MEDICAL SCIENCE MONITOR BASIC RESEARCH

PHARMACEUTICAL RESEARCH

e-ISSN 2325-4416
© Med Sci Monit Basic Res, 2024; 30: e943939
DOI: 10.12659/MSMBR.943939

Received: 2024.01.26
Accepted: 2024.05.10
Published: 2024.06.26

A Comparison of Outcomes from Antibiotic Treatment with and without Probiotics in 897 Patients with Lower Urogenital Tract Infections, Including Cystitis, Urethritis, Prostatitis, and Vulvovaginitis

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Data Collection B
Statistical Analysis C
Data Interpretation D
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Financial support: None declared
Conflict of interest: None declared

Background: Urogenital bacterial infections have a high incidence in humans. The most frequent cause of infections of the urogenital tract is gram-negative bacteria. Antibiotics are very effective in curing infectious diseases but they are accompanied by health complications. Probiotics are live microorganisms that are believed to confer a beneficial effect on human health when consumed in adequate amounts. This study aimed to compare outcomes from antibiotic treatment with and without the use of probiotics in 897 patients with lower urogenital tract infections, including cystitis, urethritis, prostatitis, and vulvovaginitis.

Material/Methods: A total of 897 patients aged 18 to 55 years were included in this research. Patients were divided into an intervention group including 460 patients (254 women, 206 men) and a comparison group including 437 patients (240 women, 197 men). The probiotics received by patients were capsules of ProBalans®. The diagnosis of cystitis, urethritis, prostatitis, vulvovaginitis, and sexually transmitted infection was done using several tests, and antibiotics were used for treatment. Qualitative data were analyzed using the chi-square or Fisher exact test.

Results: We found a significant difference regarding patients' impressions of improvement after therapy between patients in the intervention group and the comparison group.

Conclusions: Use of probiotics together with antibiotics in the treatment of urogenital tract infection can help to reduce the adverse effects of antibiotics, increase the efficiency of antibiotic therapy, and reduce bacterial resistance to antibiotics. However, further research is needed to confirm these potential health benefits.

Keywords: Probiotics • Antibiotics • Urinary Tract Infection • Reproductive Tract Infections • Health Benefits

Full-text PDF: https://www.basic.medscimonit.com/abstract/index/idArt/943939

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Introduction

Urinary tract infections (UTIs) are among the most common bacterial infections worldwide, occurring in both community and healthcare settings. Bacteria are the main causative agents of these infections, although more rarely, other microorganisms, such as fungi and some viruses, have been reported to be responsible for ITUs. Uropathogenic *Escherichia coli* is the most common causative agent of UTIs, followed by *Klebsiella pneumonia*, *Proteus mirabilis*, *Enterococcus faecalis,* and Staphylococcus spp. [1].

Urogenital infections have a high incidence in humans, as a result of many favorable factors and possible routes via which bacteria can attack organs in the urogenital tract. The urogenital tract is in direct contact with the external environment, which has affects the risk of bacterial infections. Factors that contribute to infections of the urogenital tract include congenital anomalies of the urogenital system, pathology in the urogenital tract that develops during the lifetime, age, general immune status, sexual and lifestyle habits, and iatrogenic infections, such as endoscopic or operative interventions of the urogenital tract performed for diagnostic or curative purposes. The anatomy, physiologic function, and topography of the urogenital tract strongly favors the development of infections.

The microorganisms attack the urogenital tract via anterograde, retrograde, hematogenous, lymphogenous, per continuitatem (direct spread), and iatrogenic transport pathways. The most frequent ways in which these infectious agents attack the urogenital system are via retrograde and iatrogenic routes.

Sexually transmitted infections (STIs) are disease processes by transmission through sexual contact. STIs involve the transmission of organisms between sexual partners through different routes of sexual contact, either oral, anal, or vaginal. The 8 most common cause of STIs are Chlamydia spp., *Neisseria gonorrhea*, *Treponema pallidum*, *Trichomonas vaginalis*, herpes simplex virus, HIV, and human papilloma virus [2].

Probiotics are supplements that contain non-pathogenic microbes such as bacteria and yeast that colonize the gut and can potentially yield a variety of health benefits [1,3]. There are various ways the probiotics can work inside our body, including stimulating the growth of good commensal microbes and inhibiting the growth of pathogenic microorganisms [3].

