

ORAL PROGESTOGENS

For patients for whom injectable progesterone is unacceptable, oral administration of progestogens may be more suitable. Norethisterone 5 mg TDS can be used continuously to suppress menstruation. The progesterone only contraceptive pill (POP) contains a much lower dose of progestogens and the incidence of breakthrough bleeding is so high that it is unlikely to be successful in reducing menstruation to an acceptable level. POP efficacy is reduced by enzyme inducing drugs such as carbamazepine.

CONTINUOUS USE OF ORAL CONTRACEPTIVE PILLS

The continuous extended use (greater than 28 days of active pills) of combined oral contraceptives (COC) will produce fewer menstrual periods and allow control over the timing of periods. A typical strategy would be to use a COC daily for 9 weeks, stopping on the 10th week to allow a withdrawal bleed. This practice has gained popularity in the treatment of menstrual disorders, such as endometriosis and dysmenorrhoea, and is also used in otherwise healthy women for reasons of personal preference. A recent Cochrane review of six randomised controlled trials (RCTs) comparing extended use and 28 day cycle use of COCs found no difference in safety or contraceptive efficacy.[16]

Anticonvulsants may interact with COCs causing decreased efficacy which may lead to breakthrough bleeding. An increase in the oestrogen dose in the COC may be needed.

COCs cause an increase in the risk of thromboembolism,[17] which may be a particular concern in immobile patients. The use of COCs has also been linked to a small increase in the risk of breast and cervical cancer[18] and this should be included in the risk–benefit evaluation for each individual, especially if she has other risk factors such as a family history of breast cancer. Due to these safety concerns, it is our practice to start with a COC with a dose of oestrogen of 20 μg, increasing to a higher dose if breakthrough bleeding occurs. We monitor BMD if used for more than 2 years or earlier if other specific risk factors for osteopaenia exist.

Recent concern has been raised that the use of ultra-low dose (20 μg) oestrogen COCs may be associated with a decrease in the degree of gain of BMD in adolescents[19] compared to controls. The available data on the use of higher (30–40 μg) oestrogen doses suggests normal BMD accretion.[8] This concern needs to be balanced against the potential adverse effects of using a higher dose COC and highlights the need for BMD monitoring.

GnRH ANALOGUES

The use of injectable GnRH analogues such as triptorelin or leuprorelin cause a hypogonadotrophic state which leads to suppression of menstruation. They are simple to administer by injection usually every 4 weeks and highly effective but require meticulous attention to dosage intervals to avoid intermittent breakthrough gonadotrophin release. Leuprorelin and triptorelin are also available in long acting preparations which can be

given 12 weekly. They are expensive compared to other options and lead to a profoundly hypo-oestrogenic state which causes a loss of BMD. This effect should be countered by the use of ''add-back'' hormone replacement therapy. This may be achieved with the synthetic steroid tibolone which does not cause periods, or an oestrogen-progesterone HRT combination used continuously to minimise the chances of breakthrough bleeding. A recent Cochrane review found that the use of an oestrogen–progesterone combination is protective of BMD in adult women receiving GnRH analogues for the treatment of endometriosis.[20] Some bleeding may occur in up to 37% of menopausal women after starting continuous HRT, but this is often light and tends to decrease with time.[21]

There are no data regarding the effect of GnRH analogues on BMD in adolescents with learning disabilities, however the data from the treatment of children with central precocious puberty suggest that although GnRH analogues may cause a reduction in BMD during treatment, this recovers once the treatment is stopped and peak BMD at final height is unaffected.[22 23] BMD seems to be improved in those children receiving calcium supplements[23] and so it would seem sensible to recommend calcium and vitamin D supplementation in children with learning disabilities treated with GnRH analogues.

