

# Primena antibiotske terapije u lečenju rekurentne urinarne infekcije uzrokovane bakterijom *Escherichia coli*

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# Use of antibiotic therapy for recurrent urinary tract infections caused by *Escherichia coli*

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## Sažetak

**Uvod.** Urinarne infekcije spadaju u najčešće infekcije i jedan su od vodećih razloga propisivanja antibiotika. Učestalije su kod žena sa značajnim porastom u postmenopauznom periodu. Lečenje urinarnih infekcija predstavlja značajan zdravstveni trošak, ali istovremeno utiču i na sam kvalitet života posebno kada su rekurentnog karaktera. Reinfekcije čine 80% rekurentnih infekcija, a uzročnik je najčešće flora debelog creva sa *Escherichia coli* kao dominantnim uzročnikom.

**Prikaz bolesnika.** Pacijentkinja starosti 63 godine javlja se na pregled kod izabranog lekara zbog subfebrilnosti i učestalijeg mokrenja, bez dizurije. Postavlja se dijagnoza cistitisa. Uključuje se sedmodnevna antibiotska terapija koja dovodi do sanacije infekcije urinarnog trakta. S obzirom na učestalo javljanje urinarnih infekcija, uvodi se antibiotska profilaksa nitrofurantoin tabletama od 50 mg u trajanju od šest meseci. Za vreme trajanja antibiotske profilakse pacijentkinja bez tegoba.

**Zaključak.** Mnogi protokoli pokušavaju da smanje pojavu, tj. vraćanje urinarnih infekcija. Lečenje antibioticima po antibiogramu, kao i antibiotska profilaksa (kontinuirana i postkoitalna profilaksa) su se pokazali najdelotvornijim u sprečavanju rekurentnih cistitisa. Metod i pristup lečenju зависi od učestalosti i težine simptoma.

**Ključne reči:** rekurentni cistitis, antibiotska terapija, profilaksa

## Abstract

**Introduction:** Urinary tract infections (UTIs) are among the most common infections and a leading reason for antibiotic prescriptions. They are more common in women, particularly during menopause. The cost of treating urinary tract infections significantly impacts the health system and affects the quality of life, especially when the infections are recurrent. Reinfections account for 80% of recurrent infections, with the primary cause usually being the colon bacterial flora, with *Escherichia coli* as the dominant culprit.

**Case report.** A 63-year-old female patient visited her GP with complaints of low-grade fever and frequent urination without dysuria. She was diagnosed with cystitis and was prescribed a seven-day course of antibiotics, which effectively resolved her urinary tract infection symptoms. Due to frequent urinary tract infections, she was subsequently placed on a prophylactic six-month course of nitrofurantoin, 50 mg. The patient remained symptom-free during the antibiotic prophylaxis.

**Conclusion.** Many protocols have been shown to reduce the occurrence of urinary tract infections. Antibiotic treatment based on the antibiogram, as well as antibiotic prophylaxis (continuous and post-coital), has proven to be the most effective method for preventing recurrent cystitis. The choice of treatment method and approach depends on the frequency and severity of symptoms.

**Keywords:** recurrent cystitis, antibiotic therapy, prophylaxis

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## Uvod

Prema podacima Instituta za javno zdravlje Srbije tokom 2022. godine bolesti mokračno-polnog sistema bile su na šestom mestu po učestalosti javljanja izabranom lekaru. U većini studija koje su sprovedene u našoj zemlji kao najčešći uzročnik urinarnih infekcija navodi se *Escherichia coli* (*E. coli*) (67–80%), a zatim slede *Proteus spp.* (10%), *Enterococcus spp.* (≈ 9%), *Enterobacter spp.* (≈ 6%), *Klebsiella spp.* (≈ 2–3%), *Pseudomonas aeruginosa* (≈ 2%), *Staphylococcus aureus* (1%). Infekcije urinarnog trakta predstavljaju jedan od vodećih razloga za propisivanje antibiotika kako kod nas, tako i u svetu sa posledičnim razvojem antimikrobne rezistencije<sup>1–3</sup>.