The term probiotics came into common use after 1980. The introduction of this concept is generally attributed to Nobel laureate Ilija Iljić Mećnikov, who ascribed the longevity of Bulgarian peasants to their habit of regular yogurt consumption [4]. In 1907, Mećnikov proposed that "the dependence of intestinal microbes on food makes it possible to adopt measures to modify the flora in our body and to replace harmful microbes with beneficial microbes" [5]. A large expansion of the potential market for probiotics has led to demands for scientific validation of the supposed benefits of these microorganisms [6].

It has been proven that antibiotic treatment can cause diarrhea in 20% of patients, and this development is more pronounced in children. The mechanism of diarrhea development during antibiotic therapy is a consequence of disturbance of the bacterial flora in the intestine, which then changes the metabolism of carbohydrates, leading to reduced absorption of fatty acids and osmotic diarrhea as a result.

Antibiotics attack beneficial gut microbes, resulting in altered microbiota composition [7]. Antibiotic treatment causes changes in the composition of the gut microbiota, alters the production of mucin and cytokines, and weakens the intestinal epithelial cell barrier [8]. A systematic review and meta-analysis for probiotic supplementation during antibiotic treatment conducted in 2023 showed that probiotic supplementation during antibiotic therapy was not influential on gut microbiome diversity indices [9]. However, the main limitations of the study were a limited number of studies for probiotics and antibiotic treatment, low sample sizes, use of different bacterial strains as probiotics, varied type and dose of antibiotics, inclusion of patients with different health conditions, and variation in age across the included studies.

In this study, we aimed to compare outcomes from antibiotic treatment with and without the use of probiotics in 897 patients with lower urogenital tract infections, including cystitis, urethritis, prostatitis, and vulvovaginitis.

Material and Methods

Ethics Statement

The study received approval from the Institutional Review Board at the University ''Hasan Prishtina'' Prishtine, Kosovo, ensuring that it adhered to ethical guidelines for research involving human participants. Informed consent was obtained from all participants before their involvement in the study. Participants were provided with a detailed information sheet explaining the purpose of the research, procedures, and potential risks and benefits. Confidentiality was maintained by assigning unique identification numbers, and all data were stored securely, accessible only to the research team. Additionally, debriefing was provided to participants upon study completion, clarifying the study objectives and addressing any concerns.

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Study Design

This study used a randomized controlled trial design to investigate the outcomes from antibiotic treatment with and without the use of probiotics in 897 patients with lower urogenital tract infections, including cystitis, urethritis, prostatitis, and vulvovaginitis.

Participants

A total of 897 patients aged 18 to 55 years were included in this research. Patients were randomized into an intervention group or a comparison group. Patients in both groups had infections of the lower urogenital tract, mainly cystitis, urethritis, prostatitis, or vulvovaginitis. The exclusion criteria were patients with compromised hormonal analyses, psychogenic problems, and those who had received prior therapy, such as with antibiotics or antidepressants. Patients with a history of depression, poor health, and previous allergic reactions were also excluded from the study.

Procedure

We collected information regarding patients' age, history of previous diseases, and possible allergies. Before treatment, after the end of treatment, and in follow-up visits, the following tests were conducted in all patients: urine culture, sperm culture, urethral smear, prostatic smear, and tests for chlamydia, urea plasma, mycoplasma, and *Neisseria gonorrhea*. Patients with persistent infection after treatment were tested for resistance to the administered antibiotics. Microbiological analysis for each patient was conducted 5 days after the end of antibiotic therapy. An experienced urologist and microbiologist performed all procedures.

Patients in both groups before the start of therapy underwent microbiological testing, including urine culture, sperm culture, urethral swab, vaginal or vulvar swab, expressed prostatic excretion, tests for chlamydia, urea plasma, and mycoplasma, and routine hematological and biochemical analyses. Antibiotic susceptibility testing using the disk diffusion method was conducted in patients in both groups and in patients with persistent infection after the end of therapy. All microbiological analyses were performed at the National Institute of Public Health of Kosovo and in private microbiological laboratories in Kosovo.

