

## **Effect of Hyaluronic Acid on Urine Nerve Growth Factor in Cyclophosphamide-Induced Cystitis**

**Introduction and Objective:** The purpose of this study was to investigate how hyaluronic acid (HA), a widely-used intravesical medication, affects nerve growth factor (NGF) production and bladder overactivity in a cyclophosphamide (CYP)-induced cystitis rat model.

**Materials and Methods:** Female Sprague-Dawley rats received three intermittent intraperitoneal injection of CYP (75 mg/kg) or saline. Before or after CYP injection, HA was given intravesically and urine NGF was checked with creatinine correction. Bladder function was evaluated by cystometrograms under Zoletil anesthesia. Furthermore, the effect of HA was counteracted with hyaluronidase (HYAL). Bladder structural change was compared among groups with trichrome stain.

**Results:** The intercontraction interval (ICI) significantly decreased in CYP-injected rats in comparison to the saline-injected control. In the CYP-injected groups, bladder HA instillation significantly increased the ICI, but did not change the maximum voiding pressure in comparison to the saline instillation. NGF production significantly increased in CYP-injected rats, but decreased significantly with HA treatment. Treatment of HA before CYP-injection may have a more significant effect. The use of HYAL would eliminate HA effect. Specific staining showed mucosa swelling after CYP treatment. Little HA coating on bladder mucosa could be found in HA treated rats.

**Conclusions:** The intravesical administration of HA suppressed CYP-induced bladder overactivity and also the urine NGF, which were highly correlated. The effects of HA on micturition reflex may be irrespective of being a mechanical barrier. The present findings raise the possibility that HA could be an effective treatment for CYP-related bladder overactivity through involving NGF signaling.