Rekurentne infekcije urotrakta se javljaju najmanje tri puta godišnje ili dva puta u poslednjih šest meseci. Čak 80% rekurentnih infekcija čine reinfekcije. Izvor ovih infekcija je najčešće flora debelog creva. Rekurentne urinarne infekcije remete kvalitet života i radnu sposobnost. Mogu dovesti do smanjenja samopouzdanja, depresivnog stanja, gubitka poverenja u lekara i sklonosti ka samolečenju i korišćenju preparata po preporuci nestručnih lica. Važnu ulogu u njihovom lečenju ima izabrani lekar koji pristupa pacijentu individualizovano, prateći savremene protokole lečenja.

Dijagnoza urinarne infekcije se postavlja na osnovu kliničke slike, analize urina i urinokulture, a po potrebi i radio-loškom dijagnostikom<sup>4–6</sup>.

Prva linija terapije u lečenju rekurentnih infekcija urinarnog trakta je primena antibiotika. Kod rekurentnih cistitisa može se uvesti i antibiotska profilaksa malim dozama antibiotika. Antibotska profilaksa se može započeti kada je pret-hodnom terapijom postignuta sterilizacija urina. Terapija bi trebalo da traje šest meseci ili duže. Nova epizoda reinfekcije se leči ponovo kratkim ili ultrakratkim protokolom.

Izazovi u lečenju su sada veći zbog starenja stanovništva koje je praćeno komorbiditetima, polifarmacijom, smanjenom metaboličkom rezervom jetre i bubrega, pa i većom opasnošću od nastanka neželjenih reakcija prilikom lečenja ili pak razvoja komplikacija. Poslednjih godina poraslo je interesovanje za neantibiotsku profilaksu (kao što su brusnica, D-manoza, probiotski preparati), ali su nalazi u većini studija nekonzistentni. Neophodan je i dovoljan unos tečnosti, mokrenje pre odlaska na spavanje i nakon koitusa, izbegavanje kontracepcije sa spermicidima, izbegavanje penušavih kupki i hemijskih dodataka u vodi za kupanje, tuširanje umesto kupanja u kadi, brisanje od napred prema nazad nakon defekacije da bi se sprečilo prenošenje bakterija iz rektuma, higijena nakon defekacije i lečenje opstipacije<sup>7–9</sup>.

Cilj rada je da se ukaže na značaj racionalne primene antibiotske terapije u lečenju rekurentne urinarne infekcije uzrokovane *E. coli*.

## Introduction

According to the data from the Institute for Public Health of Serbia, genito-urinary diseases were the sixth most common cause for GP visits during 2022. In most studies conducted in our country, *Escherichia coli* was the most common cause of urinary infection (67–80%), followed by *Proteus spp.* (10%), *Enterococcus spp.* (≈ 9%), *Enterobacter spp.* (≈ 6%), *Klebsiella spp.* (≈ 2–3%), *Pseudomonas aeruginosa* (≈ 2%), *Staphylococcus aureus* (1%). Urinary tract infections are one of the leading causes of antibiotic prescription in our country, as well as worldwide, with a consequent development of antibiotic resistance<sup>1–3</sup>.

Recurrent urinary tract infections occur at least three times a year, or twice in the last six months. Even 80% of recurrent infections are reinfections. The source of these infections is usually colon microflora. Recurrent urinary tract infections interfere with life quality and working ability. They may lead to loss of self-confidence, depression, loss of confidence in one's GP, and lead to self-treatment and use of substances recommended by incompetent persons. GPs play an important role in their treatment and they approach each patient individually, following current treatment protocols.

The diagnosis of urinary tract infections is based on clinical presentation, urine analysis, urine culture, and if necessary X-rays may be used<sup>4–6</sup>.

The initial treatment for recurrent urinary tract infections involves the use of antibiotics. In cases of recurring cystitis, low-dose antibiotic prophylaxis may be considered after the previous treatment has successfully sterilized the urine. This preventive antibiotic treatment should last for at least six months. If a new episode of infection occurs, it should be treated with a short or ultrashort course of antibiotics.

The challenges in treatment have become increasingly complex due to the aging population. This has led to higher instances of multiple health issues, increased medication use, decreased liver and kidney function, and a greater risk of side effects or complications during treatment. Recently, there has been growing interest in non-antibiotic prophylaxis, such as cranberries, D-mannose, and probiotics. However, the findings from studies on these methods have been inconsistent. It's also important to ensure an adequate intake of fluids, urinate before bedtime and after sex, avoid spermicide contraceptives, bubbly baths, and bath chemicals. It's better to shower rather than bathe, and wipe the genitals from front to back after using the toilet to prevent the spread of bacteria from the rectum. Good hygiene practices after using the toilet and treating constipation are also important<sup>7–9</sup>.