All patients in the intervention group were prescribed probiotics twice a day during the duration of antibiotic therapy and for 7 days after the end of the antibiotic therapy. The probiotics received by patients were capsules of ProBalans® (*Lactobacillus acidophilus* LA3, *Bifidobacterium animalis* ssp. *lactis* BLC1, and *L. casei* BGP93; 1×10^9 colony-forming units [CFU]). It was explained to each patient that probiotics should be taken 3 h after taking antibiotics and that probiotics should not be consumed together with drinks that contained alcohol or with hot foods or drinks. The diagnosis of cystitis, urethritis, prostatitis, vulvovaginitis, and sexually transmitted infection (STI) was done based on urine culture, sperm culture, urethral smear, prostatic smear, and tests for chlamydia, ureaplasma, mycoplasma, and *Neisseria gonorrhoeae*. The treatment of patients with antibiotics was done based on the results of antibiotic susceptibility testing bacterial pathogens before start of therapy, as well as their subjective tolerance, in both groups. The following antibiotics were used to treat patients in this study: amoxicillin, cefixime, ceftriaxone, cephalosporin, ciprofloxacin, levofloxacin, clarithromycin, gentamicin, azithromycin, and doxycycline. Amoxicillin, cefixime, ceftriaxione, cephalosporins, ciprofloxacin, levofloxacine, clarithromycine, gentamicin, azithromycin, and doxycycline are used for treatment of cystitis, urethritis, prostatitis, vulvovaginitis, and STIs. The duration of antibiotic therapy was 10 to 14 days. Patients in the comparison group were not prescribed probiotic therapy. All patients were supervised before therapy, during therapy, and after antibiotic and probiotic therapy.

The Clinical Global Impression of Improvement (CGI-I) and Patient Global Impression of Improvement (PGI-I) scales were also administered to patients in both groups. The PGI-I evaluates all aspects of a patient's health and assesses if there has been improvement or decline in clinical status, whereas the CGI-I provides brief assessment of the clinician's view of a patient's condition prior to and after the therapy. In the PGI-I, patients were asked to describe their experience with the treatment received (antibiotics plus probiotics or antibiotics alone). In the CGI-I, treating physicians were asked to describe their patients' experience with the treatment received. In both scales, patient experience and clinician observation are categorized in 5 scores: very good, good, no change, bad, and very bad.

The present study was conducted in accordance with the applicable laws and regulations in Kosovo, and in accordance with the ethical principles laid down in the Declaration of Helsinki. The study began in January 2020 and ended in December 2022.

Data Analysis

The data were analyzed using IBM SPSS 22.0 (IBM Corp., Armonk, NY, USA). The obtained data are presented as median and range for quantitative data and as number and percentage for qualitative data. Testing of quantitative data with a normal distribution was done using one-way analysis of variance and data with a non-normal distribution were analyzed with the Kruskal-Wallis test. Numerical variables were assessed for a normal distribution using the Shapiro-Wilk test

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of normality. Testing of quantitative data between groups with a normal distribution was performed using an unpaired *t* test, and the Mann-Whitney test was used for data with a non-normal distribution. Qualitative data were analyzed with the chi-square test or Fisher exact test. *P*<0.05 was considered statistically significant.

Results

Participation and Randomization of Patients

A total of 897 patients were included in this study. The intervention group included 460 patients (254 women and 206 men), with age range 18 to 25 years. The comparison group included 437 patients (240 women and 197 men), with age range 18 to 55 years. Patients in both groups had infections of the lower urogenital tract, mainly cystitis, urethritis, prostatitis, or vulvovaginitis. Most patients were from Kosovo. All patients from both groups responded to the examinations required by our study in **Figure 1**.

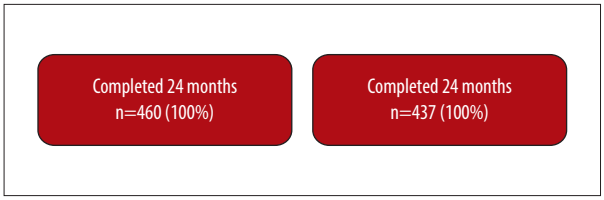

Figure 1. Patients' participation and randomization to the project's examinations.

