Signs and symptoms, evaluation, and management of genitourinary tract consequences of premature ovarian insufficiency

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Abstract

Premature ovarian insufficiency (POI) occurs in 1% of women under 40 years old. Hypoestrogenism associated with this condition may result in vaginal atrophy and urine incontinence, called genitourinary syndrome. The symptoms include: vaginal dryness, irritation, dyspareunia, and dysuria. There is relative lack of studies on the occurrence and treatment of genitourinary problems in women with POI. Prevalence rates vary from 17 to 54% depending on cause, duration of oestrogen depletion, and the treatment used. Patients with POI gain lower scores in tests measuring vaginal health or sexual function in comparison to healthy peers. Hormonal treatment in premature ovarian insufficiency is recommended until the natural age of menopause. The vaginal route of oestrogen administration is supposed to be the criterion standard in treating genitourinary symptoms. Androgen supplementation is not routinely recommended.

Key words: premature ovarian insufficiency, genitourinary syndrome, oestrogen therapy.

Introduction

Premature ovarian insufficiency (POI) is a condition characterised by sex steroid deficiency, elevated gonadotropin follicle-stimulating hormone (FSH) > 25 ml/IU four weeks apart, and oligo/amenorrhea for more than four months in women below 40 years old. The prevalence of POI varies from 0.01% in women under 20 years of age to 1% in patients under 40 years of age.

Studies on menopausal patients show that depletion of ovarian function and lack of oestradiol may result in sequelae of vaginal atrophy and urine incontinence, called genitourinary (GU) syndrome. There are few trials on urogynaecological consequences in young patients with POI, and therefore most evidence is derived from studies in postmenopausal women of older age.

Incidence

Genitourinary syndrome of menopause affects more than 50% of postmenopausal women. Data may be underestimated; the real prevalence is thought to be higher due to sexual embarrassment and the sensitive nature of the problem [3]. The exact prevalence rate of GU symptoms in women with spontaneous POI is not known. Data from an observational study, assessing GU symptoms in 31 women with POI, revealed that 54% suffered from symptoms of vulvovaginal atrophy (dyspareunia, itching, burning sensation) and 42% had urinary tract symptoms (dysuria, urinary frequency, mild urinary incontinence) [4]. In women with iatrogenic POI after breast cancer treatment the prevalence of moderate to severe dyspareunia was 42%, and the incidence of vaginal dryness was 49% [5]. Data from patients after bilateral oophorectomy showed a 24% prevalence rate for vaginal dryness, and 17% for dyspareunia. Loss of libido was reported by 22% of women without any hormonal treatment [6].

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Submitted: 15.06.2018
Accepted: 27.07.2018
Aetiopathogenesis

Oestrogen receptors are localised in the vagina, vulva, vestibule, labia majora/minora, and bladder trigone in high concentration. These parts are sensitive biological markers of serum hormonal levels [7]. Oestradiol influences synthesis of local peptides, which is of great value for vaginal microflora [8]. Moreover, oestrogens promote production of antimicrobial peptides and exfoliation of infected cells. Hypoestrogenic state is correlated with increased incidence of urinary tract infections after menopause.

Vaginal disturbances like atrophy or infections can be assessed by collecting hormonal cytology, pH measurement, amine test, bacterioscopy, and culture for bacteria and fungi. Vaginal health index (VHI) includes the assessment of overall elasticity, fluid secretion, pH, epithelial integrity, and dryness [9]. Bonetti-Pinto et al. found no statistical differences in cytology, pH, or microflora in women with POI compared to healthy controls. In both groups VHI was trophic, although POI patients were found to have statistically lower VHI scores than controls [9]. The VHI scores were lower than in the control group mainly because of less vaginal discharge and friable appearance with the presence of petechiae [10].

Progestrone in the urinary tract acts mainly by inducing beta-adrenergic receptor formation, alpha-adrenergic antagonism, and anticholinergic effect. Progestrone increases bladder capacity and dilates the urethra through relaxation of smooth muscles [11].

Symptomatology of POI depends not only of oestrogen and progesterone serum levels but is also connected with decrease in ovarian testosterone production. In premenopausal women androgens are synthetized in 50% by ovaries and 50% by adrenal glands. Androgens act centrally through dopamine and peripherally through nitric oxide pathways, and they may result in improved libido and overall quality of life [12-14].