Other concerns regarding the use of GnRH analogues in children are the formation of sterile abscesses, weight gain, menopausal symptoms and possible increased risk of polycystic ovaries.[24]

LEVONORGESTREL INTRAUTERINE SYSTEM (MIRENA)

The levonorgestrel intrauterine system (LNG-IUS) is a 32 mm long, T-shaped plastic device with a reservoir containing the progesterone levonorgestrel which is released slowly over 5 years. The device causes local oestrogen insensitivity and inhibits endometrial proliferation. It is licensed for use as a contraceptive, for the treatment of primary menorrhagia and for the prevention of endometrial hyperplasia during oestrogen replacement therapy. It causes a decrease in menstrual blood loss of around 90% over 1 year in adult women with menorrhagia[25] and up to 50% of women experience amenorrhoea.[26]

Problems associated with the LNG-IUS include unexpected breakthrough bleeding, ovarian cyst formation, weight gain, bloating and flushing.[27] The device may be spontaneously expelled and, as with any IUD, there is a small risk of infection. This may be of concern in an adolescent who may not be able to communicate symptoms easily. The system may need to be inserted under general anaesthetic if cooperation is not possible. Consent for the procedure is necessary, which can be a difficult situation if the adolescent is not deemed competent to understand the situation adequately.

SURGICAL OPTIONS

Surgical options include endometrial ablation or hysterectomy and should only be used as a last resort in an adolescent with seriously distressing symptoms which cannot be controlled by medical means. Both procedures can cause permanent sterility. The ethical situation is complicated as the right to reproduce has been cited as a basic human right and historically sterilisation of women with learning disabilities was commonplace, justified on eugenic grounds which are unacceptable to contemporary thinking.[28–30]

The situation is also difficult legally. If a patient is able to understand the issues surrounding surgery and its consequences, then she is able to give consent for the procedure. However, if she is unable to give her own consent due to intellectual impairment, consent from a parent is not acceptable under UK law and concerns have been expressed in the past that doctors performing such procedures would be liable to criminal prosecution. Several high profile cases in the 1980s helped to clarify the situation and it is currently recommended that the approval of a high court judge is necessary to enable procedures to be carried out.[31–35]

CHOICE OF THERAPY

The choice of therapy can only be made in partnership with the young woman's carers and the young woman herself. If, after explanation and reassurance, therapy is deemed necessary, a full and frank discussion outlining the advantages and disadvantages of the treatment options is necessary. An assessment of BMD status should be made to inform choice and other factors such as acceptability of injections or oral medications, anticonvulsant use, thromboembolic risk factors, family history of malignancy, patient weight, need for contraception and so on, should be ascertained.

If the absolute eradication of menses is not necessary and one period every 3 months is acceptable, then the extended use of a COC may be the simplest first choice. If this is not acceptable and baseline BMD is satisfactory, then injectable DMPA or oral norethisterone would be an acceptable alternative, with reassessment of BMD status at 1–2 yearly intervals. When BMD is compromised, then the need for ongoing therapy should be reviewed, and, if still required, a COC or GnRH agonist with tibolone add-back therapy could be considered. The intermittent discontinuation of therapy for ''treatment holidays'' could also be considered.

Surgical options should be considered a last resort when symptoms are severe and other treatment modalities have been tried and failed.

CONCLUSIONS

No perfect strategy exists to suppress menstruation in this population. Girls must be allowed to go through puberty before any attempt is made to stop periods. The various therapeutic options have different side effect profiles and the choice of therapy needs to be tailored to the adolescent's particular clinical situation regarding weight, BMD, mobility, thromboembolic risk factors and understanding. The induction of a long term profoundly hypo-oestrogenic state should be avoided either by limiting the duration of therapy or by the use of add-back oestrogens. BMD in at-risk patients needs to be assessed and monitored serially.

There is very little evidence to guide the clinician in this area and the evidence discussed has to be extrapolated from studies addressing a different patient population. There is a real need for a fuller discussion of this difficult issue and a vital requirement for studies in this area to investigate the efficacy of therapeutic interventions, adverse effects, psychological benefits and harms, and patient and family views.

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