

THE EFFECT OF TAMSULOSIN ON NEUROGENIC VOIDING DYSFUNCTION INCLUDING FROM CENTRAL MICTURITION CENTER TO PERIPHERAL BLADDER FUNCTION

Hypothesis / aims of study

Alpha-1 adrenoreceptor (α_1 AR) antagonists have generally been used for the treatment of lower urinary tract symptoms that are caused by bladder outlet obstruction including BPH. However, α_1 AR antagonists were also used for voiding dysfunctions of neurogenic origin empirically. We are to investigate the effects of tamsulosin on the neurogenic voiding dysfunction in regard to peripheral bladder function and central micturition area using intracerebral hemorrhage (ICH) induced rat model.

Study design, materials and methods

Adult female Sprague-Dawley rats, weighing 260 ± 10 g (10 weeks old) were randomly divided into five groups (n = 8 in each group): sham-operated, ICH-induced, ICH-induced and 0.01 mg/kg tamsulosin-treated, ICH-induced and 0.1 mg/kg tamsulosin-treated, and ICH-induced and 1 mg/kg tamsulosin-treated group. ICH was induced by injection of collagenase to the hippocampal CA1 region using a stereotaxic apparatus. The tamsulosin-treated groups received tamsulosin once a day for 14 consecutive days at the respective doses, starting 1 day after the ICH induction. Parameters of awake urodynamics were investigated after treatment in each group. Immunohistochemistry for c-Fos and NGF expression were performed for the detection of neuronal activity in the central micturition areas.

Results

ICH increased bladder contraction pressure and frequency significantly ($P < 0.05$), thereby contributing to the induction of voiding dysfunction of neurogenic origin. On the contrary, tamsulosin treatment ameliorated this increment of bladder contraction pressure and frequency of ICH induced rats ($P < 0.05$). After ICH induction, c-Fos and NGF expressions in central micturition areas were enhanced, which mean increase neuronal activity of corresponding site. In the same manner, tamsulosin treatment ameliorated this enhancement of c-Fos and NGF expressions of ICH induced rats, which mean tamsulosin could suppress unintended neuronal activation after ICH ($P < 0.05$).

Interpretation of results

Tamsulosin could not only decrease neuronal activation of central micturition centers but also improve cystometric parameters in neurogenic voiding dysfunction due to ICH. The present study support the basis that tamsulosin could be effective therapeutic modality for ameliorating the voiding dysfunction of neurogenic origin. And, the therapeutic effect of tamsulosin could be linked to suppress unintended neuronal activation of central micturition centers.

Concluding message

Although the pathophysiology of NLUTD is still poorly understood, a number of pieces of evidence suggest that α_1 -AR antagonist tamsulosin may be useful in NLUTD. Tamsulosin could not only decrease neuronal activation of central micturition centers but also improve cystometric parameters in neurogenic voiding dysfunction due to ICH. The present study demonstrated that the therapeutic effect of tamsulosin in NLUTD could be linked to neuronal voiding centers. We also proposes the another possible mechanism to explain the previously reported clinical efficacy of tamsulosin in NLUTD. Better understanding of the normal physiology of lower urinary tract function and the pathophysiology of NLUTD may in future help to define the exact role of tamsulosin in NLUTD more clearly.

References

1. P. Abrams, G. Amarengo, A. Bakke, A. Buczynski, D. Castro-Diaz, S. Harrison, G. Kramer, R. Marsik, A. Praisner, M. Stohrer, P. Van Kerrebroeck, J.J. Wyndaele, Tamsulosin: efficacy and safety in patients with neurogenic lower urinary tract dysfunction due to suprasacral spinal cord injury, *J Urol* 170 (2003) 1242-1251.
2. A. Athanasopoulos, K. Gyftopoulos, K. Giannitsas, J. Fisfis, P. Perimenis, G. Barbalias, Combination Treatment With an α -Blocker Plus an Anticholinergic for Bladder Outlet Obstruction: A Prospective, Randomized, Controlled Study, *The Journal of Urology* 169 (2003) 2253-2256.
3. M.M. Barendrecht, P. Abrams, H. Schumacher, J.J. de la Rosette, M.C. Michel, Do alpha1-adrenoceptor antagonists improve lower urinary tract symptoms by reducing bladder outlet resistance?, *Neurourol Urodyn* 27 (2008) 226-230.

Disclosures

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