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THE DISTRIBUTION OF THE PROSTAGLANDIN E RECEPTORS TYPE 1 AND 2 IN THE OBSTRUCTED HUMAN URINARY BLADDER

Hypothesis / aims of study

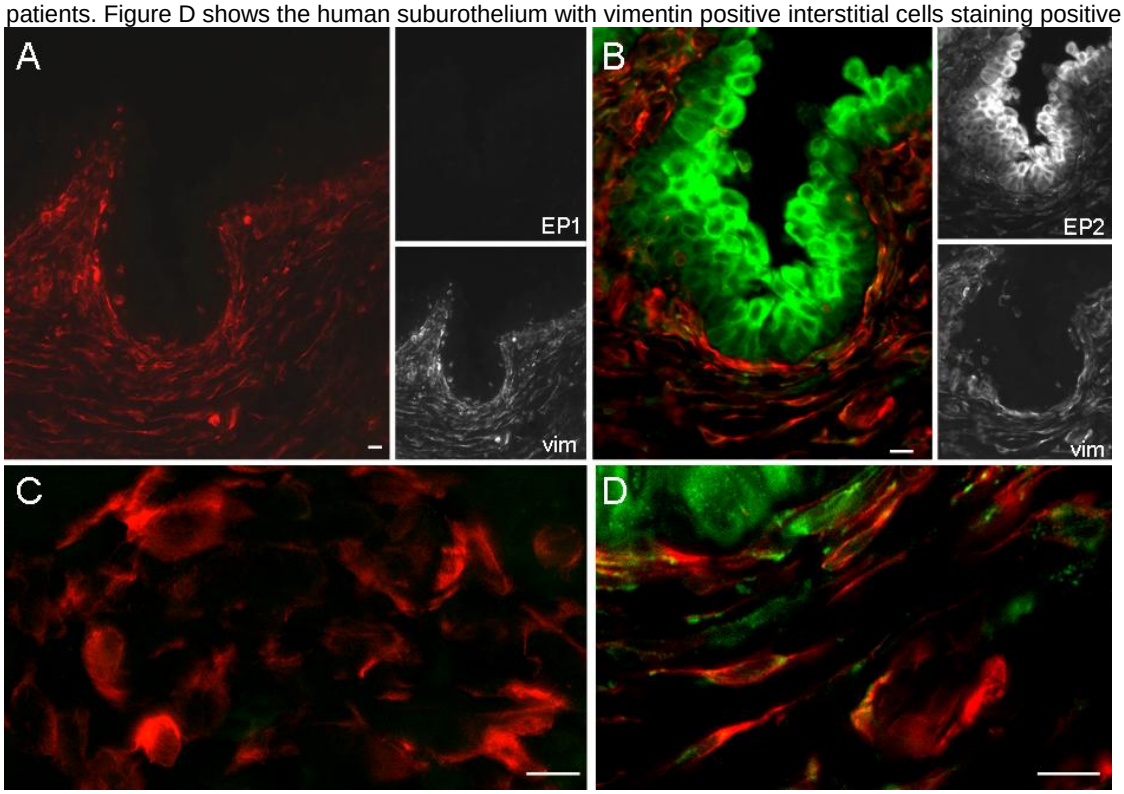
Prostaglandins are synthesised in the bladder wall and released into the general circulation and bladder lumen. They have been shown to affect the smooth muscle and cause contraction of isolated strips or modulate spontaneous phasic activity (autonomous activity). Moreover, increased levels of urine Prostaglandin E2 (PGE2) are suggested to be associated with the overactive bladder syndrome (OAB) [1]. It follows from these data that we need to understand which of the prostaglandin receptors are responsible for muscle activation and where they are located. EP1 and EP2 are shown to be present in the urothelial and suburothelial layers of the guinea pig urinary bladder [2]. This study is to our knowledge the first to investigate the distribution of prostaglandin receptors in the human urinary bladder wall.

Study design, materials and methods

With approval of the medical ethical committee, per-operative full thickness bladder strips were obtained from five patients undergoing a Hryntschak transvesical prostatectomy. Tissues were then fixed in 4% paraformaldehyde and processed for immunohistochemistry. Primary antibodies used, were antibody to the prostaglandin E type 1 and 2 receptor (EP1 and EP2) and vimentin. Specific antibody binding was visualised using the appropriate secondary antibodies.

Results

EP1 (green) is not expressed by the human urothelium (figure A). The vast majority of the suburothelial vimentin positive interstitial cells (red) are also EP1 negative (figure C). Only very few regions of the SU show vimentin positive interstitial cells expressing EP1. As shown in figure B, the umbrella cells of the urothelium stain strongly positive for EP2 (green). In some small regions EP2 negative umbrella cells were observed. Umbrella cells were washed off during the tissue workup in two of the five patients. Figure D shows the human suburothelium with vimentin positive interstitial cells staining positive for EP2 (figure D).



In all the figures presented, vimentine, a marker for interstitial cells is stained in red. The prostaglandin receptors EP1 and EP2 are stained in green. Panel A and C show the distribution of the EP1 receptor in the urothelium and suburothelium. The distribution of the EP2 receptor is shown in figure B and D. The calibration bars are 25 µm in panel A and B and 10 µm in panel C and D.

Interpretation of results

Presence of EP2 prostaglandin receptor in the human umbrella cells raises the hypothesis that prostaglandin signals can be picked up by these receptors at the urothelial layer. The interstitial cell network has been described before in animal models as a network for signal transduction through the bladder wall. As human suburothelial interstitial cells express EP2, the prostaglandin signal could be spread out through the bladder wall mediated by the EP2 receptor. The absence of EP1 in the

human urothelial and suburothelial layers suggests to rather choose the EP2 receptor blockade as a target for treating OAB symptoms.

Concluding message

The umbrella cells and suburothelial interstitial cells of the obstructed human bladder express the prostaglandin E receptor type 2 (EP2). EP1 receptor is not expressed in the urothelial and suburothelial layers of the obstructed human bladder. The physiological significance of these findings need to be cleared out through further studies, including a comparison with the normal bladder.

References

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What were the subjects in the study?	**HUMAN**
Was this study approved by an ethics committee?	**Yes**
Specify Name of Ethics Committee	**Maastricht University Medical Centre Ethical Committee**
Was the Declaration of Helsinki followed?	**Yes**
Was informed consent obtained from the patients?	**Yes**