Sexual function

Sexual function (SF) in women is under modulation of oestrogen influencing lubrication and androgen stimulating desire and arousal. A case-controlled study on sexuality in young women with spontaneous POI reported normal sexual function despite lower testosterone serum levels than in the control group. However, lower serum total testosterone levels were correlated with the decreased Derogatis Interview for Sexual Functioning (DISF) composite score [15].

Pacello et al. assessed sexual function of 36 women with POI using Female Sexual Function Index (FSFI). Women with POI showed worse sexual performance with complaints about lubrication and pain during intercourse. No differences in desire, arousal, orgasm, or satisfaction in FSFI questionnaire were found between groups. Use of systemic oestrogen in the POI group was not enough to improve sexual function, despite normal vaginal tropism assessed with VHI measurements [10].

Yela et al. examined 80 women with POI regarding their sexual function and quality of life (QoL). Psychological domains like orgasm, arousal, and sexual satisfaction were correlated with stronger impact on QoL than physical disturbances like pain or lubrication [16]. Loss of gonadal function impairs SF and QoL regardless of hormonal treatment. Early and unexpected infertility has a negative impact on sexuality by decline in self-confidence and interpersonal relationships [16-19]. The study of Bonetti-Pinto et al. on 58 women with POI showed lower sexual function scores because of decreased arousal, lubrication, orgasm, and satisfaction and higher incidence of dyspareunia. The greatest differences were shown in decline of arousal and desire, and less in dyspareunia and lubrication [20].

Management

Hormone replacement treatment

Hormone replacement therapy (HRT), both systemic and topical, is implemented to treat genitourinary symptoms. According to the National Institute of Health (NIH), the European Menopause and Andropause Society (EMAS), and the International Menopause Society (IMS), oestrogen treatment is recommended for vaginal dryness. The EMAS recommends using both systemic and topical oestrogen initially if symptoms are severe, followed by just local treatment [14, 21-23].

Early detection and individualised treatment is crucial. Oestrogen therapy is the most commonly prescribed treatment. Many different formulations are available, from pessaries, creams, and rings, to tablets. For the majority of treated women, both local and systemic HRT seem to be effective in relieving genitourinary symptoms. The vaginal route of administration delivers oestrogen locally with little or no influence on endometrium and systemic receptors. That is why no progestins are obligatory during such application [8]. According to the Cochrane review, all forms of vaginal oestrogen are equally effective [24]. Hormonal treatment reduces vaginal atrophy symptoms and corrects the physical changes, and restores the cytology, pH, and vascularity of the vagina [2]. However, the longer hypoestrogenism proceeds, the more difficult atrophy may be to treat [2].

There is lack of randomised controlled trials assessing the use of HRT in the treatment of genitourinary syndrome in women with premature ovarian insufficiency. In the Piccioni study, systemic HRT in POI patients with vulvovaginal atrophy and urinary tract
Clinical studies on the use of HRT have been performed on small groups of women with POI. The young age of patients with POI probably makes them less susceptible to urine incontinence; however, more research is needed to investigate further this issue. The sensitive nature of the problems with vaginal atrophy, sexual dysfunction, or urine incontinence may cause underestimation of the problem. The mainstay of the therapy of genitourinary syndrome is oestrogen replacement, mostly administered locally. There is a need to study real differences between the genitourinary symptoms in women of postmenopausal age and younger patients with POI and to design the most efficient treatment options.

Conclusions

The group of patients with premature ovarian insufficiency is under-researched in the context of genitourinary symptoms, and the few available studies are performed on small groups of women with POI. The young age of patients with POI probably makes them less susceptible to urine incontinence; however, more research is needed to investigate further this issue. The sensitive nature of the problems with vaginal atrophy, sexual dysfunction, or urine incontinence may cause underestimation of the problem. The mainstay of the therapy of genitourinary syndrome is oestrogen replacement, mostly administered locally. There is a need to study real differences between the genitourinary symptoms in women of postmenopausal age and younger patients with POI and to design the most efficient treatment options.

Disclosure

The authors report no conflict of interest.
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