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INTRAVENOUS NORADRENALIN FACILITATES AFFERENT ACTIVITY OF THE MICTURITION REFLEX AT THE LUMBOSACRAL CORD IN RATS

Aims of study

Lower urinary tract symptoms (LUTS), especially collecting disorders, are more severe in patients with benign prostatic hyperplasia (BPH) and hypertension when compared with BPH patients without hypertension [1]. Although adrenergic alpha-1 receptor antagonists improve both voiding and collecting disorders in BPH patients, tamsulosin (an alpha-1A receptor antagonist) is superior for voiding disorders and naftopidil (an alpha-1D receptor antagonist) is superior for collecting disorders. Since intrathecal injection of naftopidil to the lumbosacral cord level transiently abolishes bladder contractions in rats [2], noradrenalin may facilitate afferent activity of the micturition reflex at the lumbosacral cord via alpha-1D receptor. Therefore, in order to clear the influence of intravenous noradrenalin on bladder activity, the effects of intravenous and/or intrathecal injections of noradrenalin or naftopidil were examined.

Materials and methods

Twenty-four female Sprague-Dawley rats weighing about 250 g were used. The rats were anesthetized by intraperitoneal and subcutaneous injection of urethane (1.2 g/kg), and a polyethylene catheter connected to a pressure transducer was inserted into the bladder through the urethra. The urethra was ligated to the catheter near the external urethral meatus. The ureters were transected and the proximal cut ends were left open. In 9 rats, a cannula was placed in the femoral vein for the intravenous (IV) administration of noradrenalin (0.1 mg). Another cannula was placed in the femoral artery for measurement of blood pressure. In 9 rats, laminectomy was performed at L3 and a catheter was inserted into the subarachnoid space through a small hole in the dura for the intrathecal (IT) injection of noradrenalin (0.001-10 μg). The tip of the catheter was advanced to the level of the sacral cord. In 6 rats, both an intravenous cannula and an intrathecal catheter were placed for IV noradrenalin and IT naftopidil (0.1μg). The bladder was filled with physiological saline to above or just under the threshold volume, inducing rhythmic isovolumetric contractions. When the interval and amplitude of the bladder contractions had been stable for 30 min, these parameters were measured as control values. The changes of bladder activity for 15-30 min after drug injections were recorded and compared with the control recordings before drug injections.
Results are reported as the mean ± standard deviation.

Results

When the bladder was filled with saline just under the threshold volume inducing rhythmic bladder contractions (n = 3), IV noradrenalin (0.1 mg) induced rhythmic bladder contractions for several minutes. Blood pressure was transiently increased (60-80 mm Hg increase) after IV noradrenalin. However, when the bladder contracted rhythmically (n = 6), IV noradrenalin (0.1 mg) shortened the interval (from 1.6 ± 0.3 to 1.3 ± 0.2 min, $p = 0.035$) and decreased the amplitude of bladder contractions (from 42.2 ± 6.1 to 28.5 ± 5.9 cm water, $p = 0.001$). The baseline pressure was also decreased (from 14.3 ± 3.0 to 11.2 ± 1.9 cm water, $p = 0.032$) after IV noradrenalin. These changes were disappeared within 15 min after IV noradrenalin.
When the bladder was filled with saline just under the threshold volume inducing rhythmic bladder contractions (n = 3), IT noradrenalin (0.01 μg) induced rhythmic bladder contractions for several minutes. However, when the bladder contracted rhythmically (n = 6), IT noradrenalin (0.001-10 μg) transiently abolished bladder contractions for several minutes. After recovery of bladder contractions, the interval of bladder contractions was shortened (from 2.1 ± 0.6 to 1.6 ± 0.3 min, $p = 0.032$), but the amplitude of bladder contractions and the baseline pressure did not change compared with the control values (66.7 ± 11.7 cm water and 13.8 ± 2.8 cm water, respectively). The change of the interval was disappeared within 15 min after recovery of bladder contractions.
Simultaneous IV noradrenalin (0.1 mg) and IT naftopidil (0.1μg) did not change the interval of bladder contractions, but the amplitude of bladder contractions (from 58.5 ± 12.1 to 41.0 ± 8.5 cm water, $p = 0.009$) and the baseline pressure were decreased (from 16.6 ± 1.3 to 12.3 ± 1.0

cm water, $p < 0.001$).

Interpretation of results

The decrease of the amplitude of bladder contractions and the decrease of baseline pressure were recognized after IV noradrenalin but not IT noradrenalin, suggesting that IV noradrenalin inhibits the activities of the bladder smooth muscle cells. The interval of bladder contractions was shortened after IV or IT noradrenalin but not after simultaneous IV noradrenalin and IT naftopidil, suggesting that IV noradrenalin passes through the blood-brain barrier, and facilitates afferent activity of the micturition reflex at the lumbosacral cord via alpha-1D receptor. Although the mechanism that IT noradrenalin transiently abolished bladder contractions is unclear, we might have felt the effect of intravenous increase of noradrenalin as a desire to void when we felt tension. Therefore, hypertension with high serum noradrenalin level may worsen LUTS, especially collecting disorders.

Concluding message

The increase of the intravenous noradrenalin level facilitates afferent activity of the micturition reflex at the lumbosacral cord, and induces urinary frequency.

References

1. Int J Urol, 10: 569-574, 2003.
2. Neurosci Lett, 328: 74-76, 2002.