We aimed at stressing the importance of rational antibiotic use in recurrent urinary tract infections caused by *E. coli*.

## Prikaz bolesnika

Pacijentkinja starosti 63 godine. Od komorbiditeta ima hipertenziju, šećernu bolest tip 2 insulin nezavisnu, hroničnu opstruktivnu bolest pluća (lak restriktivni poremećaj ventilacije). Bivši pušač, ne konzumira alkohol, seksualno neaktivna. Negira alergije na lekove.

## Prvi pregled

Pacijentkinja se javlja na pregled kod izabranog lekara zbog povišene temperature poslednja dva dana ( $37,5^{\circ}\text{C}$ ) i učestalog mokrenja. Prethodno je bila na kontroli kod ortopeda zbog skidanja konaca nakon ugradnje proteze desnog kolena, rana zarasla uredno.

Na pregledu afebrilna, kardiopulmonalno kompenzovana (TA  $125/80 \text{ mmHg}$ ), frekvencija pulsa 80/min. Nije intoksicirana, odaje utisak lakog bolesnika. Auskultatorno nad srcem i plućima uredan nalaz. Bubrežne lože neosetljive na sukusiju, bolnost suprapubično. Pri pregledu navodi da ima česte urinarne infekcije. Prisutno učestalo mokrenje, ali bez osećaja pečenja prilikom mokrenja. Negira bol u lumbalnim ložama, mučinu i povraćanje.

Urađeni laboratorijski nalazi: sedimentacija (SE) 42 mm/h, leukociti (Le)  $6,6 \times 10^9/\text{L}$ , trombociti (Tr)  $635 \times 10^9/\text{L}$ , eritrociti (Er)  $4,05 \times 10^{12}/\text{L}$ , hemoglobin (Hgb) 119 g/L, fibrinogen 4,2 g/L, C-reaktivni protein (CRP) 20,9 mg/L, urea 9,2 mmol/L, kreatinin 97  $\mu\text{mol/L}$  (preračunato eGFR 57 ml/min/ $1,73 \text{ m}^2$ ). Urin: zamućen, relativne gustine 1,025, proteini 1 arb. jed, glukoza 0 arb. jed, metilketoni 0 arb. jed, urobilinogen 1 E.J, Hgb 0 arb. jed, nitriti 1 arb. jed, Er sveži 3, Le 20, bakterije brojne, epitelne ćelije vrlo brojne, hijalini cilindri 1. S obzirom na nalaz i klinički pregled, postavlja se dijagnoza cistitisa. Uključuje se antibiotska terapija levofloksacin 750 mg 1 x 1 sedam dana, paracetamol tablete 500 mg 3 x 1 po potrebi u slučaju bolova i febrilnosti, dat savet za dovoljan unos tečnosti. Zakazuje se kontrola sa nalazom urinokulture.

## Prva kontrola

Nakon četiri dana navodi da se bolje oseća, mokrenje manje učestalo, afebrilna. Urinokulturom izolovana *E. coli*  $> 100,000/1 \text{ ml}$  urina rezistentna na ampicilin, amoksicilin, amoksiklav sa klavulanskom kiselinom, trimetoprim-sulfametoksazol, ciprofloksacin, a osetljiva na cefaleksin, ceftriaxon, levofloksacin, nitrofurantoin, nitroxolin, fosfomicin. Kontrola se zakazuje nakon završene antibiotske terapije.

## Case report

The patient is a female 63 y/o. Her comorbidities include hypertension, diabetes, and chronic obstructive pulmonary disease (mild restrictive ventilation disorder). She is a former smoker, doesn't use alcohol, and is sexually inactive. She denies medication allergies.

## First examination

The patient visits her GP due to a two-day fever ( $37,5^{\circ}\text{C}$ ) and frequent urination. Previously, she had an orthopedic consultation to have her threads removed after the right knee prosthesis implantation. The wound healed well.

