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EXPRESSION OF PTH/PTHRP RECEPTOR 1 (PTH1R) IN NORMAL AND DISEASED BLADDER DETRUSOR MUSCLE

Hypothesis / aims of study
Parathyroid hormone related peptide (PTHrP) is a unique stretch-induced endogenous detrusor relaxant, functioning via PTH/PTHrP receptor 1 (PTH1R). We hypothesized that suppression of this axis could be involved in pathogenesis of detrusor overactivtiy. Therefore we investigated expression of PTHrP and PTH1R in rat bladder with of without outlet obstruction, and clinical specimens undergoing urological surgery.

Study design, materials and methods
1) Under authorization of animal experiment ethics committee, bladder outlet obstruction was created in 8 weeks Sprague-Dawley rats by urethral constriction. Bladders were retrieved after 5, 7, and 14 days after creation of BOO, and was compared with rat bladders 14 days after sham-operation. Expression level of PTHrP and PTH1R was mRNA was evaluated by real-time reverse transcript polymerase chain reaction. 2) Under IRB approval, bladder specimens of patients undergoing bladder augmentation were used for immnunohistochemical study for PTH1R. Healthy normal kidney specimen, and bladder specimen of the patients undergoing nephrectomy for cancer, ureteral reimplantation for vesicoureteral reflux or partial cystectomy for urachal cyst were used as control. The patients who underwent augmentation were 1-30 (median 14) years old, male:female 9 : 4. Six cases had spinal disorder, 4 posterior urethral valve and 3 non-neurogenic neurogenic bladder. On urodynamic study the bladder capacity was 5-303 (median 107) ml, maximal pressure 10-107 (median 30), and compliance 0.05-30 (median 3.9). Uninhibited contractions were noted in 6, vesicoureteral reflux in 8.

Results
1) Transcript levels of PTHrP and PTH1R showed consistent reduction after BOO compared with sham. 2) Renal tubules in kidneys, as well as detrusor muscle layer and vessels in control bladders were positively stained for PTH1R. However, in all augmented bladders, in spite of positive staining in the vessels, there was marked decrease in PTH1R staining in detrusor muscle layer.

Interpretation of results
Downregulation of PTHrP and PTH1R, mediating endogenous bladder relaxation signal, could be related with pathogenesis of bladder overactivity seen in rat obstructed bladder and human end-stage bladder diseases requiring augmentation.

Concluding message
PTHrP/PTH1R axis could be target for treating detrusor overactivity.

Figure 1

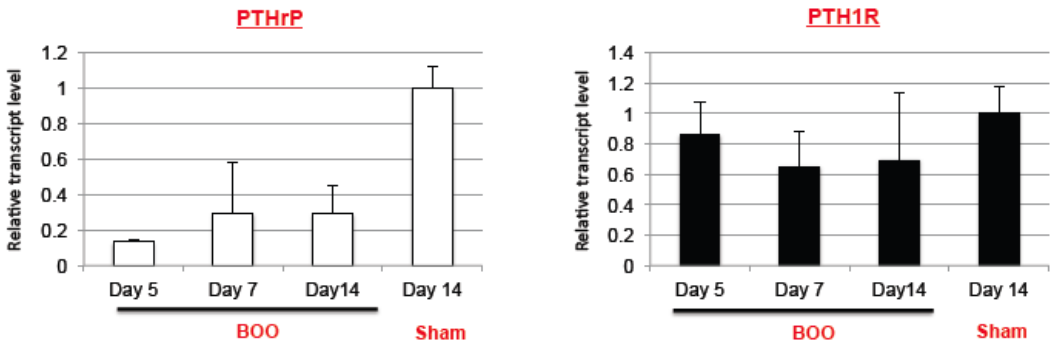
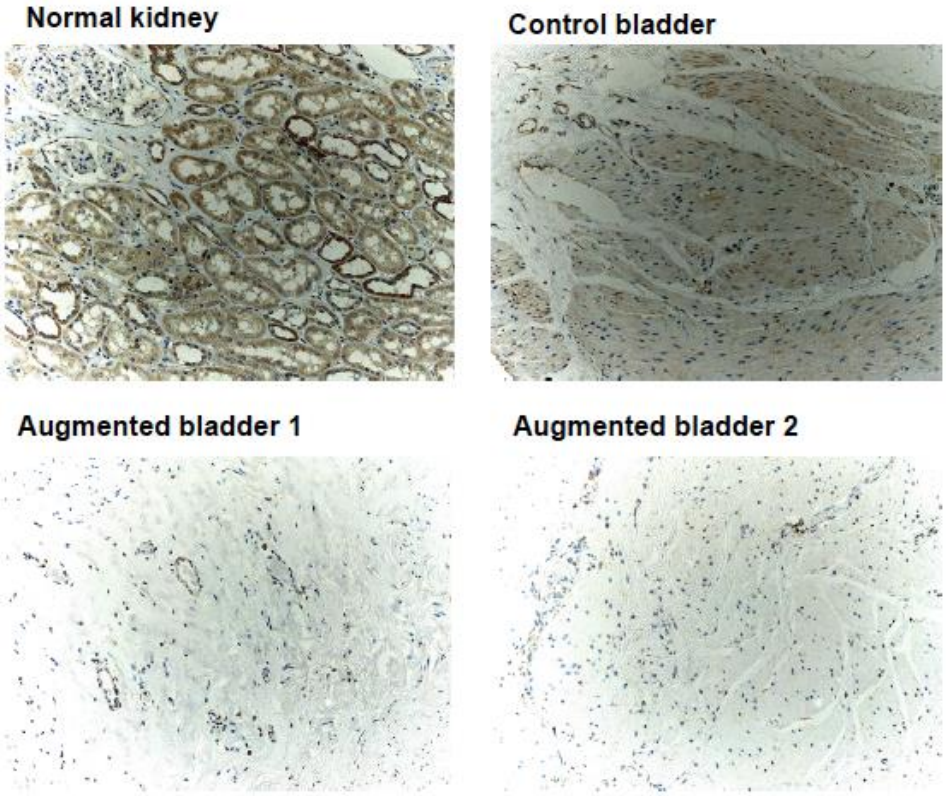


Figure 2



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Disclosures

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