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# USE OF SODIUM HYALURONATE IN THE TREATMENT OF CHRONIC CYSTITIS

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Nina Kulchenko<sup>1</sup> , Aleksandr Tolkachev<sup>2</sup>,  
Farid Mangutov<sup>2</sup> , Galina Myandina<sup>1</sup> ,  
Aleksandr Strachuk<sup>1</sup> , Hasan Alhejoj<sup>1</sup> ,  
Anton Petrov<sup>1</sup> 

<sup>1</sup> Peoples Friendship University of Russia (RUDN University), Moscow

<sup>2</sup> P. Herzen Moscow Oncology Research Institute, Moscow, Russia

✉ [kle-kni@mail.ru](mailto:kle-kni@mail.ru)

**ABSTRACT** — We prospectively evaluated the efficiency of chronic cystitis therapy in women with 0.1% sodium hyaluronate (Uro-hyal) on the basis of regression of leukocyturia, erythrocyturia, bacteriuria, subjective sensations (according to the QoL scale). We also observed all the patients during 12 months after treatment and recorded the number of recurrences. As a result, we recorded a significant improvement in the quality of life and by 2.5 times decrease in recurrences of the disease after Uro-hyal therapy compared to the control group. Conclusions. The intravesical use of 0.1% sodium hyaluronate contributes to restoring the protective properties of the mucous membrane of the bladder and maintains a long time without recurrence of the disease.

**KEYWORDS** — chronic cystitis, dysuria, bacteriuria, sodium hyaluronate (Uro-hyal, CLS International), intravesical therapy.

## INTRODUCTION

An episode of lower urinary tract infection occurs in almost every third woman under 25 years of age [1]. The inflammation of the lower urinary tract occurs in approximately every second woman during her lifetime [1]. If the patient has more than 3 episodes of chronic cystitis a year, or two episodes in six months, the urologist diagnoses chronic cystitis [2]. Frequent bouts of chronic cystitis significantly reduce the patient's quality of life [3]. The causes of chronic cystitis are the presence of a constant source of bacteriuria, impaired urinary passage, abnormalities of the urinary tract, diabetes mellitus, etc. [4, 5, 6].

The main treatment of chronic cystitis is etiotropic treatment for bacterial infection [7]. However, the frequent use of antimicrobial drugs contributes to their increased resistance, as well as the development of adverse effects (allergic reaction, nausea, diarrhea, dysbacteriosis, etc.). Therefore, antimicrobial therapy does not eliminate all issues in the problem of recur-

rent cystitis and prevention of further damage to the urothelium.

There are many medicines used to prevent and treat bladder mucous membrane damage or to restore it after chronic cystitis. These drugs can be used intravesically [8]. The necessity of such therapy is conditioned by the fact that in chronic cystitis, regardless of etiology, there is a constant destruction of urothelium, lamina propria and the submucosa of the bladder base.

In recent years, a group of drugs that can strengthen the tissue framework of the bladder wall, thereby creating conditions for the restoration of the physiological barrier properties of the urothelium have been intensively studied. One of the most frequently used drugs in this class is sodium hyaluronate.

## Aim

Evaluate the efficacy of 0.1% sodium hyaluronate (Uro-hyal, made by the company CLS International in Russia, according to the international standard EN ISO 13485) in treatment of chronic cystitis.

## METHODS

We carried out a prospective analysis of the treatment results of chronic cystitis in women (n=72). All patients agreed to the study and data processing. Inclusion criteria are the age of women from 18 to 50 years, presence of bacteriuria at least 10\*5 CFU, presence of chronic cystitis in the history at least 1 time a year, presence of cystitis attacks at least 3 times a year. Exclusion criteria are sexually transmitted diseases, cancer, urethral stricture, diabetes mellitus.

All women were divided into two groups by the blind method. The first group (basic group) included 37 women with chronic cystitis, who received five intravesical injections of 50 ml 0.1% sodium hyaluronate solution (Uro-hyal) (one procedure per week) after ten days of antibacterial therapy (taking into account the sensitivity of the detected microorganism). The second group (control group) included 35 women with chronic cystitis, who were offered only a ten-day course of antibacterial therapy (taking into account the sensitivity of the microorganism detected in them).

Patients of both groups at the time of the first visit had no reliable differences in the number of recurrences of cystitis per year (4.1+1.3), leukocyturia (26.1+3.7 cells in the field of vision), erythrocyturia (5.3+2.2 cells in the field of vision), bacteriuria (p>0.05).

We assessed the efficacy of the therapy according to the dynamics of leukocyturia, erythrocyturia, bacteriuria, ultrasound of the bladder, subjective sensations (on the QoL scale) after the end of treatment. We also interviewed women from both groups about the number of cystitis relapses within a year after treatment.

