

EXPRESSION OF STEROID HORMONE RECEPTOR ISOFORMS IN THE FEMALE LOWER URINARY TRACT

Hypothesis / aims of study

Steroid hormone action is mediated by specific receptors which form a complex with the ligand, and bind to hormone response elements within the genome. New gene transcription is activated as a result. Previous work employing immunocytochemistry identified both oestrogen (ER) and progesterone receptors (PR) within the urethra, but a lack of ER expression in the transitional epithelium of the bladder(1). Subsequently to the publication of that study, it is now known that both ER and PR are each present in two distinct subtypes: ER α and ER β and PR-A and PR-B. These isoforms may be differentially expressed in tissues and have distinct actions(2,3). New subtype-specific antibodies are now available and so the objective of this study was to characterise the distribution of these ER and PR subtypes in the female lower genital tract.

Study design, materials and methods

Ethical committee approval was obtained. Following informed consent, bladder biopsies were obtained from the bladder dome, trigone, proximal and distal urethra from women having gynaecology surgery where a urethral catheter would be placed routinely. Biopsies were formalin fixed for 16-24 hours and stored in 70% industrial methylated spirit at 4°C until processing. 100 micrometre sections were cut and stained by immunocytochemistry employing specific mouse monoclonal antibodies to ER α , ER β , PR-A, PR-B. Rabbit anti-mouse secondary antibodies linked to horseradish peroxidase staining were used and staining was revealed using 3,3'-diaminobenzidine. Slides were scored descriptively.

Results

19 patients were included in the study. 9 women were premenopausal and 11 were postmenopausal. 9 of these women were taking hormone replacement therapy. Adequate tissue was obtained from 19 dome, 16 trigone, 16 proximal urethral, and 15 distal urethral specimens.

ER α was absent from all transitional epithelium biopsies, and present in the nuclei of squamous epithelial cells in trigone and urethra. No association with menopausal status was seen.

ER β was present in nuclei of all transitional epithelium biopsies, irrespective of site or hormone status. ER β expression in squamous epithelium mimicked ER α .

Expression of PR-A and PR-B was confined to a layer of suburothelial cells in transitional epithelia. Squamous cell nuclei were positive for both subtypes in premenopausal women and those on HRT, but negative in the postmenopausal women.

Interpretation of results

Our work confirms the localisation of ER and PR subtypes to be similar in most tissues to previously published work. However, we have demonstrated the previously unrecognised expression of ER α in the transitional epithelium of the bladder. The precise role of the ER receptor and the downstream effects of activation of the receptor remain to be determined.

Concluding message

This finding suggests that oestrogen may have an action upon the epithelium of the bladder, and that targeted manipulation of the ER α receptor using drugs may provide a new approach to certain urinary tract disorders.

1. Oestrogen and progesterone receptor expression in the female lower urinary tract, with reference to oestrogen status. *BJU Int* 2000;86:32-8.
2. Immunolocalisation of oestrogen receptor beta in human tissues. *J Mol Endocrinol* 2000;24:145-55.

3. Progesterone receptors in reproduction: functional impact of the A and B isoforms. *Steroids* 2000;65:571-7.