

# Fosfomycin in the prevention of urinary tract infections. Preliminary data



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## Objective

- ❖ Recurrent urinary tract infections (rUTI) in female patients is a common and a rather challenging clinical condition [1].
- ❖ Continuous antibiotic prophylaxis with nitrofurantoin, cotrimoxazole and fluoroquinolones has been proven most effective to prevent rUTI [1,2].
- ❖ Urinary infections due to multidrug – resistant (MDR) Gram – negative Enterobacteriaceae are steeply increasing worldwide even in the community (with the presence of ESBL (+) producing bacteria), and the increasing resistance rates to fluoroquinolones has rendered therapeutic options even more limited [3].
- ❖ Fosfomycin tromethamine, an oral salt of fosfomycin, is an antibiotic utilized for urinary tract infections in women once weekly and exhibits an excellent activity against MDR uropathogens [2].
- ❖ The aim of the current study is to evaluate the efficacy of chronic therapy with fosfomycin in the treatment and prevention of recurrent UTIs.

## Material and Methods

- ❖ Female patients suffering from rUTI, defined as  $\geq 3$  UTI/year or  $\geq 2$  UTI/half year evaluated in the Outpatient ID clinic of Hygeia General Hospital were included
- ❖ Data collected included demographic characteristics, comorbidities, the isolated microorganisms and their susceptibility pattern, toxicity as well as time of recurrence.
- ❖ Strain identification and antimicrobial susceptibilities were performed with the Vitek-2 system (bioMerieux Marcy L'Étoile, France) and interpreted according to Clinical and Laboratory Standards Institute (CLSI).
- ❖ Fosfomycin MIC values were interpreted as follows: MIC  $\leq 64$   $\mu\text{g/ml}$ : susceptible (S); MIC 128  $\mu\text{g/ml}$ : intermediate (I); MIC  $\geq 256$   $\mu\text{g/ml}$ : resistant (R).
- ❖ **Oral fosfomycin was administrated as a single dose (one 3-g sachet) for 5-7 days to be followed by a 3gr dose once or twice a week**
- ❖ Urine cultures were repeated once monthly.
- ❖ Isolation of a pathogen during treatment was considered recurrence.

## Results

- ❖ Thirty women, mostly post-menopausal were included in the current study.
- ❖ The most predominant isolated pathogen was *Escherichia coli* (60,7%).
- ❖ Demographic characteristics of studied population are illustrated in Table 1.
- ❖ Resistance rates are depicted in Table 2. Resistance to fosfomycin was not observed.
- ❖ Recurrence during prophylaxis with oral fosfomycin once weekly was documented in 3 out of 4 patients (75%).
- ❖ Eight out of 25 patients (32%) receiving prophylaxis with fosfomycin twice weekly presented with relapse. (Table 3)
- ❖ The most prevalent pathogen isolated during recurrence was *K. pneumoniae* (50%).
- ❖ Risk factor for recurrence was the presence of diabetes mellitus.
- ❖ The most common adverse effect was diarrhea followed by allergic reaction (two patients).

Table 1. Demographic characteristics

Patients	Number
Women	30 (100%)
Age (median), years	66 (range: 22 – 89)
Duration from first episode (median), months	4 (range: 0,5 – 45)
Menopause	25/30 (83,3%)
Diabetes mellitus	3/30 (10%)
Nephrolithiasis	5/30 (16,7%)

Table 3. Effectiveness of prophylaxis with oral fosfomycin

Administration	Recurrence - Patients (%)	Time to recurrence, months
3gr once weekly	3/4 (75)	5
3gr twice weekly	8/25 (32)	2.57

Table 2. Resistance rates of isolated pathogen

	Patients (%)	Resistance rates (%)					
		Ampicillin	Cefuroxime	Nitrofurantoin	Norfloxacin	Cotrimoxazole	Fosfomycin
<i>E. coli</i>	17/28 (60.7)	70,6	41,2	14,3	64,71	52,9	0
<i>P. mirabilis</i>	4/28 (14.3)	50	0	100	0	25	0
<i>K. pneumoniae</i>	5/28 (17.9)	25	50	50	40	50	0
<i>Enterobacter spp</i>	2/28 (7.1)	100	50	100	0	0	0

### References.

1. Pickard R, et al. EAU Guidelines on Urological Infections. 2016 .
2. El Sakka N, et al. Expert Rev Clin Pharmacol. 2016;9:1047-56.
3. Bonkat G, et al. World J Urol. 2013;31:1427-32.

## Conclusions

- ❖ These preliminary data, suggest that oral fosfomycin prophylaxis appears as an effective regimen, particularly in the era of MDR prevalence, for the prevention of rUTI.
- ❖ From the current study, the administration of oral fosfomycin twice weekly was more effective for prophylaxis of rUTI.
- ❖ However the appropriate dosing interval for prophylaxis needs further evaluation.