As shown in **Table 1**, there were no significant differences between the intervention and comparison groups in terms of patient characteristics and results of microbiological analysis prior to therapy. In the intervention group, 187 patients had cystitis (157 women and 30 men), and 163 patients had urethritis and/or vulvovaginitis (97 women and 66 men). In the intervention group, 121 patients (78 women and 43 men) had STIs, and 110 men had prostatitis. In the comparison group, 178 patients (145 women and 33 men) had cystitis, 169 patients (95 women and 74 men) had urethritis and/or vulvovaginitis, 108 patients had STIs (66 women and 42 men), and 90 men had prostatitis. The most frequent STI in both groups

Table 1. Urogenital infections in both groups by sex (2020-2022).

Urogenital infection	Intervention group		Comparison group		Total	*P* value
	Men (n=206)	Women (n=254)	Men (n=197)	Women (n=240)	Both sexes (n=897)	
	n (%)	n (%)	n (%)	n (%)	Total N (%)	
Age (years), Median (range)	32 (18-55)	29 (18-55)	31 (18-55)	30 (18-55)	897 (100.0)	*P*>0.05
Cystitis	30 (14.6)	157 (61.8)	33 (16.8)	145 (60.4)	365 (40.7)	F, *P*>0.05 M, *P*>0.05
Urethritis	66 (32.0)	/	74 (37.6)	/	140 (15.6)	M, *P*>0.05
Vulvovaginitis	/	97 (38.2)	/	95 (39.6)	192 (21.4)	F, *P*>0.05
Prostatitis	110 (53.4)	/	90 (45.7)	/	200 (22.3)	M, *P*>0.05
Total	**206 (44.8)**	**254 (55.2)**	**197 (45.1)**	**240 (54.9)**	**897 (100.0)**	***P*>0.05**
STI	43 (20.9)	78 (30.7)	42 (21.3)	66 (27.5)	229 (25.5)	F, *P*>0.05 M, *P*>0.05
Gonorrhea	9 (4.4)	21 (8.3)	6 (3.0)	12 (5.0)	48 (5.4)	F, *P*>0.05 M, *P*>0.05
Chlamydia	10 (4.9)	20 (7.9)	23 (11.7)	35 (14.6)	88 (9.8)	F, *P*>0.05 M, *P*>0.05
Ureaplasma	16 (7.8)	18 (7.1)	10 (5.1)	14 (5.8)	58 (6.5)	F, *P*>0.05 M, *P*>0.05
Mycoplasma	8 (3.9)	19 (7.5)	3 (1.5)	5 (2.1)	35 (3.9)	F, *P*>0.05 M, *P*>0.05

M – men; F – women; STI – sexually transmitted infection.

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Table 2. Results of microbiological analyses before treatment.

Bacteria	Sperm culture**	Urine culture	Urethral smear**	Vaginal and vulvar smear***	Expressed prostatic excretion	Total
	n (%)*	n (%)*	n (%)*	n (%)*	n (%)**	N (%)
E. coli	68 (7.6)	253 (28.2)	63 (7.0)	110 (12.3)	107 (11.9)	601 (67.0)
S. aureus	151 (16.8)	206 (23.0)	160 (17.8)	98 (10.9)	53 (5.9)	668 (74.5)
S. agalactiae	70 (7.80)	/	68 (7.58)	117 (13.04)	94 (10.48)	349 (38.91)
Enterococcus spp.	115 (12.8)	240 (26.8)	113 (12.6)	168 (18.7)	150 (16.7)	786 (87.6)
Proteus mirabilis	/	198 (22.07)	/	/	/	198 (22.1)
Total	**404 (45.0)**	***897 (100.0)**	**404 (45.0)**	**493 (55.0)**	**404 (45.0)**	**2602 (100.0)**

* Percentage of total patients in both groups; ** total for men in both groups; *** total for women in both groups.

Table 3. Patients in the intervention group with persistent infection after antibiotic and probiotic therapy.

Bacteria	Sperm culture	Urine culture	Urethral smear	Vaginal and vulvar smear	Expressed prostatic excretion
	n (%)	n (%)	n (%)	n (%)	n (%)
E. coli	/	460/5 (1.1)	/	/	/
S. aureus	206/9 (2.0)	/	206/7 (1.5)	240/6 (1.3)	206/10 (2.2)
S. agalactiae	/	/	/	/	/
Enterococcus spp.	/	/	/	/	206/8 (1.7)
Proteus mirabilis	/	/	/	/	/
Total, n (%)	**206/9 (2.0)**	**60/5 (1.1)**	**206/7 (1.5)**	**240/6 (1.3)**	**206/18 (3.9)**

was chlamydia infection. There were no statistically significant differences ($P>0.05$) in the frequency of urogenital infections between the groups for either sex (**Table 2**).

