

THE EFFECTS OF NERVE GROWTH FACTOR AND VANILLOID RECEPTOR SUBTYPE 1 ON BLADDER FUNCTION AFTER RELIEF OF BLADDER OUTLET OBSTRUCTION IN RATS

Aims of Study

Bladder outlet obstruction (BOO) is a common medical disorder in man that can result from a variety of conditions including benign prostatic hyperplasia, urethral stricture disease, benign and malignant tumors and congenital abnormalities. The observation that 15 to 30% of men after surgical relief of BOO have persistent irritative symptoms should concern clinician. The changes of afferent nerves may contribute to irritative symptoms related to BOO. Nerve growth factor (NGF) is a secretory protein which plays a critical role in the development of the peripheral nervous system including the maturation of sensory pathways. Also NGF has recently been shown to regulate the expression of vanilloid receptor subtype 1 (VR1) mRNA in adult rat dorsal root ganglion neurons and acutely regulate the excitability of afferent receptor. Experimental studies in rats have revealed that alterations in the expression of NGF and VR1 in the bladder after BOO may affect on sensory signalling in the bladder and in turn influence persistent irritative symptoms and unstable bladder. Based on above facts, this study was performed to investigate the changes in NGF and VR1 after relief of BOO and how these changes participate in functional changes of bladder.

Methods

A total of 50 Wistar male rats weighing approximately 250-300 g were used for this study and divided into 10 control and 40 experimental groups. Control groups consisted of sham operated animals. Experimental groups were obstructed for 3 weeks by partial urethral ligation. After 3 weeks, obstruction was relieved by urethral deligation. Cystometrograms (CMG) were performed 3 weeks after deligation and contraction pressure, interval of contraction, presence of bladder instabilities were checked. On the basis of CMG, experimental groups were subdivided into normalized and unstable bladder groups. The cases that contraction interval decreased to ≤ 2 standard deviations below mean interval of control rat or that have uninhibited contraction were defined as unstable bladder group. The bladders of each group were dissected out and weighed. Total RNA was extracted from each bladder and semi-quantitative reverse transcriptase polymerase chain reaction (RT-PCR) was performed for analysis of NGF and VR1 mRNA.

Results

25% of experimental groups showed unstable bladder. Compared with the control group, bladder weight of the normalized and unstable bladder group were increased ($p < 0.05$). However, no significant difference was noted between normalized and unstable bladder groups. On CMG, there was no significant difference in contraction pressure among the 3 groups. The contraction interval of the unstable bladder (3.9 ± 0.47 min) was markedly decreased compared with control (10.2 ± 0.49 min) and normalized groups (10.9 ± 0.74 min) ($p < 0.05$). On RT-PCR, NGF and VR1 mRNA were detectable in all tissue. Semi-quantitative comparison was used to compare mRNA expression in each group using the housekeeping gene, GAPDH as an internal standard. Contrary to control and normalized groups, the NGF mRNA increased in unstable group ($p < 0.05$). Also, VR1 mRNA increased in unstable group compared with control and normalized groups ($p < 0.05$).

Conclusions

These data suggest that NGF and VR1 might be involved in the sensory functions of the bladder. In addition, increased NGF and VR1 may be related to persistent unstable bladder or bladder irritative symptoms after correction of BOO.

References

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