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Effectiveness of Oral Fosfomycin in the Treatment of Cystitis among Adult Cancer Patients in Outpatient Settings

Dina Khabour

DK.07128@khcc.jo

King Hussein Cancer Center

Wedad B. Awad

King Hussein Cancer Center

Salam Ashour

King Hussein Cancer Center

Rula Najjar

King Hussein Cancer Center

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Abstract

Purpose

Cancer patients are at increased risk of urinary tract infections (UTIs) due to malignancy- and treatment-related immunosuppression. Oral fosfomycin is a convenient option for cystitis amid rising antimicrobial resistance, but data on its effectiveness in cancer patients are limited. This study evaluated the effectiveness of oral fosfomycin for cystitis in adult cancer patients managed in outpatient settings.

Methods

This retrospective study was conducted at a comprehensive cancer center and included adult cancer patients (≥ 18 years) who received oral fosfomycin for cystitis in outpatient settings between January and December 2024. Clinical cure was defined as symptom resolution without additional healthcare visits within 7 days; recurrence was defined as a subsequent UTI-related healthcare encounter within 90 days.

Results

A total of 455 patients were included. Mean age was 58 ± 19 years, 60% were female, and 90% had solid tumors, mainly breast (29%) and bladder (18%) cancers. Active chemotherapy was ongoing in 39% of patients. Positive urine analysis was reported in 69% and urinary symptoms in 65%. Extended-spectrum β-lactamase (ESBL)-producing Escherichia coli was the most common isolated pathogen (63%). Fosfomycin, prescribed as targeted therapy in 63% of patients, achieved an overall clinical cure rate of 89%. Subsequent UTI-related events occurred in 43% of patients within 90 days.

Conclusion

Oral fosfomycin achieved a high clinical cure rate in adult cancer patients treated for cystitis in outpatient settings, supporting its role as a practical treatment option. Despite favorable initial outcomes, recurrence remained common, highlighting the need for further studies to identify recurrence risk factors and optimize long-term outcomes.

Introduction

Patients with cancer are immunocompromised due to their underlying malignancy and anticancer therapies, rendering them highly susceptible to infections. Urinary tract infections (UTIs), including cystitis, are one of the most common bacterial infections in this population and frequently lead to emergency department visits, antimicrobial use, and, in some cases, hospitalization [1]. Management of

UTIs in cancer patients is increasingly challenged by the global rise in antimicrobial resistance, which has reduced the reliability of many traditional oral treatment options [1, 2].

Current clinical guidelines recommend nitrofurantoin, trimethoprim–sulfamethoxazole, and fosfomycin as first-line therapies for cystitis, with fosfomycin representing a well-established and convenient outpatient option [3, 4]. Fosfomycin exerts its antibacterial activity through inhibition of the MurA enzyme, resulting in disruption of bacterial cell wall synthesis, and demonstrates broad in vitro activity against both Gram-negative and Gram-positive pathogens, including ESBL-producing Enterobacterales [5, 6]. Its pharmacokinetic properties allow for high urinary concentrations following a single 3 g oral dose, supporting its use as a single-dose regimen; however, its indication is limited to lower urinary tract infections [5, 6].

Although earlier studies have demonstrated that fosfomycin has comparable effectiveness to other oral agents, more recent randomized evidence suggests that multiple dose regimens such as nitrofurantoin may achieve superior clinical and microbiological outcomes [7]. Nevertheless, fosfomycin continues to be recommended in international guidelines due to its favorable safety profile, ease of administration, and preserved activity against resistant Escherichia coli strains [3, 4].

Despite these recommendations, data evaluating the effectiveness of fosfomycin in immunocompromised populations, particularly among cancer patients, remain limited. Most existing studies have been conducted in non-malignant populations or inpatient settings, with variable reported outcomes. A retrospective study in hospitalized patients reported a microbiological cure rate of approximately 59%, while another study in kidney transplant recipients demonstrated clinical cure rates of up to 83.9% [8, 9]. These findings highlight the variability of outcomes in high-risk populations and underscore the need for further investigation in oncology patients treated in the outpatient setting.

