The Effect of Hormones on the Lower Urinary Tract

Department of Urogynaecology, King's College Hospital, London, UK
Linda Cardozo

The female genital and lower urinary tract share a common embryological origin, arising from the urogenital sinus. Both are sensitive to the effects of female sex steroid hormones. Oestrogen is known to have an important role in the function of the lower urinary tract throughout adult life with oestrogen and progesterone receptors demonstrated in the vagina, urethra, bladder and pelvic floor musculature. This is supported by the fact that oestrogen deficiency occurring following the menopause is known to cause atrophic changes within the urogenital tract and is associated with urinary symptoms such as frequency, urgency, nocturia, incontinence and recurrent infection. These may also co-exist with symptoms of vaginal atrophy such as dyspareunia, itching, burning and dryness.

OESTROGENS AND THE MANAGEMENT OF INCONTINENCE

Oestrogen preparations have been used for many years in the treatment of urinary incontinence although their precise role remains controversial. In order to clarify the situation a meta-analysis from the Hormones and Urogenital Therapy (HUT) Committee has been reported. There was an overall significant effect of oestrogen therapy on subjective improvement in all subjects and for subjects with urodynamic stress incontinence alone. Subjective improvement rates with oestrogen therapy in randomised controlled trials ranged from 64% to 75% although placebo groups also reported an improvement of 10% to 36%. However, when assessing objective fluid loss there was no significant effect. The most recent meta-analysis of the effect of oestrogen therapy on the lower urinary tract has been performed by the Cochrane group. Overall 28 trials were identified, including 2926 women. In the 15 trials comparing oestrogen to placebo there was a higher subjective impression of improvement rate in those women taking oestrogen, and this was the case for all types of incontinence (RR for cure 1.61; 95% CI 1.04–2.49). Equally, when subjective cure and improvement were taken together there was a statistically higher cure and improvement rate for both urge (57% Vs 28%) and stress (43% Vs 27%) incontinence. In those women with urge incontinence the chance of improvement was 25% higher than in women with stress incontinence and, overall about 50% of women treated with oestrogen were cured or improved compared to 25% on placebo.

However, recent large-scale epidemiological studies investigating the use of oral HRT do not support these findings. The Heart and Estrogen/progestin Replacement Study (HERS) assessed 2763 postmenopausal women <80 yrs and ischaemic heart disease. Incontinence improved in 26% of women assigned to placebo as compared to 21% receiving HRT while 27% of the placebo group complained of worsening symptoms compared with 39% in the HRT group (p = 0.001). The incidence of incontinent episodes per week increased an average of 0.7 in the HRT group and decreased by 0.1 in the placebo group (p<0.001).

These findings have also been confirmed in the Nurse's Health Study which followed 39 436 post-menopausal women aged 50—75 years over a four year period. The risk of incontinence was found to be elevated in those women taking HRT when compared to those who had never taken HRT. There was an increase in risk in women taking oral oestrogen (RR 1.54; 95% CI 1.44—1.65), transdermal oestrogen (RR 1.68; 95% CI 1.41—2.00), oral oestrogen and progesterone (RR 1.34; 95% CI 1.24—1.34) and transdermal oestrogen and progesterone (RR 1.46; CI 1.16—1.84). In addition, whilst there was a small risk after the cessation of HRT (RR 1.14; 95% CI 1.06—1.23) by ten years the risk was identical (RR 1.02; 95% 0.91—1.41) and was identical to those women who had never taken HRT.

The recent report on the WHI study examining 27,347 women aged 50—79 years of age, has also been shown to support these findings. Overall HRT increased the risks of all types of urinary incontinence in those women continent at baseline and this was true for conjugated equine oestrogens alone and also for their use in combination with medroxyprogesterone acetate. In addition HRT was also found to worsen all types of urinary incontinence in those women symptomatic at baseline.
CONCLUSION

Oestrogen therapy alone has been shown to have little effect in the management of urodynamic stress incontinence alone. More recently the development of duloxetine, a balanced serotonin and noradrenaline re-uptake inhibitor, may offer a synergistic approach in women complaining of mild stress incontinence when combined with oestrogen replacement therapy. When considering the irritive symptoms of urinary urgency, frequency and urge incontinence oestrogen therapy may be of benefit although this may simply represent reversal of urogenital atrophy rather than a direct effect on the lower urinary tract.

At present the current evidence would suggest that oestrogen replacement may have a small synergistic effect in the management of women with lower urinary tract symptoms although the evidence is not robust enough to support its use alone. Evidence from large epidemiological studies investigating the long term effects of hormone replacement would appear to contradict some of the studies specifically investigating incontinence. However, these should be judged with caution as their primary role was not to investigate the role of oestrogen in women with incontinence and consequently the results may be affected by other confounding factors which have not yet been fully elucidated. Certainly there would appear to be no evidence to suggest a causative role for oestrogen in the pathogenesis of urinary incontinence indicating again that these findings may be spurious.

Neither menopausal symptoms nor urinary incontinence are life-threatening conditions although both have a significant effect on quality of life. The current evidence from all trials suggests that oestrogen replacement therapy may have a minor role in lower urinary tract dysfunction.