Conclusion: The overall decreased blood flow to the bladder smooth muscle appears to be an etiological factor in bladder contractile dysfunction secondary to partial outlet obstruction. The ability to increase blood flow after emptying the bladder could be an important determinant of compensation in the early phase of outlet obstruction. Loss of the ability to increase the blood flow after emptying might be the turning point from reversible to irreversible damage of the bladder due to outlet obstruction.

45

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BLADDER DYSFUNCTION IN ACUTE URINARY RETENTION AND SUBSEQUENT CATHETERIZATION

AIMS OF STUDY: Previously we have reported that ischemia-reperfusion causes bladder dysfunction, and that free radicals including nitric oxide play an important role on ischemia-reperfusion injury in the bladder.[1,2] It is well known that bladder ischemia is caused by urinary retention, but bladder dysfunction due to acute urinary retention is still unclear. In this study, we attempted to investigate bladder function, blood flow and vesical pressure in acute urinary retention and subsequent catheterization in rat urinary bladder. Furthermore, we attempted to measure malonaldehyde (MDA) and 4-hydroxyalkenals (4-HNE) as makers of lipid peroxidation in the bladder.[3]

METHODS: Eight weeks male Wistar rats were used in this study. Rat penile urethra was clamped with a small clip and cystostomy was performed to infuse 3ml of saline (infusion speed 24 ml/hour) to induce acute urinary retention. Thirty minutes after the induction of urinary retention, cystostomy was opened to make the bladder empty. In functional studies, contractile responses to carbachol and 100 mM KCl were measured in these conditions (before (A), 3ml of urinary retention (B), 3ml of urinary retention exposed 30 minutes (C), and subsequent 30 minutes after catheterization (D). Moreover, in vivo real-time monitoring of blood flow and vesical pressure were measured in the bladder with a laser Doppler flowmeter and cystometography, respectively. MDA and 4-HNE were measured by colorimetric assay in these groups (A-D). Statistical analysis of the differences between groups was performed using analysis of variance and the multiple comparison Fisher's test. $P < 0.05$ was regarded as the level of significance.

RESULT: Data of functional study and MDA, and 4-HNE are shown in the TABLE. In functional study, Emax values of carbachol to bladder in A, B, C and D groups were 11.8 $\pm$ 1.3, 11.9 $\pm$ 1.7, 9.8 $\pm$ 0.8, and 6.9 $\pm$ 0.7 g/mm^2, respectively (TABLE). Contractile response to 100mM KCl showed in the same manner as Emax values of carbachol. In real-time monitoring of blood flow and vesical pressure, acute urinary retention significantly decreased blood flow and increased vesical pressure, and subsequent catheterization increased blood flow and decreased vesical pressure in the bladder. The concentrations of MDA and 4-HNE in the bladder in the group D were significantly higher than that in groups A, B, and C (TABLE). Our data indicated that Emax value in the group D is siginificantly lower than the other groups, and lipid peroxidation in the group D is significantly higher than the other groups.

CONCLUSION: Our data indicate that urinary retention and especially subsequent catheterization cause bladder injury. This bladder injury is, in some part, caused by ischemia-reperfusion, and lipid peroxidation may play an important role in the bladder dysfunction.

TABLE

	Emax (g/mm²)	MDA (μM/g tissue)	4-HNE (μM/g tissue)
A	11.8 ± 1.3	1.27 ± 0.11	1.19 ± 1.02
B	11.9 ± 1.7	1.24 ± 0.06	1.30 ± 0.98
C	9.8 ± 1.3	1.08 ± 0.08	1.33 ± 0.77
D	6.9 ± 0.7*	1.75 ± 0.24*	8.31 ± 2.09*

*) significantly different from group A, B and C. $P < 0.05$ is level of significance.

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46

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PHARMACOLOGICAL EFFECTS OF A NEW MUSCARINIC RECEPTORS ANTAGONIST: KRP-197 ON HUMAN ISOLATED URINARY BLADDER

Aims of Study

KRP-197 (4-(2 methlimidazolyl)-2,2-diphenylbutyramide) is a newly synthesized antimuscarinic drug, and clinical trials for the treatment of pollakisuria and urinary incontinence are now going. The pharmacological studies have demonstrated that this compound has a potent affinity and selectivity for M3 muscarinic receptor subtypes and no calcium antagonistic actions. Furthermore, this drugs exhibited a favorable selectivity for the bladder as compared with the salivary glands. However, there is little information available on the effects of KRP-197 on human detrusor smooth muscles. Therefore, the present study was undertaken to determine the effects of KRP-197 on the human isolated urinary bladder using muscle bath technique. Furthermore, the pharmacological action of KRP-197 was compared with that of other antimuscarinic drugs (atropine, oxybutynine and propiverine).

Methods

In this study, human urinary bladders were obtained from 20 patients (18 male and 2 female: mean age 67.8 years) undergoing radical cystectomy due to bladder carcinoma. Smooth muscle strips were dissected from