Therefore, this study aims to evaluate the effectiveness of oral fosfomycin use for the treatment of acute cystitis among adult cancer patients managed in outpatient settings.

Methods

This retrospective observational study was conducted at King Hussein Cancer Center (KHCC), a 352-bed comprehensive cancer center in Amman, Jordan. All adult cancer patients (≥ 18 years) who received oral fosfomycin, either empirically or as targeted therapy, for the treatment of cystitis (UTI) between January and December 2024 were included. Patients who received fosfomycin as suppressive therapy were excluded.

Fosfomycin orders were prescribed across ambulatory care settings, including outpatient clinics and the emergency department (ED). Data was retrieved from the pharmacy billing system and electronic patient medical records. The following variables were collected: patient demographics, primary diagnosis, comorbidities, clinical presentation, laboratory findings, microbiological data, fosfomycin treatment details, and clinical outcomes. Fosfomycin regimens included either a single 3 gm oral dose or multiple-

dose regimens (e.g., every 48–72 hours for 3 repeated doses), depending on clinician preference and patient clinical characteristics.

Definitions

Cystitis was defined as documentation of at least one clinical symptom consistent with lower urinary tract infection such as dysuria, urinary frequency, urgency, or suprapubic tenderness, in addition to positive laboratory finding (urine analysis) and/or microbiological culture confirmation [1, 2]. Microbiological confirmation required a positive urine culture yielding Escherichia coli, Enterococcus faecalis, or other pathogens such as Klebsiella spp. and Pseudomonas aeruginosa. Laboratory confirmation by urine analysis included pyuria (≥ 10 leukocytes/μL) or a positive leukocyte esterase and/or nitrite test, the latter indicating the presence of Enterobacteriaceae capable of reducing urinary nitrates to nitrites.

Clinical cure was defined as resolution of UTI-related symptoms without the need for additional antimicrobial therapy or a return visit to the emergency department or outpatient clinic within 7 days of treatment initiation.

UTI recurrence was defined as a subsequent inpatient or outpatient healthcare encounter for symptoms consistent with urinary tract infection occurring within 90 days of the initial episode.

Statistical Analysis

Descriptive statistics were used to summarize patient characteristics, microbiological findings, and clinical outcomes. Continuous variables were reported as mean ± standard deviation (SD) or median with interquartile range (IQR), as appropriate. Categorical variables were presented as frequencies and percentages. A P-value of < 0.05 was considered statistically significant.

Results

During the study period, 455 patients met the inclusion criteria and were enrolled. Of these, 246 patients (54%) were prescribed fosfomycin in outpatient clinics, while 209 patients (46%) received prescriptions in the emergency department. The mean ± SD age was 58 ± 19 years, and 273 patients (60%) were female. Most patients had solid tumors (n=412, 90%), with breast (n=119, 29%) and bladder cancers (n=75, 18%) being the most common type. A total of 177 patients (39%) were receiving active chemotherapy. Cardiovascular (92%), endocrine (43%), and renal (36%) conditions were among the most frequent comorbidities, and 241 patients (53%) had normal renal function. Recent urological procedures were reported in 97 patients (21%), and 67 patients (15%) had urinary catheters. A prior history of fosfomycin use within the past 6 months was documented in 22% of patients. Table 1 summarizes the baseline characteristics of the included patients.

Positive urine analysis results were identified in 313 patients (69%), while typical UTI symptoms were reported in 296 patients (65%). Among patients with positive urine cultures, ESBL-producing Escherichia

coli was the most frequently isolated pathogen (n=285, 63%), followed by Enterococcus faecalis (n=25, 6%), Klebsiella (n=7, 1.5%), and Pseudomonas aeruginosa (n=6, 1.3%). Other pathogens were infrequently identified. Table 2 shows the infectious data and treatment outcomes. There was no significant association between female sex and the intended clinical outcome, with a crude odds ratio (OR) of 1.43 (95% CI: 0.75–2.72; p = 0.28).