During the examination, she showed no signs of fever and had normal heart and lung function. Her blood pressure was  $125/80 \text{ mmHg}$ , and her heart rate was 80 beats per minute. She was not under the influence of any intoxicating substances and did not appear to be in urgent need of medical attention. Her heart and lung sounds were normal upon auscultation. Although she did not experience any tenderness in her costovertebral angles, she did report pain upon palpation in the suprapubic region. She mentioned that she often suffers from urinary tract infections (UTIs) and currently complains of frequent urination without pain. She denied experiencing any lumbar pain, nausea, or vomiting.

Lab work panel: Sedimentation rate (ESR) 42 mm/h, leukocytes (Le)  $6,6 \times 10^9/\text{L}$ , platelets (Ptl)  $635 \times 10^9/\text{L}$ , erythrocytes (Er)  $4,05 \times 10^{12}/\text{L}$ , hemoglobin (Hgb) 119 g/L, fibrinogen 4,2 g/L, C-reactive protein (CRP) 20,9 mg/L, urea 9,2 mmol/L, creatinine 97  $\mu\text{mol/L}$  (calculated eGFR 57 ml/min/ $1,73 \text{ m}^2$ ). Urine: cloudy, specific gravity 1,025, proteins 1 arb. unit, glucose 0 arb. unit, methylketones 0 arb. unit, urobilinogen 1 E.U, Hgb 0 arb. unit, nitrites 1 arb. unit, Er fresh 3, Le 20, abundance of bacteria and epithelial cells, hyaline casts 1. Based on the findings and clinical examination, she was diagnosed with cystitis. She was prescribed a seven-day course of levofloxacin 750 mg, once daily, paracetamol tablets 500 mg, 3 x 1, as needed, in the case of fever or pain, and advised to up her fluid intake. Her follow up was scheduled after receiving the urine culture results.

## First follow-up

After four days of therapy, she is feeling better with reduced urination frequency and is no longer running a fever. The urine culture showed the presence of *E. coli* at a concentration of  $> 100,000/1 \text{ ml}$ . The bacteria were resistant to ampicillin, amoxicillin, amoxicillin/clavulanic acid, trimethoprim-sulfamethoxazole, and ciprofloxacin, but sensitive to cephalexin, ceftriaxone, levofloxacin, nitrofurantoin, nitroxoline, and fosfomycin. A follow-up examination was scheduled after completing the course of antibiotics.

## Druga kontrola

Nakon završene antibiotske terapije pacijentkinja negira prisustvo urinarnih tegoba, bez osećaja jeze i febrilnosti. Kontrolni laboratorijski nalazi: CRP 3,6 mg/L; urin: bistar, bez bakteriurije, Le 3, nitriti 0 arb. jed, Er 0, malo epitelnih ćelija. Nedelju dana od završene antibiotske terapije kontrolna urinokultura negativna. Na kontrolnom pregledu navodi se da je ovo četvrta urinarna infekcija ove godine. U urinokulturi uvek izolovana *E. coli*. Prethodne infekcije sanirane antibiotskom terapijom, po preporuci drugog izabranog lekara, a na osnovu antibiograma trimetoprim-sulfametoksazolom, ciprofloxacinom u dva navrata i u jednom navratu samoinicijativnog uzimanja cefiksima od 400 mg. Terapija je trajala 10 dana. Pacijentkinja zabrinuta da neće moći da bude sprovedena planirana medicinska rehabilitacija u banjskim uslovima posle operacije kolena. Da se ne bi ponovo javila urinarna infekcija, lekar se odlučuje za uvođenje antibiotske profilakse nitrofurantoinom od 50 mg, jedna tableta uveče narednih šest meseci uz higijensko-dijjetetske mere. Data je preporuka, ukoliko se javi recidiv, da se započne lečenje po kratkom režimu uz uzimanje uzorka za urinokulturu pre započinjanja antibiotske terapije.

## Drugi pregled

Nakon tri meseca kod pacijentkinje se javljaju akutni respiratori simptomi sa pogoršanjem disanja. Urađenom reakcijom lančanog umnožavanja (engl. *polymerase chain reaction* - PCR) nazofaringealnog brisa potvrđeno je prisustvo Covid-19 infekcije. Od strane pneumoftiziologa ordiniran azitromicin kapsule 500 mg i pronison po šemi uz korekciju dezopstruktivne terapije i zakazana kompjuterizovana tomografija pluća. Preventivnu antibiotsku profilaksu za rekurentru urinarnu infekciju nastavlja po preporuci. Posle preležane Covid-19 infekcije dolazi do pogoršanja bubrežne funkcije sa nalazom uree 15,9 mmol/L i kreatinina 169 µmol/L. Savetovan dovoljan unos tečnosti i da se ponove parametri bubrežne funkcije i elektroliti za dve nedelje.

