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Topical estrogen therapy for UTIs

Urinary tract infections (UTIs) are common among older people in residential aged care. The 2021 *Fourth Australian report on antimicrobial use and resistance in human health* reported 23.1% of residents with a suspected UTI and prescribed antimicrobial treatment. Antimicrobials were consistently and most commonly prescribed for UTI prophylaxis. The report highlighted prolonged prophylaxis not recommended by guidelines.

Antimicrobial resistance (AMR) continues to be one of the most significant challenges that healthcare services face in Australia, and around the world. Use of low-dose vaginal estrogen is an option in postmenopausal women with recurrent UTIs, and provide benefits for other symptoms of genitourinary syndrome.

Genitourinary syndrome

Genitourinary syndrome of menopause (GSM) is highly prevalent, occurring in 20-45% of menopausal women. GSM was previously referred to as vulvovaginal atrophy. Symptoms of GSM include:

- genital symptoms of dryness, burning, and irritation
- sexual symptoms of lack of lubrication, discomfort or pain, and impaired function
- urinary symptoms of urgency, dysuria and recurrent urinary tract infections

Urinary incontinence is one of the factors associated with recurrent UTIs in postmenopausal women.

The risk of UTIs in older women is associated with a decrease in oestrogen levels. As estrogen levels decline during menopause, the vaginal epithelial lining becomes thinner, with reduced blood supply. Hormonally-induced changes in the vaginal flora associated with menopause are thought to play an important part in the pathogenesis of urinary tract infections among older women. In pre-menopausal women, circulating estrogens encourage colonization of the vagina by lactobacilli, which produce lactic acid from glycogen and maintain a low vaginal pH that inhibits the growth of many urinary tract pathogens. After menopause, however, the vaginal pH increases with subsequent changes in vaginal flora. The vagina is predominantly colonized by Enterobacteriaceae, especially Escherichia coli after menopause. This change in vaginal flora increases the susceptibility to UTIs.

Genitourinary syndrome of menopause does not improve without treatment and increases in severity over time.

Low-dose vaginal estrogen therapy

Local low-dose vaginal estrogen therapy is useful for the treatment menopausal symptoms with only vaginal symptoms. They have been shown to improve vaginal atrophy, dryness and dyspareunia. These agents restore the atrophic vaginal, urethral, and trigonal mucosa; increase vaginal lubrication, lower the vaginal pH; and may reduce the occurrence of urinary tract infections.

Local estrogen therapy may provide a more rapid or complete relief of genitourinary symptoms than do oral or transdermal (patches) preparations.

Menopausal hormone therapy (MHT), previously called hormone replacement therapy (HRT), is indicated for the relief of troublesome vasomotor symptoms (hot flushes, night sweats). Starting MHT in woman aged 60 years or more, or more than 10 years after menopause is no longer recommended. MHT should be commenced around menopause, unless there are contraindications, and continued for the shortest period of time. Systemic estrogen, even at higher doses, fails to relieve symptoms of GSM in 10% to 25% of women. Treatment with both systemic and local estrogen is usually not necessary.

Vaginal estrogens products include:

- estradiol pessary 10mg (*Vagifem Low*)
- estriol pessary 500mcg (*Ovestin Ovula*)
- estriol vaginal cream 0.1% (*Ovestin*)

Vagifem Low pessaries should initially be inserted once daily for 2 weeks, then maintained twice weekly. *Ovestin Ovula pessaries* are inserted intravaginally nightly at bedtime for 2-3 weeks, then continue 1-2 times weekly. *Ovestin vaginal cream* is used nightly at bedtime for 3 weeks, then used twice weekly.

Vaginal pH falls to low levels by the third week of topical estrogen treatment. An increase in lactobacilli in the vaginal flora occurs in this time period. Symptom relief can be expected within 3 to 4 weeks but may occur sooner. Vaginal dryness can improve within 2 weeks of beginning therapy.

Dose and delivery formulation (pessary, cream) should be individualised. Vaginal creams may be more soothing immediately after application.

Benefits

A study published in the New England Journal of Medicine nearly thirty years ago confirmed the benefit of long-term use of vaginal estrogen in preventing recurrent UTIs. Topical estrogen treatment had a dramatic effect on the incidence of recurrent UTIs – 0.5 in users versus 5.9 episodes per year in non-users. Significantly more women were *Lactobacillus* positive in the vaginal oestrogen group compared to placebo.

The considerable reduction in the frequency of symptomatic episodes of UTI in patients treated with estrogen also greatly reduced their use of antibiotics - 6.9 versus 32.0 days per patient over 8 months.

Across many studies, vaginal estrogen has been shown to reduce urinary frequency, urge incontinence, stress incontinence and nocturia. Topical estrogens typically reduce the risk of UTIs by about 50% and possibly as significant as 5 fewer UTI episodes per year.

Safety

Local low-dose vaginal estrogen therapy is well tolerated for treating GSM. Side effects are limited to localised irritation, pruritus or burning. Non-hormonal moisturisers and lubricants are recommended in women with hormone-dependent cancers, although some guidelines endorse use of low-dose vaginal estrogen.

There is no need for progestogen with low-dose vaginal estrogen therapy for women with an intact uterus. Systemic absorption is negligible, especially in low doses. Estradiol levels remain within the normal postmenopausal range with low-dose vaginal estrogen therapy.

Systemic estrogen increases the risk of venous thromboembolism (VTE), stroke and breast cancer (with combination estrogen / progestogen). The safety of vaginal estrogen was confirmed in the large Women's Health Initiative study. Among women with an intact uterus, the risks of stroke, invasive breast cancer, colorectal cancer, endometrial cancer, and pulmonary embolism/deep vein thrombosis were not significantly different between vaginal estrogen users and nonusers. Low-dose vaginal estrogen did not increase the risk of coronary heart disease (CHD) or death.

Summary

Estrogen deficiency is a major contributor to recurrent urinary tract infections in postmenopausal women. Prolonged estrogen replacement with a topically applied vaginal cream is safe and effectively prevents urinary tract infections. Preventive approach can be considered an alternative to the use of long-term low-dose antibiotics. Topical estrogen may be particularly useful in residents in whom the prolonged use of antibiotics induces side effects, allergic reactions, drug interactions, or the emergence of multidrug-resistant microorganisms. Low dose vaginal estrogen therapy can reduce inappropriate and prolonged use of antimicrobials, leading to antimicrobial resistance.

References

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