According to age group, there was no significant difference in terms of morbidity in both groups.

Results Before Treatment

Table 2 shows the results of microbiological analyses before the start of treatment for both groups. In the analysis of 2602 microbiological samples, urinary tract infections were most frequently caused by *Enterococcus* spp., followed by *Staphylococcus aureus* and *E. coli*.

Results After Treatment

Table 3 presents the results of antibiotic susceptibility testing for patients with persistent infection after 10 to 14 days of therapeutic treatment with antibiotics together with probiotics.

Among 460 patients with persistent infection, only 45 (9.8%) required further treatment. The pathogen most frequently showing antimicrobial resistance was *S. aureus*.

Among 437 patients in the comparison group with persistent infection after treatment with antibiotics alone, 114 (26.1%) required further treatment. The results of antibiotic susceptibility testing showed that *S. aureus* was most frequently resistant to antibiotic treatment (**Table 4**). The findings in both groups showed that treatment with antibiotics administered together with the probiotics was superior to treatment with antibiotics alone in treating urinary tract infections, including chlamydia, ureaplasma, and mycoplasma infections, as well as STIs.

Bacterial Antibiotic Resistance Before and After Treatment

Table 5 shows that low bacterial resistance was present in the total sample in our study. After antibiotic treatment together with probiotic therapy in the intervention group, patients

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Table 4. Patients with persistent infection in the comparison group after antibiotic therapy alone.

Bacteria	Sperm culture	Urine culture	Urethral smear	Vaginal and vulvar smear	Expressed prostatic excretion
	n (%)	n (%)	n (%)	n (%)	n (%)
E. coli	/	437/10 (2.3)	/	/	/
S. aureus	197/8 (1.8)	/	197/11 (2.5)	240/14 (3.2)	197/13 (3.0)
S. agalactiae	/	437/3 (0.7)	197/4 (0.9)	240/11 (2.5)	/
Enterococcus spp.	197/7 (1.6)	437/6 (1.4)	197/6 (1.4)	240/12 (2.8)	197/9 (2.1)
Proteus mirabilis	/	/	/	/	/
Total, n (%)	**197/15 (3.4)**	**437/19 (4.4)**	**197/21 (4.8)**	**240/37 (8.5)**	**197/22 (5.0)**

Table 5. Bacterial antibiotic resistance before treatment in both groups.

Bacterial/ antibiotic resistance	*E. coli*	*S. aureus*	*S. agalactiae*	*Enteroc.* Spp.	*Proteus Mirab.*	Chlamydia	Ureo-plasma	Myco-plasma	Gonorrhea
Amoxicillin	+++	+++	+++	+++	R	R	R	R	+++
Cefixime	++	++	+++	+++	+++	R	R	R	++
Ceftriaxone	++	+++	+++	+++	++	R	R	R	+++
Cefalexin	+	++	+++	++	+	R	R	R	+
Ciprofloxacin	+++	++	+++	+++	+++	++	++	+	++
Levofloxacin	+++	+++	+++	+++	+++	+++	+++	++	+
Clarithromycin	++	++	++	+++	+++	+++	+++	+++	++
Gentamicin	+++	+	+++	+++	++	+	+	/	+
Azithromicin	++	+++	++	+	++	+++	+++	+++	+
Doxycycline	++	+	+++	+++	+++	++	+++	+++	/

+ – Weak sensitivity; ++ – intermediate sensitivity; +++ – very high sensitivity; R – resistant.

with persistent infection did not show significant bacterial resistance (**Table 6**).

A significant difference was observed between the intervention group and comparison group in terms of antibacterial resistance, which was much higher in the comparison group for *E. coli*, *S. aureus*, and *Enterococcus* spp. (**Tables 6, 7**).

Therapy Experience and Adverse Effects in Both Groups

Table 8 shows the results for both patient groups in describing their experiences while receiving each type of therapy. A significant difference was found in the PGI-I and CGI-I scales between the intervention and comparison groups. **Table 9** shows there was a very large difference in adverse effects between the intervention group and comparison group, with much fewer adverse effects in the intervention group, especially for diarrhea.