Statistical analysis was performed using Excel and STATISTICA 6.0 spreadsheets. The significance of differences between quantitative indicators was assessed using the Mann–Whitney test. The differences were considered significant at  $p < 0.05$ .

## RESULTS

During the intravesical injection of Uro-hyal, not a single woman reported any discomfort during the procedure or an allergic reaction. After the treatment, we found no leukocyturia or erythrocyturia in women of both groups. Urinary bladder wall thickness at transvaginal ultrasound access in women of the first group was  $3.6 \pm 0.4$  mm, in the second group —  $4.2 \pm 0.6$  mm ( $p > 0.05$ ). Patients of the first observation group noted a significant improvement in the quality of life after Uro-hyal therapy in comparison with the second group (Fig. 1). Thus, in the first group the quality of life improved by 65,5%, in the second group by 51,9% ( $p < 0,01$ ).

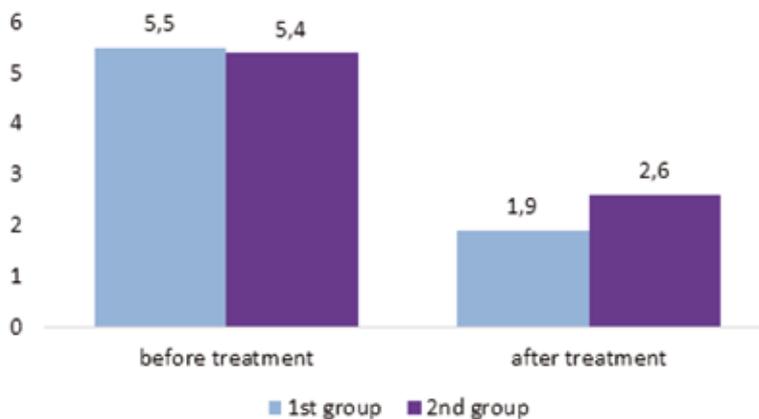


Fig. 1. Dynamics of quality of life of patients (according to the QoL scale) depending on the selected therapy

No urination urges after treatment were reported in 29 (82.8%) control group patients and none of the women in the first group ( $p < 0.001$ ). None of the observed women complained of intolerable or very severe urination pain. However, discomfort after urination persisted in 11 (31.4%) and 6 (16.2%) women in the second and first monitoring groups after the end of treatment ( $p < 0.05$ ). The average number of recurrences of cystitis after Uro-hyal therapy decreased to  $1.2 \pm 0.5$  times per year in the first group of the study, against  $2.5 \pm 0.8$  times in the second group during the whole period of observation ( $p < 0.05$ ).

Discussion. The main pathogenetic component for all variants of chronic cystitis is permanent damage of the mucous membrane of the bladder, which leads to hyperplastic and dysplastic processes in the membrane and increases the frequency of cystitis episodes [1]. Atrophic

and dystrophic changes in the mucous membrane of the bladder create a favourable environment for the development of the bacterial component and progression of urothelial damage. It is known that chronic cystitis results in an increase and change of leukocyte infiltration in mucous and submucous membranes of the bladder. Therefore, in the treatment of chronic cystitis, it is important to use substances that provide protection for urothelium [9]. Currently, medications based on hyaluronic acid (0.1% sodium hyaluronate) have some success. The main clinical effects of sodium hyaluronate are the establishment of mechanical barrier (lubrication), enhancement of regeneration due to restoration of glycosaminoglycan layer of the urothelium, moistening of the mucous bladder due to high degree of water binding, interruption of the pathological circle of inflammatory reaction [10].

Studies by Rooney P. et al. have shown that hyaluronic acid is capable of reducing the production of cytokines by 4–5 times, reduces the intensity or generally prevents the development of inflammatory processes. There has also been an increase by 2 times in the formation of sulfated glycosaminoglycans and a decrease in urothelium permeability without damaging natural barriers [11].

The results of our study showed that when 0.1% sodium hyaluronate was used in the treatment of acute interstitial cystitis, there was a significant improvement in the quality of urination in 70.5% of patients, none of the women had complaints of intolerable or very severe pain ( $p < 0.05$ ) [12].

## CONCLUSIONS

Intravesical use of sodium hyaluronate in the therapy of chronic cystitis significantly improves the effectiveness of treatment. Pathogenetically justified combined therapy of chronic cystitis should be carried out in two stages. The first stage is a ten-day course of antibacterial therapy. The second stage is a course of intravesical injections

(at least five) of sodium hyaluronate solution. The use of sodium hyaluronate in the complex treatment of chronic cystitis increases the duration of the recurrence-free intervals of the disease.

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