THE CURATIVE EFFECT OF INTRAVESICAL IRRIGATION OF HYALURONIC ACID FOR TREATMENT OF NON-BACTERIAL CYSTITIS

Hypothesis / aims of study
The non-bacterial cystitis includes interstitial cystitis, chemical cystitis, radioactive cystitis, other non-bacterial and chronic cystitis, with bladder irritative symptoms (urinary frequency, urgency and dysuria) as major clinical manifestations. Research shows that bladder mucous membrane's glycosaminoglycan (GAG) layer can protect the bladder wall from damaging of ion, microorganism, crystals and other toxic molecular [1,2]. Based on this mechanism, protecting the bladder mucous membrane's barrier maybe become main therapeutic method for bacterial cystitis.

Hyaluronic acid (HA) is important composition of bladder glycosaminoglycan (GAG), therefore intravesical irrigation of hyaluronic acid can patch defective glycosaminoglycan layer (GAG) in bladder mucous membrane to relieves bladder irritation symptoms[3]. In order to evaluate the efficacy and safety of intravesical irrigation of hyaluronic acid (brand name: Cystistat), From May 2009 to October 2011, we proceed a study through intravesical irrigation of Cystistat for 16 cases of non-bacterial cystitis patients.

Study design, materials and methods
Selection criteria: 25-60 years old, bladder irritative symptoms maintain over 3 months, routine urine and blood were normal, urine culture for the middle segment urine samples was negative, tests of the liver and kidney functions showed normal findings. This group has 16 cases, male in 2 cases, female 14 cases; from 32 to 55 years old; with an average age of 44 years old; the course of disease is from 3 months to 5 years, and more than one year in 13 patients (81%). Clinical manifestations mainly were urinary frequency, urgency, dysuria.

Exclusion criteria: any clear pathogeny of causing bladder irritative symptoms: such as bladder cancer without surgery, acute or chronic bacterial cystitis, urethritis, prostatitis, bladder neck sclerosis, urethrosténosis, benign prostate hyperplasia, neurogenic bladder, history of tuberculosis, serious low blood pressure patients, mental patients, pregnant women and allergic constitution, serious systemic disease or chronic consumptive disease, serious smoking and drinking habits, drug addiction patients, and the patients of other drug test.

Treatment methods: after patients urinate, urethral catheter is inserted right with aseptic technique, then pumping out residual urine, slowly injecting hyaluronic acid sodium solution with 50 ml (40 mg) (brand name: Cystistat). Drugs in bladder is retained for at least 30 to 40 min, patients keep horizontal position and change a position after 5-10 min to make medicine as long as possible contact with the bladder wall. Perfusion weekly, period of treatment is 4 weeks. Once follow-up every two weeks, to the 8nd week.

Effect evaluation: respectively evaluate before and after the perfusion. Urethral pain (or bladder area pain) use visual analogue scale (VAS) [4], range with 0-10, 0 represents painless, 10 represents the maximal pain, patients choose a number represents feel the pain before and after treatment. Urinary frequency and urgency use LUTS (lower urinary tract symptoms) score system [5], this system includes 18 questions, and score 0-5 every question. Patients take Self-assessment with symptoms before and after treatment.

Results
All patients completed perfusion and follow-up, bladder irritation symptoms obviously relieve, all patients are into the final statistical analysis. And the results of all follow-up periods show on table 1.

<table>
<thead>
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<th>Table 1. the results of all follow-up periods for 16 cases of non-bacterial cystitis</th>
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<td>VAS score</td>
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<td>LUTS score</td>
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*p value compared with before-treatment

At 1st week, the VAS score dropped from 6.50±2.129 to 6.19±2.007 (p=0.096>0.05), LUTS score dropped from 36.13±15.633 to 35.44±16.079 (p=0.077>0.05), the difference was not statistically significant. At 2nd week, the VAS score dropped from 6.50±2.129 to 5.94±1.692 (p=0.014<0.05), LUTS score dropped from 36.13±15.633 to 35.38±15.331 (p=0.009<0.05), the difference was statistically significant. At 8th week, the VAS score dropped from 6.50±2.129 to 2.75±0.931 (p<0.001), LUTS score dropped from 36.13±15.633 to 19.68±5.642 (p<0.001), the difference was extremely significant.

During the process, 1 case (6%) patient recurrence at the end of the follow-up, symptoms relieved after perfusion 2 weeks. 3 cases (19%) patients appear urethral discomfort when irrigation, after 24h disappear. In the process of drug infusion, 2 cases (13%) patients felt fullness sensation of bladder area. Patients did not appear adverse reaction such as headache, syncope, skin rash. Review the routine urine and kidney function all normal.
**Interpretation of results**

The study that intravesical irrigation of hyaluronic acid (Cystistat) treat the non-bacterial cystitis, has achieved good effect. The first week, patients' pain, frequency and urgency didn't improve obviously ($p > 0.05$), it maybe is relevant that perfusion time is short. However, we observed patients' symptoms improved obviously after the second week ($p < 0.05$), after 8th week, the symptoms score improved significantly ($p < 0.05$), this full show that intravesical irrigation of cystistat is a feasibility method for non-bacterial cystitis, it can, in bladder mucous membrane temporarily replace defect GAG to relieve symptoms.

Some bad situation appeared during the process was not associated with drug. Urethral pain may be the result of inserting catheter; Bladder fullness sensation disappeared within one hour, may be the result of ejecting drug too fast cause bladder capacity change. The study confirms that intravesical irrigation of Cystistat to treat the non-bacterial cystitis has good curative effect and safety, but the research has focused on the non-bacterial cystitis, not limited to a cystitis type, and the cases less, this may lead to lack of specificity and pertinence for statistical results. In addition, the period is short, one patients with recurrence extended the cycle only can relieve symptoms, this suggests that the long-term efficacy and life quality of patients is worth further study, at the same time, suggest that the plan how to make after symptoms improved.

**Concluding message**

The short-term curative effect and safety that intravesical irrigation of Cystistat treat the non-bacterial cystitis is worth affirmation, it can significantly relieve symptoms, to improve the quality of life.

**References**

3. Na yanqun; Guo zhenhua; Practice of Urology; People's medical publishing house; May 2009, 1st edition: 301-320

**Disclosures**

**Funding:** none  
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