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Matsumoto S[1], Hanai T[1], Shimizu N[1], Sugimoto K[1], Watanabe E[1], Uemura H[1]
1. Kinki University School of Medicine

PDE5 INHIBITOR (VARDENAFIL) PROTECTS RAT BLADDER FROM PARTIAL OUTLET OBSTRUCTION-INDUCED CONTRACTILE DYSFUNCTION.

Hypothesis / aims of study
Evidence has been accumulating that PDE5 inhibitors improve lower urinary tract symptoms (LUTS) in BPH patients or ED patients with BPH [1)]. A possible mechanism why PDE5 inhibitors are effective for both ED and LUTS would be the improvement of NO/cGMP pathway in the penis and bladder, respectively, which is impaired by the low blood flow in the pathological conditions such as aging and arteriosclerosis [2)]. However, no experimental investigation has been reported yet how PDE5 inhibitors affect bladder functions. In this study, we investigated our hypothesis that a PDE5 inhibitor would increase the bladder blood flow which might result in the protection of bladder function in a 4 week rat BOO model in which decompensatory change of bladder functions is induced.
Study design, materials and methods
Bladder outlet obstruction (BOO) was introduced to 12-week old female SD rats. Vardenafil (0.5, 2 or 8 mg/kg/day) was given by drinking water from the day of BOO surgery. Four weeks after the introduction of BOO, vardenafil was washed out by giving water for 24-48 hr, and then bladder was excised and dissected into 4 longitudinal strips for isometric organ bath assay. Contractile profile of bladder strips to electrical field stimulation, carbachol and KCl was investigated in group 1: sham-operated rats given with water, group 2: BOO rats given with water, group 3: BOO rats treated with vardenafil 0.5 mg/kg/day, group 4: BOO rats treated with vardenafil 2 mg/kg/day, and group 5: BOO rats treated with vardenafil 8 mg/kg/day.
Results
BOO induced the increase in the bladder weight by 4.4-fold in group 2 compared to group 1. Bladder weights of group 3-5 were not significantly different from that of group 2. Contractile forces in response to electrical field stimulation, carbachol and KCl in group 2 was 30-50% of those in group 1. Vardenafil treatment in group 3-5 dose-dependently improved the reduction in contractile response by BOO compared to group 2 (Contractile forces in group 5 were 40-80% of those in group 1).
Interpretation of results
Vardenafil treatment protects rat bladder from partial outlet obstruction-induced contractile dysfunction compared to vehicle treatment. These results were consisted with recently reported results, in which chronic treatment with vardenafil prevented the development of non-voiding contractions in BOO rats [3)]. Further analyses are necessary how vardenafil prevented these changes in BOO rats.
Concluding message
These functional analyses showed that vardenafil possesses bladder protective effects in BOO rats and this could be a mechanism why PDE5 inhibitors are effective to LUTS in BPH patients.

References
1) AUA (2006), Abstract #1637.
2) BJU Int (2005) 96;1073-1078.
3) Endocrinology (2007)148;1019-1029.

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