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EFFECTS OF CONNEXIN EXPRESSION ON DETRUSOR FUNCTION AFTER RELIEF OF BLADDER OUTLET OBSTRUCTION IN RAT

Aims of Study

Bladder outlet obstruction is a common medical disorder which leads to rearrangements of smooth muscle and epithelial cells of the bladder wall and to alterations in their function. Detrusor overactivity and storage symptoms are frequently associated with bladder outlet obstruction and often remain unchanged even after relief of the bladder outlet obstruction. This may be related with increased electrical coupling. Connexins (Cx) constitute a family of transmembrane proteins that form gap junction channels allowing metabolic and electrical coupling of cellular networks. Several Cxs have been identified so far in bladder smooth muscle and epithelium. This study was undertaken to evaluate the changes of connexin (Cx26, Cx37, Cx40, Cx43, and Cx45) expression after relief of bladder outlet obstruction and whether these changes are affected by functional changes of detrusor.

Methods

A total of 50 Wistar male rats weighing approximately 250-300 g were used for this study and divided into two groups: 10 control and 40 experimental groups. Control group consisted of sham operated animals. The experimental group was partially obstructed for 3 weeks. After 3 weeks, the obstruction was relieved by urethral deligation. 3 weeks after deligation, the cystometrograms (CMG) was performed and contraction pressure, interval of contraction, presence of detrusor overactivity were checked. On the basis of CMG, the experimental group was subdivided into normalized and overactive 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 overactive group. The bladder of each group were dissected out after CMG and weighed. Messenger RNA (mRNA) expression of Cx26, Cx37, Cx40, Cx43 and Cx45 were analysed in each group by reverse transcriptase polymerase chain reaction (RT-PCR). Semi-quantitative comparison was used to compare mRNA expression in each group using the housekeeping gene, GAPDH as an internal standard.

Results

25% of experimental group was defined as overactive group. The bladder weights of normalized and overactive group increased compared with control group ($p<0.05$). However, no significant difference was noted between normalized and overactive groups.

On CMG, the contraction interval of overactive group was markedly decreased compared with that of the control and normalized groups ($p<0.05$). There was no significant difference in contraction pressure among control, normalized, and overactive groups.

Cx26, Cx37, Cx40, Cx43 and Cx45 mRNAs were detectable in all tissue. Semi-quantitative RT-PCR revealed that the expression of Cx26 mRNA decreased in normalized group compared with control and overactive groups ($p<0.05$). However, there was no significantly difference between control and overactive group. The expressions of Cx26 and Cx43 mRNA in overactive group increased significantly compared with control and normalized group ($p<0.05$). However, the expressions of Cx26 and Cx43 mRNA were not significantly different between control and normalized groups. The expressions of Cx37 and Cx40 mRNA were not significantly different among all three groups.

Conclusions

The present data demonstrate that the several connexins may be related to functional changes of detrusor and are differentially regulated. Also, these changes may be related to persistent overactive bladder or storage symptoms after relief of bladder outlet obstruction.