Fosfomycin was prescribed as targeted therapy in 164 patients (63%), achieving a clinical cure in 409 patients (89%). A total of 17% of patients received multiple dose fosfomycin regimens, while the majority received a single-dose regimen. Recurrence of UTIs occurred in 195 patients (43%) within 90 days following treatment. Recurrence-free rates were higher among female patients (59%) compared to male patients (54%).

Stratified analysis demonstrated variability in recurrence-free rates across cancer types. Patients with breast cancer had the highest proportion of no recurrence (68%), followed by renal cell carcinoma (58%) and bladder cancer (57%). Intermediate recurrence-free rates were observed in gastrointestinal cancers (53%) and lymphoma (52%), while lower rates were seen in vaginal or vulvar cancers (48%), leukemia (47%), and prostate cancer (45%). Table 3 shows the recurrence-free rates stratified by cancer type.

Among patients with urinary catheters, recurrence-free rates were generally low across catheter types, with modest differences observed between nephrostomy tubes (42%), Foley catheters (35%), and suprapubic catheters (33%). Table 4 shows the recurrence-free rates stratified by catheter type.

Discussion

In this cohort of adult cancer patients treated for acute cystitis in the outpatient setting, oral fosfomycin achieved a high clinical cure rate of 89%, despite the substantial prevalence of antimicrobial resistance, particularly extended-spectrum β-lactamase (ESBL)-producing Escherichia coli. These findings provide valuable real-world evidence supporting the effectiveness of fosfomycin in an oncology population that is frequently underrepresented in prospective studies. As cancer patients are at increased risk of infection-related morbidity because of immunosuppression and repeated healthcare exposure, the availability of effective oral treatment options is particularly important for supportive cancer care. Our findings are consistent with emerging evidence supporting the use of fosfomycin for infections caused by ESBL-producing uropathogens. In a multicenter retrospective cohort study, Wald-Dickler et al. [10] reported comparable clinical success rates between oral fosfomycin and intravenous ertapenem for complicated urinary tract infections, the majority of which were caused by ESBL-producing Escherichia coli and Klebsiella pneumoniae. Moreover, patients treated with fosfomycin experienced fewer adverse events and shorter durations of antimicrobial therapy. These findings support the role of fosfomycin as a potential carbapenem-sparing treatment option in selected patients.

More recently, Seo et al. [11] conducted a multicenter randomized non-inferiority trial evaluating oral fosfomycin as a step-down therapy compared with intravenous carbapenems or β-lactam/β-lactamase inhibitor combinations for complicated UTIs caused by ESBL-producing Enterobacterales. Their results

further support the effectiveness of oral fosfomycin as an alternative to prolonged intravenous therapy in patients with susceptible organisms.

The clinical cure rate observed in our study is consistent with previously reported outcomes in the general population, where fosfomycin has demonstrated cure rates ranging from approximately 80% to 90% for the treatment of cystitis [7, 12, 13]. This finding suggests that fosfomycin may retain its effectiveness in patients with cancer despite potential host-related factors that could compromise treatment outcomes. Similar results have been reported in studies involving immunocompromised populations and infections caused by multidrug-resistant pathogens, including transplant recipients and patients with resistant Enterobacterales infections [8, 9]. Given the growing prevalence of antimicrobial resistance and the limited availability of oral treatment options, fosfomycin remains an attractive therapeutic choice because of its broad antimicrobial activity, ease of administration, and favorable tolerability profile [3, 4]. A minority of patients (17%) received multidose fosfomycin regimens, likely reflecting clinical judgment in patients perceived to be at higher risk of persistent infection or recurrence. However, outcomes were not analyzed according to dosing strategy, and therefore no conclusions can be drawn regarding the comparative effectiveness of single dose versus multidose regimens in this population.

