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STRETCH OR DISTENSION- INDUCED INCREASE IN NON-NERVE EVOKED NORADRENALINE RELEASE IN RAT AND HUMAN BLADDER

Hypothesis / aims of study

In the storage phase, the inhibition of bladder contraction is mediated by noradrenaline through the β-adrenoceptors in the detrusor smooth muscle. Several reports demonstrated the important role of β_3-adrenoceptor in human bladder. However there were few reports about the noradrenaline release from urinary bladder in the storage phase. In the present study, we attempted to measure the distension- or stretch-induced noradrenaline release from in vivo rat bladder and isolated human bladder strips, using microdialysis procedure.

Study design, materials and methods

1) In vivo rat study: In the anesthetized SD rat, under lower abdominal incision, hypogastric nerve was identified and cut under microscope. A cannula was inserted into the bladder transurethrally and physiological saline was infused into the bladder constantly. Microdialysis probe was inserted into the bladder wall, Ringer solution was perfused into the probe at a constant flow rate of 2.0 μl/min, and the dialysate was collected in various bladder capacities (0, 0.25, 0.5 and 1.0 ml).
2) In vitro human bladder strip study: Human bladders were obtained from 5 patients (all male: 62- 74 years old) who were performed bladder operation due to malignancy. After insertion of microdialysis probe, smooth muscle strip with or without urothelium was suspended in organ bath, and an isometric force was recorded. Perfused dialysate was collected every 10 minutes. The effects of bladder distension and elevation of the resting tension (0 to 40 mN) on noradrenaline release were evaluated.

The measurement of noradrenaline in the dialysate was performed using HPLC-ECD system in both experiments.

Results

1) In vivo rat study: Noradrenaline release from rat bladder in vivo was determined at 0 ml bladder capacity (basal release). With the increase in bladder capacity, the amounts of noradrenaline release were gradually increased. The amount of noradrenaline release at 0.5 and 1.0 ml in bladder volume were 0.062 ± 0.010 and 0.080 ± 0.012 pmol, respectively, which were significantly higher ($P<0.02$) than that of 0 ml (0.028 ± 0.005 pmol).
2) In vitro human bladder strip study: In human bladder strips with urothelium, significant noradrenaline release was observed at 0 mN resting tension (0.224 ± 0.058 pmol/g tissue weight; basal release). The basal release did not inhibited by treatment with tetrodotoxin (10^{-6} M) pre-treatment. Removal of urothelium caused a significant reduction (85±9.2%) of the release of strip with urothelium. There was stretch-dependent increase in tetrodotoxin-insensitive noradrenaline release from human bladder strip with urothelium. The maximum % increase in noradrenaline release was 464 ± 58 % in 40 mN resting tension, as compared with the release in 0 mN resting tension.

Interpretation of results

In vivo rat study, we cut hypogastric nerves. Therefore, it may be possible that the released noradrenaline may not be a synthetic nerve origin. In addition, the failure of inhibitory effect of tetrodotoxin on noradrenaline release in human bladder strip suggests that basal and stretch-induced noradrenaline release might be non nerve-evoked release.

Concluding message

The present data demonstrate that there are tetrodotoxin-insensitive basal noradrenaline releases in rat and human bladders. Distension- or stretch-induced increases in noradrenaline release in rat and human bladder may suggest that the increased non nerve-evoked noradrenaline release contributes to the bladder function in the storage phase.

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HUMAN SUBJECTS: This study was approved by the Ethics committee of Kumamoto University and followed the Declaration of Helsinki Informed consent was obtained from the patients.