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HYDROGEN PEROXIDE-INDUCED DETRUSOR OVERACTIVITY INVOLVES NITROSATIVE STRESS, LOSS OF UROTHELIAL INHIBITORY FUNCTION AND UP-REGULATION OF RHO KINASE

Hypothesis / aims of study
Intravesical application of hydrogen peroxide has been shown to induce detrusor overactivity. This study investigated whether H2O2-induced overactivity involves nitrosative stress and alterations in urothelial function and Rho kinase expression.

Study design, materials and methods
Continuous cystometry of male New Zealand rabbits (N=6) was performed with 1% hydrogen peroxide (H2O2). The infusion was continued for 1 hour. The control group (N=6) received normal saline infusion. Bladder tissues from bladder body were then obtained. Contractile responses to 120mM KCl, field stimulation and bethanechol were tested on bladder strips with (Uro+) and without (Uro-) urothelial layer in tissue bath. Expressions of nitrotyrosine, Rho kinase II and CPI-17 in the detrusor were determined with western blotting.

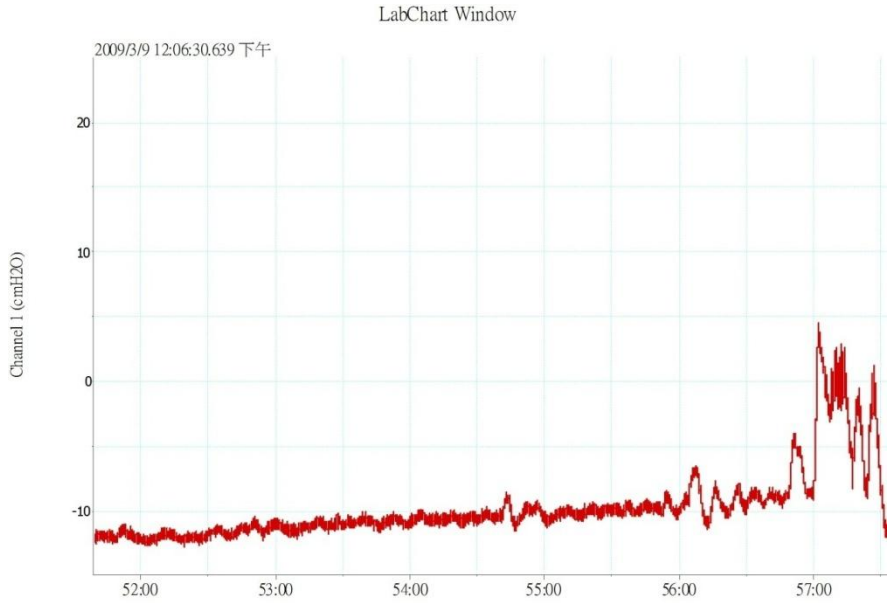
Results
(1) Comparing with normal saline group, instillation of H2O2 significantly reduced the cystometric bladder capacity and inter-contraction interval (figure 1). (2) In control group the responses to field stimulation and bethanechol of Uro- strips were significantly greater than those of Uro+ strips. However, in H2O2 treated bladder strips, the contractile responses were not different between Uro+ and Uro- strips. The contractile response of H2O2 treated Uro+ strips to bethanechol was significantly higher than that of control Uro+ strips. (3) The results of western blot showed that following H2O2 instillation, there was an increased nitrotyrosine expression in both urothelium and detrusor and an up-regulation of Rho kinase II expression in the detrusor. Expression of CPI-17 was not different between two groups.

Interpretation of results
Intravesical instillation of H2O2 induces detrusor overactivity and nitrosative stress as evidenced by the increased nitrotyrosine expression . Inhibitory modulation of the urothelium on the detrusor was also modified by intravesical instillation of H2O2.

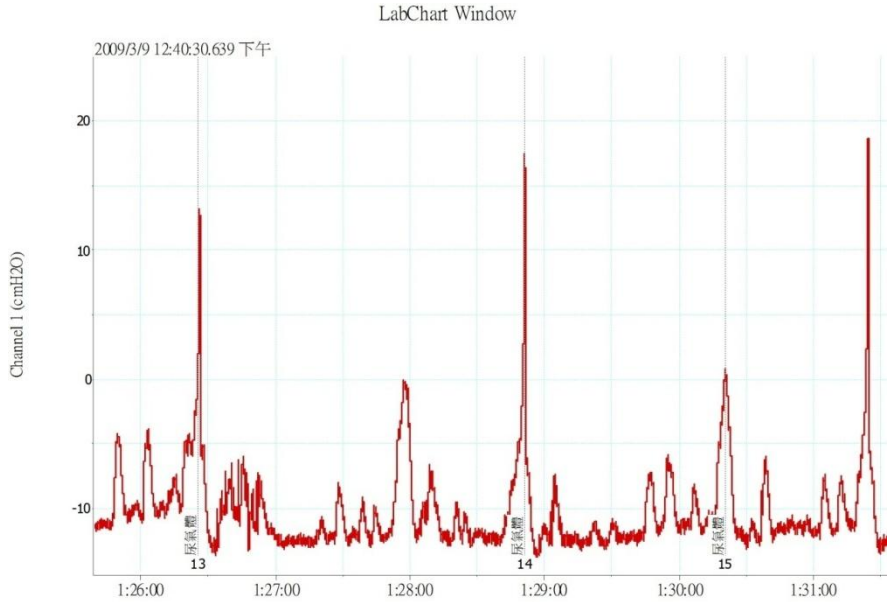
Concluding message
Intravesical application of hydrogen peroxide induces nitrosative stress and detrusor overactivity. Disappearance of inhibitory modulation of the urothelium on the detrusor and up-regulation of Rho kinase might contribute to overactivity of the bladder.

Figure 1.

(a) Cystometry with normal saline infusion



(b) 1% H2O2 infusion



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What were the subjects in the study?	**ANIMAL**
Were guidelines for care and use of laboratory animals followed or ethical committee approval obtained?	**Yes**
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