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## A complex approach to the chronic recurrent cystitis treatment

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### Abstract

**Background.** Chronic cystitis is the dominating urinary tract disease. Due to its high prevalence among women, this issue remains topical in medicine.

**Aim.** To evaluate the effectiveness of the sodium hyaluronate in the complex treatment of chronic recurrent cystitis.

**Material and methods.** The research included 60 patients with a confirmed clinical diagnosis of “chronic recurrent cystitis” in the clinic of Kazan State Medical University for the period from July 2020 to July 2021. To evaluate the effectiveness of treatment, the patients were divided into groups using the copy-pair method. The first (main) group included 30 women receiving anti-inflammatory therapy and local treatment with collargol instillations. After that, the patients were prescribed the topical use of sodium hyaluronate: 40 mg (50 ml) once a week for 1 month. The second (control) group also included 30 patients who received only anti-inflammatory therapy and local treatment with collargol. The average age of the observed patients was  $30.5 \pm 1.5$  years: in the first group —  $31.1 \pm 1.5$  years, in the second group —  $31.9 \pm 1.3$  years. All patients underwent control cystoscopy, ultrasound and urodynamic examinations on the 15th and 30th day of treatment. The Welch's t-test, Fisher's test, analysis of variance with repeated observations were used as statistical data analysis methods.

**Results.** Treatment was completed by all patients in both groups. The patients' management showed a significant decrease in the number of urination (up to 6 times a day), and urgent uriesthesia was recorded in 86.6% of women in the main group compared to 60% in the control group ( $p < 0.05$ ). The control cystoscopy performed on the planned 15th day of treatment showed positive dynamics in the bladder mucosa recovery under the collargol influence. All patients of the first group had no changes in the mucous membrane of the bladder. There was a positive dynamics of urodynamic parameters in the first group compared to the control group.

**Conclusion.** The sodium hyaluronate, which was included in the complex therapy of chronic recurrent cystitis, accelerates the process of the bladder mucosa regeneration after local treatment with collargol and reduces the time of its recovery.

**Keywords:** chronic recurrent cystitis, sodium hyaluronate.

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### Background

Cystitis, an infectious and inflammatory condition of the bladder involving damage to its mucous membrane, is a widespread disease that poses a considerable challenge to the female body. Chronic cystitis is also an important socio-economic problem, as its complex treatment is a long and difficult process. Treatment of chronic cystitis should include comprehensive therapy, considering the disease etiology and pathogenesis.

In 40% of patients, chronic cystitis is diagnosed at working age (20–40 years) [1, 2], and in 50% of cases, it results in impaired job performance [3–5]. In all, 50% of women present with a urinary tract infection at least once in their lives [1]. At the same time, half of them have a recurrence of infection

within 6–11 months, and in 50% of patients, recurrence occurs in 50% of patients three times or more per year [6, 7].

To achieve therapeutic efficiency, comprehensive treatment, including antibiotic therapy, as well as stabilization of the glycosaminoglycan layer with immunotherapy and phytotherapy, is advisable [8–10]. In addition, local treatment in the form of instillations of various drugs is often used in hospitals [11, 12] and is one of the most effective treatment methods [13].

However, collargol, often used as a local therapy, can cause mild burning of the bladder mucosa [13]. Currently, a hyaluronic acid preparation, Urogial, developed by MKS Laboratories, is registered on the Russian pharmaceutical market. Sodium

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**Table 1.** Characteristics of patient indicators

Indicators	Group 1, <i>n</i> = 30	Group 2, <i>n</i> = 30	<i>p</i>
Patient age, years	31.9 ± 3.8	30.8 ± 2.7	0.1473
Average duration of chronic cystitis, days	5 (4; 5.72)	5 (4; 5)	0.5803
Bacteriuria up to 10 <sup>3</sup> CFU	15	14	≈1
Bacteriuria over 10 <sup>3</sup> CFU	13	14	≈1
Frequent urination up to 18 times a day	8	9	≈1
Frequent urination up to 16 times a day	22	21	≈1
Urgency up to 30 times a day	15	13	0.7966
Urgency up to 26 times a day	15	17	0.7966

Note: CFU, colony forming units.

**Table 2.** Characteristics of patient data according to cystoscopy results

Cystoscopy data	Group 1, <i>n</i> = 30	Group 2, <i>n</i> = 30	<i>p</i>
Diffuse hyperemia	7	8	≈1
Swelling of the mucous membrane	14	12	0.7920
Changes in the trigone of urinary bladder	17	15	0.7940
Mucosal trabecularity	25	26	≈1

hyaluronate is a viscoelastic protector of the intercellular substance of the urothelium of the bladder and urethra; it creates a film on the mucous membrane surface and accelerates its regeneration [14, 15].

### Aim

The study aimed to investigate the efficiency of sodium hyaluronate in the complex treatment of patients with chronic recurrent cystitis.

### Materials and methods

The study involved 60 female patients with a diagnosis of chronic recurrent cystitis, distributed into two groups (30 patients each). The sample was formed using the copy-pair method; when forming the groups, the age of the patients, the average duration of chronic cystitis, the level of bacteriuria, the frequency of urination, and the presence of urgency were considered.