## Prva kontrola nakon drugog pregleda

Laboratorijski nalazi uree 11,2 mmol/l i kreatinina od 121 µmol/l (eGFR 43 ml/min/1,73 m<sup>2</sup>, CKD stadijum 3b), natrijum i kalijum u granicama referentnih vrednosti, fizičko-heminski nalaz urina uredan. Preporučeno je da nastavi sa antibiotskom profilaksom uz dovoljan unos tečnosti, neslanu dijetu i upućuje se na dalje praćenje kod nefrologa. Na ultrazvuku gornjeg abdomena, bubrega i male karlice opisuje se uredan nalaz osim početne steatoze jetre.

## Second follow-up

After the course of antibiotics, the patient was without UTI symptoms, fever, and chills. Control lab work panel: CRP 3,6 mg/L; urine: clear, no bacteriuria, Le 3, nitrites 0 arb. units, Er 0, few epithelial cells. A week after the course of antibiotics her control urine culture remained negative. At this follow-up, she states that this is her fourth UTI this year. Every time *E. Coli* was isolated. Previous infections were cured using antibiotics, prescribed by another GP (general practitioner), based on the results of the antibiogram - trimethoprim-sulfametoxazole, ciprofloxacin twice and once she took cefixim, 400 mg, on her own. The therapeutic course lasted 10 days. The patient was worried that she wouldn't be able to go through with rehabilitation in the spa facilities after her knee surgery. In order to prevent a new UTI, GP decided to start her on the prophylactic antibiotic course, nitrofurantoin, 50 mg, once in the evening, for six months, with all the necessary hygienic measures. She was advised to start a short-term course of antibiotics in accordance with the findings of urine culture, in the case of recidive.

## Second examination

After three months she experienced an acute respiratory infection with breathing deterioration. The polymerase chain reaction – PCR test of the nasopharynx was performed and she was diagnosed with Covid-19 infection. She was prescribed azithromycin, 500mg, and prednisone (until the resolution of her obstructive symptoms), by a pulmonologist. She was scheduled for a lung CT scan. She continued with her prophylactic antibiotic course for recurrent UTIs, as recommended. After Covid-19, her kidney function deteriorated with urea levels as high as 15,9 mmol/L and creatinine 169 µmol/L. She was advised to take enough fluids and repeat kidney panel lab work in two weeks.

## First follow-up after the second examination

Lab work panel: urea 11,2 mmol/l, creatinine 121 µmol/l (eGFR 43 ml/min/1,73 m<sup>2</sup>, CKD stage 3b), sodium and potassium were within the reference range, as well as urine. She was advised to continue with her prophylactic antibiotic course and take enough fluids, follow a low-sodium diet, and was referred to a nephrologist. Her abdominal ultrasound showed no abnormalities except for fatty liver.

## Druga kontrola nakon drugog pregleda

Pacijentkinja dolazi kod izabranog lekara nakon dva meseca sa izveštajem nefrologa. U analizi krvi nakon dva meseca diferencijalna krvna slika uredna, hepatogram, elektroliti u granicama referentnih vrednosti, dobra regulacija lipidnog statusa (LDL 1,8 mmol/L), glikemija 6,1 mmol/L, HbA1C 33 mmol/L, kreatinin 101 µmol/L, klirens kreatinina 50 ml/min.

Na pregledu nefrologa savetovan nastavak nitrofurantoin kapsula od 50 mg i dalje najmanje šest meseci i planirana kontrola sa nalazima uree, kreatinina, mokraćne kiseline, elektrolita, krvne slike, fizičko-hemijske analize urina i urinokulturom.

Izabrani lekar savetuje praćenje bubrežne funkcije, glikemije, lipidnog statusa i arterijske tenzije. Nakon završene antibiotske profilakse razmotriti upotrebu neantibiotiske profilakse. U slučaju ponovne pojave urinarnih tegoba savetovano da se uradi urinokultura i započne lečenje sa jednokratnom primenom fosfomicin granula 3 g, jedna doza uveče pre spavanja na prazan stomak i bešiku. U slučaju da ne dođe do poboljšanja u naredna 2–3 dana ili pojave febrilnosti, preporučuje se lečenje drugim lekom, sedmodnevnim režimom na osnovu nalaza urinokulture u cilju sprečavanja komplikacija.