Despite the favorable initial response, recurrence within 90 days of treatment occurred in almost half of the patients (43%). This rate is considerably higher than recurrence rates reported in the general population following treatment for cystitis, which are typically estimated at 10% to 25% [1, 2]; however, in cancer patients recurrence rates were reported in ranges between 14–40%, which is similar to our results [14, 15]. The increased recurrence observed in our cohort likely reflects the unique clinical characteristics of patients with cancer, including ongoing immunosuppressive therapies, frequent healthcare encounters, urinary tract instrumentation, and underlying structural or functional urological abnormalities. These findings highlight the need for close follow-up and individualized strategies to reduce recurrence risk in oncology patients, as previously reported by Grafia et al. as well [16].

Subgroup analyses demonstrated variability in recurrence-free outcomes across different patient populations. Higher recurrence-free rates were observed among patients with breast and renal malignancies, whereas lower rates were noted among patients with prostate cancer, leukemia, and other malignancies. Although these observations should be interpreted cautiously because of the descriptive nature of the analysis, they may reflect differences in disease characteristics, treatment-related immunosuppression, and involvement of the urinary tract. Recurrent UTI represents a substantial clinical burden in women and has been consistently identified as a predominantly female condition across multiple studies and reviews. However, these observations were not replicated in our cohort. Although female patients demonstrated numerically higher rates of recurrence, this was not statistically significant. This lack of statistical significance may reflect differences in patient characteristics, underlying risk factors, or treatment-related variables within our study population, suggesting that sex alone was not an independent predictor of clinical outcome in this cohort [17, 18].

Urinary catheterization was also associated with lower recurrence-free rates across all catheter types. Patients with nephrostomy tubes, Foley catheters, and suprapubic catheters experienced similarly high recurrence rates, suggesting that catheterization itself may be an important contributor to recurrent infection. Potential mechanisms include biofilm formation, chronic bacterial colonization, prolonged device use, and the presence of underlying urological pathology. These findings emphasize the multifactorial nature of recurrent cystitis in patients with cancer and support the importance of ongoing assessment of catheter necessity whenever clinically feasible. Furthermore, approximately one-fifth of patients had undergone recent urological procedures, which may have contributed to the elevated recurrence rates observed in our cohort [16]. The relatively high proportion of patients with genitourinary malignancies may also have influenced recurrence risk through mechanisms such as urinary tract obstruction, mucosal disruption, local tumor effects, and repeated urological interventions.

Although Escherichia coli, particularly ESBL-producing isolates, was the predominant pathogen identified; the microbiological profile was otherwise relatively consistent across the cohort. The high prevalence of resistant organisms further highlights the importance of preserving effective oral treatment options such as fosfomycin within antimicrobial stewardship programs, particularly for vulnerable populations such as patients with cancer [7, 12].

Limitations

This study has several limitations. First, its retrospective, single-center design may limit generalizability and is subject to potential information bias related to incomplete clinical documentation in patient records. Second, although subgroup trends were explored, formal multivariable analyses were not performed to identify independent predictors of recurrence. Third, differentiation between cystitis relapse and reinfection was not possible because molecular microbiological data were unavailable at the center. An additional limitation is that the selection of a one-dose or three-dose regimen was determined by physician preference rather than predefined guideline recommendations, potentially introducing treatment selection bias and affecting the comparability of the study groups. Furthermore, safety data related to fosfomycin use could not be evaluated because adverse drug reaction reporting was not consistent in patients' records, if present at all.