The average age of the patients was 30.5 ± 1.5 years (31.1 ± 1.5 years in group 1 and 31.9 ± 1.3 years in group 2). There were no statistically significant differences in age. Upon admission, all patients complained of painful frequent urination in small volumes, discomfort and pain over the womb, and urgency of urination. The disease duration was 3–7 years.

Patients were examined according to the standard diagnostic algorithm in the hospital setting, which included a complete blood count, clinical urinalysis, bacteriological examination of the urine with determination of antibiotic sensitivity, biochemical blood analysis, completion of a urination

diary for 3 days, ultrasound examination of the kidneys and bladder, and uroflowmetry.

The inclusion criteria were the following:

- diagnosis of chronic recurrent cystitis established in a hospital;
- frequent urination more than 10–15 times a day;
- a volume of residual urine not exceeding 100 ml according to ultrasound examination;
- urgency of urination, pain during urination;
- bacteriuria, leukocyturia.

The exclusion criteria were the following:

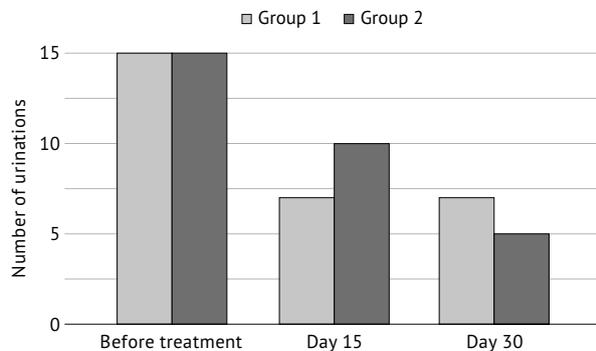
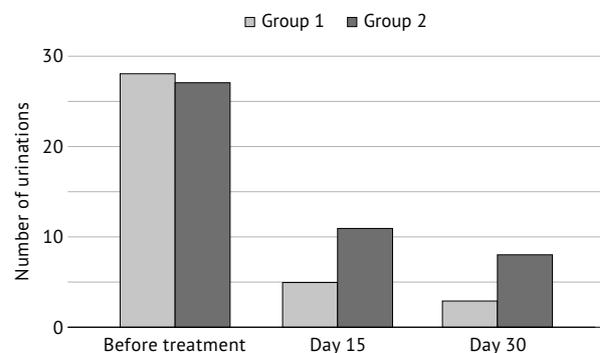
- tumors of the bladder;
- neurogenic bladder;
- bladder stones;
- the use of drugs for the treatment of chronic cystitis;
- urinary incontinence;
- gynecological diseases;
- radiation cystitis.

Patients who met our inclusion criteria were distributed into two groups (30 patients each), which were compared according to history, age, clinical symptoms, and laboratory data. These indicators were almost identical between the two groups. The comparability of the main and control groups according to their baseline indicators is presented in Tables 1 and 2.

Antibacterial drugs were prescribed to the main group patients in accordance with the microflora sensitivity, followed by the use of local treatment with instillations of 1% aqueous solution of silver No. 10 (collargol). Sodium hyaluronate was prescribed immediately after completion of topical

**Table 3.** Main bacterial pathogens according to bacterial culture before treatment (%).

Pathogen	Group 1, <i>n</i> = 30	Group 2, <i>n</i> = 30	<i>p</i>
<i>Escherichia coli</i>	72.0	73.1	0.91
<i>Proteus mirabilis</i>	5.4	4.8	0.91
<i>Klebsiella pneumoniae</i>	7.0	7.4	0.91
<i>Staphylococcus epidermidis</i>	5.8	5.7	0.91
<i>Enterococcus spp.</i>	5.1	6.3	0.91
Other	4.7	2.7	0.91

**Fig. 1.** Number of urinations according to urination diaries.**Fig. 2.** Number of urges according to urination diaries.

treatment with collargol, in an empty bladder, once a week for 1 month, on an outpatient basis, at a dose of 40 mg (50 ml). The total exposure time of sodium hyaluronate in the bladder was 1.5–2 hours [7].

Group 2 (control), which included 30 patients, received antibiotic therapy according to the sensitivity of bacterial culture and instillation with collargol. The duration of follow-up was 30 days. Antibacterial therapy was performed for 10 days with drugs depending on bacterial culture sensitivity.

The efficiency of treatment with sodium hyaluronate in the main group compared with the control group was evaluated 15 and 30 days after treatment initiation. The indicators frequency of urination and urgency, volume of residual urine, and volume of urination were recorded. The quantitative indicators were compared using the Welch *t*-test; for qualitative indicators, Fisher's exact test was used. Repeated measures analysis of variance was used to assess the significance of statistical differences between dependent indicators. Differences were considered statistically significant at  $p < 0.05$ . The study material consisted of copies of data from laboratory studies of patients from case histories.

### Results and discussion

According to the results of bacteriological examination of urine, bacteriuria was detected in all patients (Table 3).

