

<https://doi.org/10.35630/2199-885X/2019/9/3.22>

# ANTIMICROBIAL THERAPY OF ACUTE UNCOMPLICATED CYSTITIS WITH NIFURATEL

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**ABSTRACT** — The article evaluates the effectiveness of the antimicrobial therapy of acute cystitis with nifuratel in 35 women (400 mg — 3 times a day orally). The control group of the study included 31 women who used nitrofurantoin (100 mg — 2 times a day) to treat acute uncomplicated cystitis. We examined the women on the third and seventh day of the intake. Three days after the use of nifuratel (1200 mg/day), the majority of patients (94.2%) subjectively noted the disappearance of urgency, leukocyturia disappeared in 82.8%. 22.8% of women remained uncomfortable when urinating, and we decided to extend the course of antimicrobial therapy with nifuratel up to 7 days. Three days after intake of nitrofurantoin (200 mg/day), 83.8% of women subjectively noted the disappearance of urgency, leukocyturia was stopped in 77.4%. Thus, in 12 (38.7%) cases the decision was taken to extend the course of antimicrobial therapy with nitrofurantoin up to 7 days. In the first group of patients side reactions occurred only in 3 (8.5%) cases, in the second — in 13 (41.9%). Efficiency, favorable safety profile and absence of allergic reactions make nifuratel reliable in the treatment of acute uncomplicated cystitis.

**KEYWORDS** — Nifuratel, acute uncomplicated cystitis (Acute uncomplicated cystitis), antimicrobial therapy.

## INTRODUCTION

Acute uncomplicated cystitis remains one of the most common indications for antimicrobial drugs [1, 2]. Inappropriate treatments for urinary tract infections may lead to the spread of new strains of multidrug-resistant bacteria. It is not always possible to prescribe a patient an antimicrobial drug due to individual bacterial sensitivity [3]. Therefore, according to the guidelines of the European Association of urologists for the treatment of uncomplicated lower urinary tract infections, patients should be prescribed antimicrobials on an empiric basis. It is proved that the effectiveness of empiric treatment regimens for acute uncomplicated cystitis is possible in the absence of antimicrobial resistance in the population around 80–90% [2, 4]. Preference is given to antimicrobial

agents that combine a reduced level of side effects and low resistance to the predominant causative agent of acute uncomplicated cystitis — *Escherichia coli* (*E. coli*) [2]. According to the latest recommendations, nitrofurans and phosphomycin trometamol are the first-choice drugs in the treatment of acute uncomplicated cystitis [1, 5].

*Aim*

To evaluate the effectiveness of antimicrobial therapy of acute uncomplicated cystitis with nifuratel.

## METHODS

We examined 130 female patients with clinical signs of acute uncomplicated cystitis. The study was prospective and comparative. All women were divided into two groups on the principle of blind selection of antimicrobial drug from nitrofurans group for 3–7 days according to the guidelines of the European Association of urologists for the treatment of acute uncomplicated lower urinary tract infections. Criteria for inclusion in the study: pain during urination, frequent urination, urgency, leukocyturia, age from 18 years. Exclusion criteria: no episode of acute cystitis in the previous 3 months, no episode of acute pyelonephritis in the previous month, frequent relapses of cystitis, no pain in the lumbar region, uncomplicated gynecological history, no sexually transmitted diseases.

All patients were divided into two groups. The first group included 35 (53%) women who were prescribed nifuratel 400 mg — 3 times a day orally for the treatment of acute uncomplicated cystitis. In the second group of the study there were 31 (47%) patients who were prescribed nitrofurantoin 100 mg — 2 times a day for the treatment of acute cystitis.

We examined all patients on the 3<sup>rd</sup> and 7<sup>th</sup> day of antimicrobial therapy. During the follow-up period, we evaluated the effectiveness of antimicrobial therapy, drug tolerance, risk of side effects, allergic reactions. At the same time, we focused both on the subjective feelings of patients and on the regression of laboratory parameters. Since pain during urination was the predominant complaint in all women when they came to the doctor, we evaluated the subjective disappearance of pain on a visual analog scale (VAS). Statistical processing of the material was carried out using spreadsheets "EXCEL" and the program "STATISTICA 6.0". The reliability of the differences between quantitative indicators was assessed using the Mann-

Whitney criterion. The differences were considered significant at  $p < 0.05$ .

