*JKAU: Med. Sci.*, **Vol. 20** No. 2, pp: 3-12 (2013 A.D. / 1434 A.H.)
DOI: 10.4197/Med. 20-2.1

# Single Oral Dose of Fosfomycin Trometamol versus Ciprofloxacin for UTI prophylaxis in Invasive Urodynamics: A Prospective Randomized Double Blind Clinical Trial

**Hisham A. Mosli,** FRCSC, FACS**, Hasan M.A. Farsi,** FRCSC, FACS**, Taha A.Abdulmagied,** MBBCh, MD**, Abdulmalik M.S. Tayib,** FACHARTZ, FACS**, Ahmed J. Al-Sayyad,** MD, FRCSC**, M. Mamdoh Rezk,** MBBCh, MD**, Adel K. Altwarigi,** MBBS, SBU**,** and **M. Hani Abdulwahab,** MBBCh, MSC

*Department of Urology, Faculty of Medicine, King Abdulaziz University, Jeddah, Saudi Arabia*
*hmosli@hotmail.com*

*Abstract.* The aim is to test the efficacy of a single oral dose of fosfomycin trometamol in preventing urinary tract infection as compared to ciprofloxacin in patients undergoing invasive urodynamics studies. Patients were randomized into 2 groups: A and B. Group A: a random group of patients undergoing urodynamics studies received a single pre-procedure dose of fosfomycin trometamol 3 gms orally 3 hours before the study. Group B: a random group of patients received a single pre-procedure dose of 500 mg ciprofloxacin 3 hours before the study. A total of 65 patients enrolled in the study (45 females and 20 males); the age range from 10 to 75 years with a mean of 50.32 ± 13.5. There were 39 patients in group A and 26 patients in group B. The post-procedure urine analysis showed increased presence of WBCs in Group A (fosfomycin trometamol) compared to group B (ciprofloxacin). Post-procedure, the negative urine cultures were reduced from 59% to 20.5% for group A and comparably from 57.7% to 23.1% in group B. A single dose of both fosfomycin trometamol and ciprofloxacin were equally in-effective in the prophylaxis against UTI in patients undergoing urodynamics studies.

*Keywords:* Antibiotic prophylaxis, UTI, Urodynamics, Fosfomycin trometamol, Ciprofloxacin.

Correspondence & reprint request to: Prof. Hisham A. Mosli
P.O. Box 80215, Jeddah 21589, Saudi Arabia
Accepted for publication: 15 January 2013. Received: 03 October 2012.

## Background

Invasive urodynamics studies including cystometrogram (CMG) and pressure flow studies necessitate urethral catheterization and insertion of a rectal tube. Prophylactic antibiotics are indicated to prevent urinary tract infection (UTI) in a possibly diseased urinary bladder. Hence, single prophylactic dose is preferred. This prospective randomized double blind clinical trial compared head-to-head the efficacy of 2 antibiotics administered in a single oral dose for the prophylaxis against UTI in patients undergoing invasive urodynamics studies (UDS).

### *Objective*

To test the efficacy of a single oral dose of fosfomycin trometamol in preventing UTI as compared to ciprofloxacin in patients undergoing invasive UDS.

### *Study Design and Methodology*

A prospective randomized double blind study comprising 65 patients undergoing urodynamics studies for various indications were randomized into 2 groups: A & B.

Group A: a randomly selected group of patients undergoing invasive UDS received a single pre-procedure dose of fosfomycin trometamol 3gms orally 3 hours before the study. Pre-administration urine analysis and clean catch urine was collected for culture from those patients and 3 days post-procedure. Another urine analysis and midstream specimens of urine were collected and processed.

Group B: a randomly selected group of patients received a single pre-procedure dose of 500 mg ciprofloxacin 3 hours before the study, and underwent the same protocol as Group A.

### *Inclusion Criteria*

Patients undergoing invasive urodynamics procedure that required the insertion of a bladder catheter and rectal tube were included in the study.

### *Exclusion Criteria*

The exclusion criteria were: Chronically catheterized patients (more than one week of indwelling catheter), concomitant use of other antibiotics, patients in chronic renal failure (serum creatinine higher than

120 nmol/L or 1.2 mg/dl.), and patients allergic to any of the agents under investigation, pregnant women and breast feeding mothers.

### *Statistical Analysis*

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA) by a qualified biostatistician at the Clinical Research Unit (CRU) at King Abdulaziz University Hospital, Jeddah. The age was expressed as mean, and the standard deviation and the standard error of the mean were calculated. Levene's test for the equality of variances and "student's" *t*-test for equality of mean were used. Chi- Square tests (Pearson's chi-squared test ($\chi^2$) / Fisher's exact test) were used for comparisons between groups.