## Diskusija

Urinarne infekcije, iako se u najvećem broju slučajeva završavaju povoljnim ishodom, značajne su zbog svoje učestalosti i mogućnosti nastanka komplikacija. Najveći problem je sve češća zloupotreba antibiotika i sve veća rezistencija bakterija na iste, posebno *E. coli*. Čak i ako se novi antibiotici pojave na tržištu, postoji mogućnost da se brzo razvije rezistencija *E. coli* na ove antibiotike. Mehanizmi pomoću kojih *E. coli* postaje otporna na antibiotike variraju. Stoga je praćenje preporuka za upotrebu antibiotika u odgovarajućem trajanju ključno da bi se minimizirala mogućnost za rezistenciju i da bi se smanjili recidivi.

Da bi se sprečila prekomerna upotreba antibiotika, dostupnost samoinicijativnog uzimanja lekova treba da bude ograničena propisima. Obraćanje pažnje na higijenu, posebno kod pojedinaca koji putuju u endemska područja ili osoba koje su često u okolnostima sa visokim rizikom od izloženosti bakterijama otpornim na antibiotike (npr. zdravstvene jedinice) može smanjiti zaražavanje. Upotreba neantimikrobne profilakse mogla bi efikasno da smanji upotrebu antibiotika<sup>10, 11</sup>.

Iz izloženog prikaza se može zaključiti da je u terapijskom pristupu kod urinarnih infekcija, a posebno rekurentnih, najbitnija primena antibiotske terapije po antibiogramu. U slučaju rekurentnih uroinfekcija moguće je dugotrajno давanje antibiotika u manjim dozama, tzv. profilaksa. Profilaksa može biti kontinuirano uzimanje profilaktičke doze leka svako veče ili tri puta nedeljno. Od antibiotika se u profilaksi

## Second follow-up after the second examination

The patient visited her GP after two months, with a nephrologist report. Her lab work panel was mainly within reference range (complete blood count, hepatogram, electrolytes, lipid status (LDL 1,8 mmol/L)), glycemia 6,1 mmol/L, HbA1C 33 mmol/L, creatinine 101 µmol/L, creatinine clearance 50 ml/min.

A nephrologist recommended that she should continue taking nitrofurantoin, 50 mg, for at least six months. She should also come in for a follow-up including lab work (urea, creatinine, uric acid, electrolytes, CBC, urine, and urine culture).

Her general practitioner recommended a follow-up to monitor her kidney function, blood sugar levels, cholesterol, and blood pressure. Once she finished the antibiotic treatment, she was advised to consider non-antibiotic prevention methods. If she experiences recurring urinary symptoms, she should undergo a urine culture and, if necessary, start treatment with a one-time dose of fosfomycin granules (3 g) before bedtime on an empty stomach. If the symptoms persist beyond 2-3 days or if a fever develops, she should take another medication for seven days based on the urine culture results to prevent complications.

## Discussion

Urinary tract infections, though often resolving on their own, are concerning due to their frequency and potential for complications. The main problem is the overuse of antibiotics and the increasing resistance of bacteria, particularly *E. coli*. Even with the development of new antibiotics, there is a risk that *E. coli* may rapidly develop resistance to these as well. The mechanisms of antibiotic resistance in *E. coli* are diverse. Therefore, it is crucial to follow the recommended duration of antibiotic treatment in order to minimize the risk of antibiotic resistance and recurrent infections.

To prevent the overuse of antibiotics, their availability should be limited by legal regulations if patients wish to use them on their own accord. Paying attention to hygiene, especially for people traveling through areas with high rates of infection or those in high-risk situations, such as in healthcare facilities, may decrease infections. The use of non-antibiotic prophylaxis could effectively reduce the use of antibiotics<sup>10, 11</sup>.

Our case report highlights the importance of using antibiotics based on the antibiogram in treating urinary tract infections, particularly in cases of recurrent UTIs. For recurrent UTIs, it's recommended to prescribe antibiotics in low doses, known as prophylaxis. Prophylaxis can involve the continuous use of prophylactic doses of the medication every night or

koriste: nitrofurantoin 50–100mg, kotrimoksazol 480 mg, cefaleksin 250 mg i norfloksacin 200 mg. Ako se rekurentni cistitisi javljaju u menopauzi, moguće je davanje hormonske terapije (intravaginalna primena estrogena) kao rešenje uzroka<sup>12</sup>.