Observations of both groups of patients showed that disease symptoms tended to improve during

treatment, but the improvement was more pronounced in patients in the main group during treatment with sodium hyaluronate ( $p < 0.05$ ).

On day 15, there was a decrease in the number of urinations of up to six times a day in 28 (93.3%) patients in the main group and of up to nine times a day in 24 (80%) patients in group 2 ( $p < 0.05$ ). There was a decrease in the number of urges of up to six times a day in 26 (86.6%) patients in group 1 and of up to 10 times a day in 18 (60%) patients of group 2 ( $p < 0.05$ ), according to the results of urination diaries. On day 30 after treatment initiation, a decrease in the number of urinations of up to five times a day was registered in 30 (100%) patients of group 1 and of up to eight times a day in 27 (90%) patients of group 2. The results for frequency of urination and the number of urges, according to urination data, are presented in Figures 1 and 2.

Cystoscopy performed in both groups before the start of treatment showed a presentation typical of chronic cystitis. In both groups 1 and 2, diffuse hyperemia of the bladder mucosa, hyperemia of the mucous membrane in the region of the trigone of the urinary bladder, trabecularity, and swelling of the mucous membrane were noted (Table 2). On day 15 of treatment, a control cystoscopy was performed, the results of which showed the absence of pathological changes in all 30 patients in group 1. In the control group, seven (23.3%) patients retained trabecularity of the bladder mucosa.

**Table 4.** Average uroflowmetry parameters of female patients of groups 1 and 2 before and during treatment.

Parameter	Before treatment		Day 15		Day 30		P
	Group 1	Group 2	Group 1	Group 2	Group 1	Group 2	
TQ, s	6.8 ± 0.5	6.6 ± 0.4	7.5 ± 0.3	7.2 ± 0.3	8.6 ± 0.3	8.1 ± 0.2	0.040
Q <sub>Max</sub> , ml/s	37.2 ± 0.4	37.3 ± 0.6	35.0 ± 0.2	35.8 ± 0.3	30.1 ± 0.1	33.1 ± 0.2	0.037
V <sub>Comp</sub> , ml	102.1 ± 3.0	102.1 ± 2.4	122.0 ± 2.2	123.1 ± 2.0	137.0 ± 1.7	131.0 ± 1.7	0.015

Note: TQ, urination time; Q<sub>Max</sub>, maximum volume flow rate of urine; V<sub>Comp</sub>, volume of excreted urine.

All patients underwent an ultrasound examination to determine the volume of urination, the amount of residual urine, and the bladder wall thickness. After 15 days of treatment in the main group, the functional capacity of the bladder increased in 28 (93.34%) patients and amounted to 125.5 ± 3.4 ml. The volume of residual urine decreased to no more than 53.0 ± 10.1 ml. The bladder wall thickness also decreased to 5.0 ± 0.5 mm. In 17 patients in group 2, the bladder capacity was 130.5 ± 2.9 ml. Residual urine in the amount of 63.0 ± 8.2 ml was detected in 15 patients.

On day 30, increases in bladder capacity (185.3 ± 18.7 ml) and urination volume (142.8 ± 24.6 ml) were registered. The thickness of the bladder wall was 3.4 ± 0.3 mm. In six (20%) patients in group 2, 64.0 ± 8.2 ml of residual urine remained, indicating one of the symptoms of a urination disorder. Urodynamic control with the determination of the average and maximum urine flow rate after treatment showed a significant improvement in the rate of urination.

Before treatment, ultrasound examination revealed that 17 (56.6%) patients in the main group had residual urine in the amount of 60.2 ± 0.2 ml. In the control group, the same volume of residual urine was determined in 19 (63.3%) patients. On day 30 of treatment, 1 (3.0%) patient in the Uro-gial treatment group had a residual urine volume of 52 ml. In the control group, in seven (23.3%) patients, the amount of residual urine was 68.2 ± 0.2 ml.

All patients underwent a urodynamic study with the obligatory determination of the average and maximum urination rate. Urodynamic control on days 15 and 30 of treatment showed a significant improvement in uroflowmetry values. Before treatment, all patients in both groups had an increase in the maximum flow rate of urine, a decrease in the volume of urination, and a decrease in the duration of urination. After treatment, a pronounced decrease in the flow rate and increase in the volume and duration of urination were significant in the main group of female patients who received Uro-gial.

Table 4 presents the dynamics of uroflowmetry parameters of the main and control groups before and during treatment.

The follow-up results showed that comprehensive therapy was more effective in the main group than in the control group. The efficiency of sodium hyaluronate was confirmed by positive results in the recorded symptoms of the disease. A two-fold decrease in the frequency of urination and urges was noted, as well as a decrease in the average volume of residual urine and an increase in the volume of urination. Dynamic ultrasound examination showed a change in the thickness of the bladder wall.

### Conclusion

The use of sodium hyaluronate in the complex therapy of chronic recurrent cystitis accelerates bladder mucosa regeneration, improves urodynamic indices, and normalizes the number of urinations and urgency of urination.

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**Conflict of interest.** The authors declare no conflict of interest.

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