Discussion

This was the first study comparing the effect of treatment with 10 to 14 days of antibiotic therapy administered with probiotics vs antibiotics alone on urogenital tract infections. Antibiotics were used according to the results of microbiological analyses and antibiotic susceptibility testing prior to therapy. In the intervention group, probiotics were given twice a day for 3 weeks, administered 3 h after taking antibiotics. Among 2602 microbiological samples, urinary tract infections

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Table 6. Antibacterial resistance 1 week after therapy (intervention group).

Bacterial/ antibiotic resistance	*E. coli*	*S. aureus*	*S. agalactiae*	*Enteroc.* Spp.	*Proteus Mirab.*
Amoxicillin	+++	++	/	+++	/
Cefixime	+	++	/	+++	/
Ceftriaxone	++	+++	/	+++	/
Cefalexin	+	++	/	+	/
Ciprofloxacin	+++	++	/	+++	/
Levofloxacin	+++	++	/	+++	/
Clarithromycin	+	++	/	+++	/
Gentamicin	++	+	/	++	/
Azithromicin	+	++	/	+	/
Doxycycline	+	+	/	++	/

+ – Weak sensitivity; ++ – intermediate sensitivity; +++ – very high sensitivity.

Table 7. Antibacterial resistance 1 week after therapy (comparison group).

Bacterial/ antibiotic resistance	*E. coli*	*S. aureus*	*S. agalactiae*	*Enteroc.* Spp.	*Proteus Mirab.*
Amoxicillin	+	R	/	+	/
Cefixime	R	+	/	++	/
Ceftriaxone	+	++	/	R	/
Cefalexin	R	R	/	R	/
Ciprofloxacin	++	R	/	+++	/
Levofloxacin	+++	+	/	++	/
Clarithromycin	R	R	/	+	/
Gentamicin	+	R	/	++	/
Azithromicin	R	+	/	+	/
Doxycycline	R	R	/	++	/

+ – Weak sensitivity; ++ – intermediate sensitivity; +++ – very high sensitivity; R – resistant.

were most frequently caused by *Enterococcus* spp., followed by *S. aureus* and *E. coli*. STIs were more frequent in patients aged 20 to 40 years.

In a comparison between groups of the therapeutic effectiveness of antibiotics in urogenital infection, the intervention group showed much better antibiotic efficacy than the comparison group. Bacterial resistance to antibiotics was also significantly lower in the intervention group. Patients' and physicians' impressions of improvement, according to the PGI-I and CGI-I scales, were also more favorable in the intervention group, which received antibiotic therapy administered together with probiotics. The adverse effects of the therapy also showed a marked reduction in the intervention group.

According to the literature, there are no clinical study data on the effect of probiotics in the therapeutic management of urogenital tract infections. Despite developments in modern

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Table 8. Global therapeutic and clinical impressions.

Global therapeutic and clinical impressions	Intervention group	Comparison group	*P* value
PGI-I, n (%)	**n=460 (100%)**	**n=437 (100%)**	
Very good	230 (50.0)	80 (18.3)	*P*<0.05
Good	180 (39.1)	100 (22.9)	*P*<0.05
No change	45 (9.8)	130 (29.7)	*P*<0.05
Bad	5 (1.1)	97 (22.2)	*P*<0.05
Very bad	0 (0.0)	30 (6.9)	*P*<0.05
CGI-I, n (%)	**n=460 (100%)**	**n=437 (100%)**	
Very good	220 (47.8)	83 (19.0)	*P*<0.05
Good	172 (37.39)	102 (23.34)	*P*<0.05
No change	61 (13.26)	121 (27.69)	*P*<0.05
Bad	7 (1.52)	99 (22.65	*P*<0.05
Very bad	0 (0.0)	32 (7.32)	*P*<0.05

PGI-I – patient global impression of improvement; CGI-I – clinical global impression of improvement.

Table 9. Adverse effects in both groups.

