

Menopause and its effect on the female lower urinary tract

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Abstract

Significant hormonal changes occur at the time of menopause and this has an impact on all oestrogen-sensitive tissue. The female lower urinary tract (LUT) is no exception. Decreasing levels of oestrogen characteristic of the menopause produce symptomatic, histological and functional changes of the vulva, vagina and lower urinary tract together. Examples of specific urogenital problems include urgency, urinary incontinence and susceptibility to urinary tract infection. Oestrogen therapy works by preventing or reversing urogenital atrophy and provides symptomatic improvement although it may need to be combined with other treatments for certain conditions such as incontinence. Oestrogen therapy requires time to become effective with vaginal preparations probably superior to systemic therapy. Prophylactic oestrogen therapy has not been shown to be clearly of benefit for specific types of urinary incontinence.

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Introduction

The word 'menopause' is derived from the Greek *men* (month) and *pausis* (cessation). It literally means cessation of the monthly cycle. The prelude to menopause has its roots in the foetal stage already. It is during the 20th week of foetal life that ovarian function starts to decline due to oocyte atresia. In adult life, oestrogen falls to a critical level during a period commonly known as the climacteric, but more appropriately termed the menopausal transition. The average age of menopause is 50 years. There are currently over four million (16%) women aged 50 years or older in South Africa.¹ Female life expectancy is increasing worldwide, but this trend has been curtailed in Southern Africa due to the effect of HIV/AIDS, which prevents many women from reaching postmenopausal status.

Significant hormonal changes occur at the time of menopause and this has an impact on all oestrogen sensitive tissue.² The female lower urinary tract (LUT) is no exception. Oestrogen deficiency becomes clinically more overt over time and is associated with a number of LUT symptoms. These include frequency, nocturia, urinary incontinence (UI), urinary tract infections (UTIs), and urgency. These symptoms

often coexist with those of vulvovaginal atrophy, such as vaginal dryness, pruritus, burning, and dyspareunia.

Embryology and physiology of the female lower urinary and genital tracts

The LUT and genital tracts develop in very close proximity in the female embryo. They both arise from the primitive urogenital sinus in the first trimester. Oestrogen receptors are expressed in the squamous epithelium of the urethra and vagina and in areas of the trigone of the bladder that have undergone squamous metaplasia.² These receptors are however not present in the urothelium of the bladder dome, reflecting the different embryological origin of this tissue. The levator ani muscle of the pelvic floor is also oestrogen sensitive.³

Oestrogen increases cell cycle activity in all of these tissues, and a lack of oestrogen results in a decrease in the number of epithelial cells in the urethra, bladder and vagina.⁴ Cyclical variation in oestrogen levels during the menstrual cycle may lead to both symptomatic as well as urodynamic changes, with the premenstrual period being the most bothersome.⁵

Prevalence of postmenopausal urinary symptoms

LUT symptoms due to oestrogen deficiency tend to develop over time and may only present many years after the menopause. Urogenital complaints increase with age, and although nearly half of elderly women will be symptomatic, they often delay seeking treatment for several years.⁶ Also, two thirds of women do not relate their vaginal or urinary complaints to the menopause. The prevalence of postmenopausal UI is between 16 and 29%,⁷ and urge urinary incontinence (UUI) in particular occurs more frequently after the menopause.⁸ Aging is clearly a significant factor in the pathogenesis of UI, but evidence seems to indicate that menopause and oestrogen deficiency are also implicated.^{9,10} Most studies show that many women develop UI at least 10 years prior to menopause and that stress urinary incontinence (SUI) actually starts to become less after the menopause.¹¹ These findings emphasise that UI is a multifactorial process, and that menopause is just one of a number of aetiological factors.

Menopause and urinary continence

Effects of aging

The majority of women perceive the development of urinary symptoms and specifically UI as a normal part of aging, rather than a pathological process.^{12,13} It is important to note that the aging population is at risk for a number of systemic illnesses that may present with LUT symptoms, including diabetes mellitus, congestive cardiac failure, and renal disease (Table I). Symptomatic changes in the LUT do occur as part of aging, and it is often difficult to distinguish these from those due to oestrogen deficiency. Nocturia increases in prevalence from 10% at the age of 50 to 50% at the age of 80 years.¹⁴ The bladder also becomes less efficient with age. Older women experience a reduced flow rate, incomplete emptying of the bladder, a higher first sensation to void, and decreased detrusor pressures.¹⁵ Histology reveals an increase in fibrosis and a reduction in muscle fibres and density in the aging bladder.¹⁶ A similar picture is seen in the muscles of the pelvic floor.

Table I: Transitional causes of urinary symptoms in the elderly

- UTI
- Faecal impaction
- Oestrogen deficiency
- Restricted mobility
- Drug therapy
- Depression
- Mental impairment/confusional state

Sex hormones and urinary continence

Continence requires that the urethral pressure exceeds the intravesical pressure at all times except during micturition. Sex steroids influence the central nervous system control of the continence mechanism and these hormones also seem to have a direct effect on the detrusor muscle.^{17,18} Animal studies has shown that oophorectomy alters the pressure-flow characteristics of micturition. This effect may only be partly reversed by oestrogen supplementation.¹⁹ Oestrogen also targets the functional layers of the urethra (epithelium, vasculature, connective tissue and muscle) which are integral for maintaining continence.