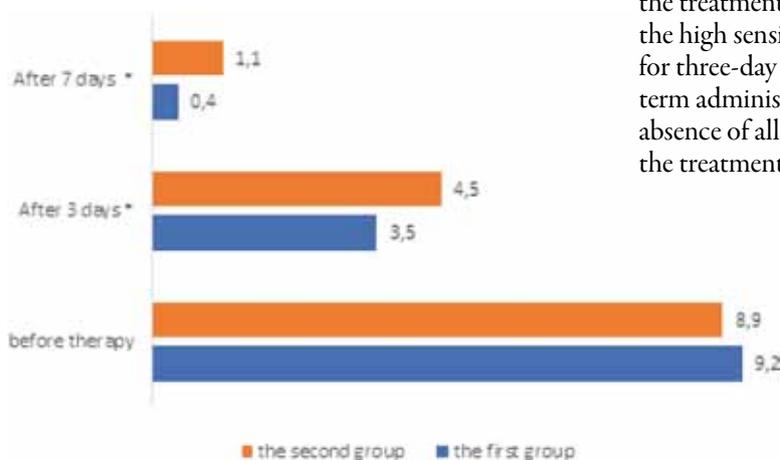
## RESULTS

All patients were between the ages of 18 and 44. The median age was  $28.7 \pm 8.2$  years. This suggests that in our study, acute uncomplicated cystitis is more common in young women. According to the nature of complaints (frequent, painful urination), urgency of pathology, indicators of laboratory studies, both groups of patients at the beginning of the study were comparable ( $p > 0.05$ ). The intensity of pain in BOTH groups was  $9.1 \pm 0.8$  points.

In the first group of the study, three days after taking nifuratel (1200 mg/day), 33 (94.2%) women subjectively noted the disappearance of urgency, the intensity of pain was  $3.5 \pm 1.1$  points, leukocyturia was stopped in 29 (82.8%) patients. Thus, in 8 (22.8%) cases it was decided to extend the course of antimicrobial therapy with nifuratel to 7 days.

In the second group of the study after three days of taking nitrofurantoin (200 mg/day), 26 (83.8%) women subjectively noted the disappearance of urgency, the intensity of pain according to VAS —  $4.5 \pm 0.9$  points, leukocyturia was stopped in 24 (77.4%) people. Thus, in 12 (38.7%) cases it was decided to extend the course of antimicrobial therapy with nitrofurantoin up to 7 days. The average course of antimicrobial therapy in both groups was  $5.2 \pm 1.4$  days.

After 7 days of treatment of acute uncomplicated cystitis with nifuratel, the urgency of symptoms disappeared in all patients, leukocyturia was stopped in 34 (97.1%). In the group of patients treated with nitrofurantoin urgency disappeared in all patients as well, but leukocyturia ( $15.3 \pm 3.1$  leukocytes in the field of view) was recorded in 3 (9.6%) women. The dynamics of regression of subjective symptoms (based on the results of testing on VAS) is presented in fig. 1.



**Fig. 1.** The dynamics of regression of subjective symptoms (based on the results of testing on VAS).  
\* at  $p < 0.05$  in comparison of values between groups

Throughout the course of antimicrobial therapy of acute uncomplicated cystitis, we evaluated side effects in both study groups (table. 1). As can be seen from table 1 side effects prevailed in the second group of patients (on the background of nitrofurantoin use) 3 times compared to the first group (treated with nifuratel). In the first group of patients, adverse reactions were observed in only 3 (8.5%) people, but they were insignificant and all women completed the full course of treatment. Against the background of taking nitrofurantoin, adverse reactions of varying severity developed in 13 (41.9%) people.