Adverse effects	Intervention group	Comparison group	*P* value
	n (%)	n (%)	
Total, N (%)	**460 (100)**	**437 (100)**	
Adverse effects, n (%)			
– Headache	2 (0.43)	7 (1.60)	*P*<0.05
– Diarrhea (AAD)	3 (0.65)	86 (19.68)	*P*<0.05
– Muscle pain	2 (0.43)	3 (0.69)	*P*>0.05
– Dizziness	1 (0.22)	3 (0.69)	*P*>0.05
– Dyspepsia	4 (0.87)	12 (2.75)	*P*<0.05
Serious adverse effects, n (%)	0 (0.0)	2 (0.46)	*P*<0.05

medicine and the discovery of new antibiotics, the incidence of urinary tract infections remains high.

The benefit of probiotics in the treatment and prevention of many infections and disorders has been confirmed in previous clinical studies. Probiotics strengthen the epithelial barrier and prevent pathogenic microorganisms from colonizing the epithelial mucosa and producing antimicrobial substances, which prevents diarrheal diseases, inflammatory bowel disease, and urogenital infection and helps in the treatment of gastric ulcers, management of obesity, and strengthening of the immune system [10].

The effects of *L. acidophilus* and *L. casei* are not limited to promoting human health; these probiotics also have antibacterial effects against pathogenic bacteria [11]. *L. acidophilus* and *L. casei* directly interact with cancer cells and indirectly inhibit the growth of *E. coli* by releasing natural bacteriocin and various metabolites [11]. The use of probiotics also normalizes the vaginal microbiota and helps to cure existing infections and prevent the recurrence of urinary tract infection [12]. However, Barrons and Tassone emphasized that lactobacilli for urinary tract infection prophylaxis remains inconclusive owing to the small research sample [13]. Nevertheless, the combination of *L. rhamnosus* GR-1 and *L. reuteri* RC-14 can colonize the vagina and decrease the presence of coliform bacteria and mycotic pathogens, preventing the occurrence of recurrent urinary tract infection [14].

Most studies in this field have focused on the prevention and cure of urinary tract infection in women; there are few data on the prevention of urinary tract infection in children. This is an important problem, considering the connection between renal fibrotic changes and febrile urinary tract infection in

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children [15]. According to a meta-analysis conducted in 2016 including data from 10 clinical studies, probiotics used as monotherapy did not have a beneficial effect in reducing the incidence or recurrence of urinary tract infection, but moderate efficacy was observed when probiotics were used together with antibiotics [16].

According to Reid et al and Bruce et al, consumption of probiotics containing *L. acidophilus*, 5 to 10 billion colony-forming units/day helps in maintaining gastrointestinal and immune health [17-20]. Darouiche et al investigated the use of probiotics in patients with neurogenic bladder. In treated patients, they noticed a decrease in urinary bladder infections [17,21,22]. Certain strains of lactobacilli probiotics can help reduce inflammation by regulating the function of cytokines as well as the creation of enzymes that destroy harmful bacteria [18,22-24]. Probiotics also stimulate the secretion of immunoglobulin A and regulatory T cells that increase human immunity [24].

Bacitracin produced by probiotics reduces colonization of the mucosa with pathogenic bacteria and regulates the biofilm by increasing the action of antibiotics [25-27]. Yet, no published research has clarified the mechanism of antibiotic resistance prevention by probiotics; however, the maintenance of normal flora during the administration of antibiotics can reduce the spread of resistance to antibiotics [28].

Antibiotics are very effective in curing infectious diseases, but they are accompanied by health complications, the most common of which is antibiotic-associated diarrhea. Global rates of antibiotic-associated diarrhea vary between 5% and 39%, depending on the specific type of antibiotic used [29-31]. The use of probiotics within 2 days during antibiotic treatment significantly reduces the incidence of antibiotic-associated diarrhea in adults, and their use is safe [32]. Use of antibiotics together with probiotics for the prevention of diarrhea would lead to direct medical cost savings that would substantially compensate for the cost of probiotics therapy [33].

The limitations in this study include a lack of included patients with catheter-associated urinary tract infection caused by prolonged use of a urinary catheter as well as those with recurrent urinary tract infection. Future prospective studies should investigate the effect of other types of probiotics in therapy for urinary tract infection.

Conclusions

According to our data, the use of probiotics together with antibiotics in the treatment of urinary tract infections could significantly reduce the adverse effects of antibiotics, increase the efficiency of antibiotic therapy, reduce bacterial resistance to antibiotics, and improve patients' impressions of improvement after antibiotics therapy.

Acknowledgment

We thank Edanz (https://www.edanz.com/ac) for editing a draft of this manuscript.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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