T. Hanai, S. Matsumoto, H. Kiwamoto,T.Sugiyama, Y.C.Park, T. Kurita1) F.H.Ma, H.Hoshi, Y.Ukai, J.Yano2)

1) Department of Urology, Kinki University School of Medicine,Osaka,Japan

2) Research Laboratories, Nippon Shinyaku Co.Ltd, Kyoto, Japan

BLADDER OUTLET OBSTRUCTION CAUSED BLADDER HYPERTROPHY ASSOCIATED WITH CHANGES OF MUSCARINIC ACETYLCHOLINE AND β-ADRENALINE RECEPTORS

AIMS OF STUDY

Partial obstruction of the rat-bladder outlet induces thickening of the bladder wall characterized by increased bladder weight and smooth-muscle content in addition to increased collagen deposition. To help to elucidate the mechanisms of this hypertrophy, we investigated the histopathological changes in the bladder wall and changes in the binding properties of muscarinic acetylcholine (mACh) and β-adrenaline (β-Ad) receptors after chronic bladder outlet obstruction .

METHODS

Bladder outlet obstruction was produced in female SD rats as previously described (J. Clin. Invest. 88: 1709, 1991). Bladders were removed and weighed 3,6,10,14 and 30 weeks after obstruction. The collagen content of the tissues was measured. Isolated bladder bodies were homogenized and centrifuged at 48.000xg and the resulting pellet was used as a membrane preparation for binding experiments. Various concentrations of the mACh receptor antagonist (3H)N-methylscopolamine and the β-Ad receptor antagonist (3H) CGP12177 were incubated with membranes and the bound radioactivity was measured.

RESULTS AND CONCLUSIONS

The mean weight of the bladder has been increased by 6weeks after outlet obstruction compared as sham operated bladder and from10 weeks to 30weeks after outlet obstruction, kept on plateau. Macroscopically, marked thickening of the bladder wall was observed after outlet obstruction. Fibrosis and muscle-layer thickening were also observed.Quantitative analysis of collagen provided further evidence for these changes. The thickening of the bladder wall with 3 and 6 weeks after outlet obstruction was a result of the proliferation of smooth muscles layers. A significant increase in the maximum number of mACh receptors associated with a decrease in the affinity was observed 6 weeks after, results contrary to those in 3 weeks after, the obstruction of the bladder outlet. On the other hand, there were significant decreases in the Bmax and affinity of β-Ad receptors both in 3 and 6 weeks after obstruction.Both of them got similar to control at 30 weeks after obstruction.It is suggest that these changes in the mACh and β-Ad receptors may contribute to the functional changes in the bladder that compensate for bladder outlet resistance.

	sham operated		obstruction									
			3 weeks		6 weeks		10 weeks		14 weeks		30 weeks	
	Kd[a]	Bmax[b]	Kd[a]	Bmax[b]	Kd[a]	Bmax[b]	Kd[a]	Bmax[b]	Kd[a]	Bmax[b]	Kd[a]	Bmax[b]
[3H]NMS	0.28	322	0.17	180	0.50	586	0.67	442	0.48	173	0.30	200
[3H]CGP	0.09	71	0.22	25	0.17	36	0.10	41	0.15	29	0.09	53

a: nM, b: fmol / mg protein

Table 1: [3H]NMS and [3H]CGP bindings to the membranes from female rat bladder body with obstruction.