The addition of progestogens might negate any positive (inhibitory) effect which oestrogen has on the detrusor muscle. Progestogen is associated with an increase in irritative bladder symptoms and UI in women taking combined hormonal therapy.²⁰

Urethral function

Oestrogen improves the important functional layers of the urethra, as mentioned in the previous paragraph, which are necessary for continence.²¹ Connective tissue metabolism is also stimulated by oestrogen. This increases collagen production in the peri-urethral tissues and thereby limits, and even reverses to some extent, age-related changes.²² The oestrogen status of the patient can therefore have a significant effect on urethral function and this is particularly important when there is already some urethral impairment present.

Oestrogen treatment for urinary incontinence

Oestrogen therapy has been shown to be useful for the treatment of LUT symptoms and UI for a number of reasons (Table II). Despite recent scientifically rigorous research, the benefits of oestrogen for the treatment of postmenopausal urinary incontinence remain controversial.

Table II: The beneficial effects of oestrogen on the lower urinary tract

- Increased urethral closure pressure
 - Increased urethral cell maturation
 - Increased blood flow
 - Increased α -adrenergic receptor sensitivity in urethral smooth muscle
- Improved abdominal pressure transmission to proximal urethra
- Stimulation of peri-urethral collagen production
- Improved neuronal control of micturition
- Increased sensory threshold of the bladder
- Improved mood and quality of life
- Reduced incidence of urinary tract infection

Oestrogen for SUI

The role of oestrogen for treating SUI is not clear. Published data have revealed conflicting results.²³ This may be due to inferior study design, different types, dosages and routes of oestrogen used, and the addition of progestogen in women with an intact uterus. There was little evidence from the trials on the severity of SUI in the period after completion of oestrogen treatment and none on long-term effects. However, treatment with local oestrogen cream seems to have an overall beneficial effect on the severity of SUI.

Oestrogen for UUI

Oestrogen has been used for many years to treat postmenopausal urgency and UUI, but few controlled trials have been performed to confirm its benefit.²⁴ Its benefit is in reversing the atrophic changes in the LUT and genital tract. A recent study evaluated the effect of a 25 mg oestradiol implant versus a placebo implant on the symptom of urgency. There was a significant subjective improvement in LUT symptoms in both the oestradiol as well as the placebo group, but no apparent objective benefit due to the oestrogen therapy could be recorded. It did however result in a much higher systemic oestrogen level.²⁵ Local oestrogen therapy again appears to be the most beneficial route of administration. Oestrogen is of particular benefit for women with UUI, with the chance of cure or improvement being approximately 25% higher than in women with SUI.²⁶

Hormonal therapy as prophylaxis against the development of UI

It is not clear whether oestrogen supplementation is beneficial when used as prophylaxis against the development of UI in peri- and postmenopausal women, and also not whether the effect lasts past the treatment period.^{27,28} Data from a few studies suggest that combined hormonal therapy can, in fact, be associated with worsening stress and urge UI.^{29,30} The relative risk of developing UI with oral oestrogen is 1.54, transdermal oestrogen is 1.68, combined oral therapy is 1.34, and combined transdermal therapy is 1.46. At 10 years after cessation of therapy the risk is identical to those women who have never used hormonal therapy.^{29,30}

Oestrogen deficiency and recurrent UTI

UTIs occur in women of all ages, but are a particular problem in postmenopausal women. Pathophysiological explanations for this finding are impaired bladder emptying, poor perineal hygiene, faecal and urinary incontinence, and altered vaginal flora. Oestrogen reverses the microbiological changes seen in the flora of postmenopausal women. It

can therefore be used for prophylaxis as well as treatment adjunct.³¹ Local (vaginal) oestrogen preparations are more effective for this purpose than systemic therapy.

Urogenital atrophy

Urogenital atrophy is a manifestation of oestrogen withdrawal after the menopause. It becomes worse over time and by age 75 years, the majority of women will report vaginal or LUT symptoms due to atrophy.³² It is however important to realise that symptoms of atrophic vaginitis can start to manifest soon after menopause in some women. Symptomatic atrophy occurs when the endogenous oestrogen levels are lower than those required for endometrial proliferation.³³ It is therefore possible to use local oestrogen treatment to give relief of these symptoms, without adding progestogen for endometrial protection.³⁴ Low dose vaginal oestradiol seems to be the most effective in reducing patient symptoms.

Conclusion

Significant hormonal changes occur at the time of menopause and this has an impact on all oestrogen-sensitive tissue. The female LUT is no exception. Decreasing levels of oestrogen characteristic of the menopause produce symptomatic, histological and functional changes of the vulva, vagina and lower urinary tract together. Examples of specific urogenital problems include urgency, urinary incontinence and susceptibility to urinary tract infection. Oestrogen therapy works by preventing or reversing urogenital atrophy and provides symptomatic improvement although it may need to be combined with other treatments for certain conditions such as incontinence. Oestrogen therapy requires time to become effective with vaginal preparations probably superior to systemic therapy. Prophylactic oestrogen therapy has not been shown to be clearly of benefit for specific types of urinary incontinence.

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