The results of this clinical study confirmed the high effectiveness of nifuratel in the treatment of uncomplicated urinary tract infections, as it was praised for its good tolerance and minimal risk of allergies and adverse effects. In this observation, we received different side effects (nausea, dizziness, allergic reaction, etc.) in the group of nitrofurantoin patients (41.9%). These results are comparable with the observations of other researchers [6, 7].

According to previous studies, it was shown that nifuratel has no effect on lactobacteria and does not cause an imbalance in the equilibrium of normal physiological flora, and resistance to it develops slowly [5]. In addition, nifuratel is approved for use during pregnancy due to its low toxicity and has vaginal dosage forms, which allow it to be used in treatment of uro-gynecological diseases [8].

Given the wide range of nifuratel and its effect not only on urinary tract infections (*E. coli*, *Klebsiella*, enterococci and others), but also on the pathogenic flora of the intestine and vagina, including candidiasis, nonspecific vulvovaginitis, bacterial vaginosis [8], this drug is of great interest for further study of its effectiveness in patients with recurrent cystitis.

## CONCLUSIONS

Antimicrobial activity of nifuratel is significant in the treatment of acute uncomplicated cystitis. Due to the high sensitivity of *E. coli*, nifuratel is effective both for three-day therapy of acute cystitis and for longer-term administration. The favorable safety profile and absence of allergic reactions makes nifuratel reliable in the treatment of urinary tract infections.

**Table 1.** Comparison of side effects in patients after treatment of uncomplicated lower urinary tract infection with nitrofurans

Types of Side Effects	Group 1 patients (n=35) – nifuratel therapy	Group 2 patients (n=31) – nitrofurantoin therapy	p
Nausea	1(2,8%)	6(19,3%)	P<0,05
Dizziness	2(5,7%)	4(12,9%)	P<0,05
Feeling of discomfort in the epigastric region	0	2(3,2%)	P<0,05
Allergic reaction	0	1(3,2%)	P>0,05

## REFERENCES:

1. **MARKOWITZ MA, WOOD LN., RAZ S., MILLER LG., HAAKE DA., KIM JH.** Lack of uniformity among United States recommendations for diagnosis and management of acute, uncomplicated cystitis. *International urogynecology journal*. 2019; 30(7): 1187–1194. DOI: 10.1007/s00192-018-3750-z
2. **GUPTA K., HOOTON T.M., NABER K.G., WULLT B., COLGAN R., MILLER L.G., ET AL.** International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis*, 52 (2011), pp. e103–e120.
3. **COLGAN R, WILLIAMS M.** Diagnosis and Treatment of Acute Uncomplicated Cystitis. *American family physician*. 2011; 84(7): 771–776.
4. **SOBKE A., MAKAREWICZ O., BAIER M., BAR C., PFISTER W., GATERMANN S.G., PLETZ M.W., FORSTNER C.** Empirical treatment of lower urinary tract infections in the face of spreading multidrug resistance: in vitro study on the effectiveness of nitroxoline. *International journal of antimicrobial agents*. 2018; 51(2): 213–220. DOI: 10.1016/j.ijantimicag.2017.10.010
5. **PEREPANOVA T.S.** Nitrofurans in the urological practice: are they all the same and why are we getting back to them today? *Experimental and Clinical Urology*. 2018; 3: 91–100.
6. **MENDLING W, MAILLAND F.** Microbiological and pharmacotoxicological profile of nifuratel and its favourable risk/benefit ratio for the treatment of vulvo-vaginal infections – A review. *Arzneimittelforschung-drug research*. 2002; 52(1): 8–13.
7. **SAKAAN S.A., TWILLA J.D., USERY J.B., WINTON J.C., SELF T.H.** Nitrofurantoin-induced hepatotoxicity: a rare yet serious complication. *South Med J*. 2014; 107:107–113.
8. **MENDEZ J.L., NADROUS H.F., HARTMAN T.E., RYU J.H.** Chronic nitrofurantoin-induced lung disease. *Mayo ClinProc*. 2005; 80: 1298–1302.