Meta-analiza sedam studija (875 pacijenata) pokazala je da je povećan unos tečnosti smanjio ukupan rizik od rekurentnih urinarnih infekcija za 64%<sup>13</sup>.

*E. coli* oslobađa toksine koji oštećuju tkiva domaćina, što dovodi do infekcija gornjeg urinarnog trakta. Teški slučajevi mogu da dovedu do opasnih bolesti, kao što su bakterijemija, septikemija i urosepsa. Sve veća otpornost na antibiotike doveo je do recidiva i hroničnosti infekcije, čineći lečenje izazovnim i komplikovanim. Stoga, najveći prioritet u istraživanju infekcija urinarnog trakta treba da bude razvoj novih, efikasnih alternativnih terapija, jer imaju potencijal da značajno poboljšaju kvalitet života miliona ljudi i smanje ukupnu upotrebu antibiotika<sup>14</sup>.

Savremena literatura pruža dosta podataka o fitoterapiji<sup>15</sup>. Prema podacima 50 studija sa 8 857 učesnika, proizvodi od brusnice smanjuju rizik od simptomatskih, rekurentnih infekcija kod žena, dece i odraslih podložnih infekcijama urinarnog trakta posle intervencija. Trenutno dostupni dokazi ne podržavaju upotrebu kod starijih osoba, pacijenata sa problemima pražnjena bešike i trudnica<sup>15</sup>. Čini se da D-manoza ima veliki potencijal u smanjenju rekurentnih infekcija sa minimalnim neželjenim efektima. Ukupna slika pretkliničkih i kliničkih studija sa D-manozom je povoljna, i pokazalo se da je D-manoza relativno bezbedna i dobro se podnosi. Ipak, kvalitet ovih studija ostavlja nešto za dodatna ispitivanja<sup>16</sup>.

## Zaključak

Mnogi protokoli pokušavaju da smanje pojavu, tj. vraćanje urinarnih infekcija. Lečenje antibioticima po antibiogramu, kao i antibiotska profilaksa (kontinuirana i postkoitalna profilaksa) su se pokazali najdelotvornijim u sprečavanju recidivantih cistitisa. Metod i pristup lečenju zavise od učestalosti i težine simptoma.

three times a week. Antibiotics used in prophylaxis include: nitrofurantoin 50–100mg, cotrimoxazole 480 mg, cephalixin 250 mg, and norfloxacin 200 mg. For recurrent cystitis during menopause, hormonal therapy such as intravaginal estrogen may be prescribed as a solution<sup>12</sup>.

Meta-analysis of seven studies (875 patients) showed that a high intake of fluids reduced the total risk of recurrent UTIs by 64%<sup>13</sup>.

*E. coli* releases toxins that damage the host tissues, leading to infections of the upper urinary tract. Severe cases may lead to dangerous conditions, such as bacteremia, septicemia, and urosepsis. Ever growing resistance to antibiotics led to recidives and chronic infections, making the treatment even more challenging and complicated. Therefore, the highest priority in UTI research should be the development of new, effective alternative therapies because they have the potential to significantly improve life quality of millions of people and reduce the use of antibiotics<sup>14</sup>.

Contemporary literature offers a lot of data on phytotherapy<sup>15</sup>. According to data from 50 studies, with 8.857 participants, cranberry products reduce the risk of symptomatic recurrent infections in women, children, and adults susceptible to UTIs after interventions. Currently, available data do not support its use in older persons, patients with bladder emptying problems, and pregnant women<sup>15</sup>. It seems that D-mannose has great potential to reduce recurrent infections with minimal side effects. The summing picture of pre-clinical and clinical studies with D-mannose is favorable and it proved relatively safe and well tolerated. Nevertheless, the quality of these studies leaves some questions without answers<sup>16</sup>.

## Conclusion

Many protocols have been shown to reduce the occurrence of urinary tract infections. Antibiotic treatment based on the antibiogram, as well as antibiotic prophylaxis (continuous and post-coital), has proven to be the most effective method for preventing recurrent cystitis. The choice of treatment method and approach depends on the frequency and severity of symptoms.

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