Conclusion

Oral fosfomycin showed excellent clinical cure rates in adult outpatient cancer patients treated for cystitis. This supports its effectiveness as a practical first-line oral treatment option as targeted therapy in cancer patients. These findings emphasize the importance of individualized patient assessment when managing urinary infections in cancer patients. Future studies should focus on identifying predictors of recurrence, evaluating optimal dosing strategies, and developing targeted preventive approaches to improve long-term outcomes in this high-risk population.

Abbreviations

CI Confidence interval

ED Emergency department

ESBL Extended-spectrum β-lactamase

IQR Interquartile range

KHCC King Hussein Cancer Center

OR Odds ratio

SD Standard deviation

UTI Urinary tract infection

Declarations

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Competing Interests

The authors have no relevant financial or non-financial interests to disclose.

Author Contributions

DK, WA, and RN developed research questions and the research protocol. DK and SA were involved in data collection. All authors were involved in data analysis, interpretation of the results, and manuscript writing, and all have reviewed and approved the final manuscript.

Ethics Approval

The study protocol was approved by the Institutional Review Board of King Hussein Cancer Center (reference number 25 KHCC 074). The Institutional Review Board granted a waiver of informed consent and permission to access the raw data and patients' electronic medical records. Data were coded and anonymized before analysis. The study was conducted in accordance with good clinical practice guidelines and the requirements of the Institutional Review Board.

Consent to Participate

Not applicable (retrospective study with a waiver of informed consent granted by the Institutional Review Board).

Consent to Publish

Not applicable.

Availability of Data and Materials

The datasets generated and analyzed during the current study are available from the corresponding author on reasonable request.

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Tables

Table 1: Baseline patient characteristics

Characteristic	(N = 455)
Age (mean ± SD), years	58 ± 19
Female gender, n (%)	273 (60%)
Solid cancer	412 (90.5%)
Hematological cancer	43 (9.5%)
Cancer type, n (%)	
Breast cancer	119 (29%)
Bladder cancer	75 (18%)
Gastrointestinal cancer	60 (13%)
Lung Cancer	10 (2%)
Prostate Cancer	48 (10.5%)
Renal Cell Carcinoma	29 (6%)
Vaginal & Vulvar Cancer	27 (5.9%)
Leukemia	19 (4.7%)
Lymphoma	25 (5.5%)
Others	43 (9.5%)
Active Chemotherapy, n (%)	177 (39%)
Comorbidities, n (%)	
Cardiovascular	421 (92%)
Endocrine	196 (43%)
Renal	166 (36%)
Hematological	14 (3%)
Respiratory	26 (6%)
Neurological	14 (3%)
Normal renal function, n (%)	241 (53%)
Recent Urological Procedures, n (%)	97 (21%)

Table 2: Infection data and treatment outcomes

Outcome	Findings, n (%)
Positive Urine Analysis	313 (69%)
Typical UTI Symptoms Presence	296 (65%)
Urinary Catheter Presence	67 (15%)
Pathogens	
ESBL-producing E. Coli	285 (63%)
Enterococcus faecalis	25 (6%)
Klebsiella spp	7 (1.5%)
Pseudomonas aeruginosa	6 (1.3%)
Targeted Treatment	164 (36%)
Clinical Cure Rate	409 (89%)
UTI Recurrence (within 90 days)	195 (43%)

Table 3: Recurrence-free rates stratified by cancer type

Cancer Type (n)	Recurrence Free n (%)
Breast cancer (119)	81 (68%)
Renal cell carcinoma (27)	17 (58%)
Bladder cancer (75)	43 (57%)
Gastrointestinal cancer (60)	32 (53%)
Lymphoma (25)	13 (52%)
Vaginal or Vulvar cancer (29)	13 (48%)
Leukemia (19)	9 (47%)
Prostate cancer (48)	22 (45%)

Table 4: Recurrence-free rates stratified by catheter type

Catheter Type (n)	Recurrence Free n (%)
Nephrostomy tubes (19)	8 (42%)
Foley’s catheter (45)	16 (35%)
Suprapubic catheter (3)	1 (33%)