### *Ethical Issues*

All patients or parents signed an informed consent. The approval of the medical ethics committee of the institution was obtained.

## Results

A total of 65 patients were enrolled in the study, 45 females and 20 males, the age range from 10 to 75 years with a mean of 50.32 ± 13.5. 39. Patients in Group A received fosfomycin trometamol, and 26 patients in Group B received ciprofloxacin.

The two groups were comparable in age and sex distribution as shown in Table 1. The types of invasive urodynamics studies performed are shown in Table 2. The clinical indications for UDS are shown in Table 3.

Pre-procedure urine analysis was classified as negative when the white blood cells (WBCs) are absent from urine on microscopic examination or, if present but reported as rare, occasional or trace only. While urine analysis was considered as positive when WBCs are present and reported as high, moderate or if they were microscopically seen in lumps. The two Groups A and B were comparable in terms of pre-procedure urine analysis as shown in Table 4.

**Table 1. Age and sex in groups A and B.**

**Group Statistics**

| | Group | | N | Mean | Std. Deviation | Std. Error Mean |
|---|---|---|---|---|---|---|
| Age | | A | 39 | 49.77 | 13.564 | 2.172 |
| | | B | 26 | 51.15 | 13.631 | 2.673 |

| | | | Sex | | Total |
|---|---|---|---|---|---|
| | | | Female | Male | |
| Group | A | Count | 26 | 13 | 39 |
| | | % of Total | 40.0% | 20.0% | 60.0% |
| | B | Count | 19 | 7 | 26 |
| | | % of Total | 29.2% | 10.8% | 40.0% |
| Total | | Count | 45 | 20 | 65 |
| | | % of Total | 69.2% | 30.8% | 100.0% |

**Table 2. Types of invasive urodynamics procedure performed.**

| Procedure | Frequency | Percent |
|---|---|---|
| CMG | 53 | 81.5 |
| Press-flow | 12 | 18.4 |
| **Total** | 65 | 100.0 |

**Table 3. The clinical indications for the procedures.**

| Diagnosis | Frequency | Percent |
|---|---|---|
| Urge Incontinence | 10 | 15.4 |
| Mixed Urinary Incontinence | 12 | 18.5 |
| Neurogenic Bladder | 7 | 10.8 |
| Nocturnal Enuresis | 1 | 1.5 |
| Over Active Bladder | 15 | 23.1 |
| Postoperative Urinary Incontinence | 3 | 4.6 |
| Posterior Urethral Valves | 1 | 1.5 |
| Urethral Stricture | 1 | 1.5 |
| Stress Urinary Incontinence | 12 | 18.5 |
| Total Urinary Incontinence | 3 | 4.6 |
| **Total** | 65 | 100.0 |

The post-procedureurine analysis showed increased presence of WBCs in Group A (fosfomycin trometamol) compared to group B(ciprofloxacin) as seen in Table 5. Negative urine culture is defined as no growth of microorganisms or colony forming organisms less than 100,000 per mL urine when cultured on standard media for 24 hrs. The pre-procedure midstream urine (MSU) culture revealed sterile urine in

59% of patients in Group A (fosfomycin trometamol), as per the urine of comparative 57.7% of Group B (ciprofloxacin) patients. Since the urine was collected just before the prophylactic antibiotic dose was administered in the same day prior to the procedure, therefore, the culture results were not known until later. Thus, all patients were admitted to the study regardless of their initial status of bacteriuria. This allowed us to learn about the true natural history of patient undergoing urodynamics studies even if they previously had sterile urine.

**Table 4. Pre-procedure urine analysis showing comparative results of the two groups.**

| | | | Pre-procedure Urine analysis result | | | Total |
|---|---|---|---|---|---|---|
| | | | Not done | Negative | Positive | |
| Group | A | Count | 1 | 33 | 5 | 39 |
| | | % within Group | 2.6% | 84.6% | 12.8% | 100.0% |
| | B | Count | 2 | 20 | 4 | 26 |
| | | % within Group | 7.7% | 76.9% | 15.4% | 100.0% |
| Total | | Count | 3 | 53 | 9 | 65 |
| | | % within Group | 4.6% | 81.5% | 13.8% | 100.0% |

**Table 5. Post-procedure urine analysis showing comparative results of the two groups.**

| | | | Post-procedure Urine Analysis Results | | | Total |
|---|---|---|---|---|---|---|
| | | | Not done | Negative | Positive | |
| Group | A | Count | 16 | 15 | 8 | 39 |
| | | % within Group | 41.0% | 38.5% | 20.5% | 100.0% |
| | B | Count | 15 | 10 | 1 | 26 |
| | | % within Group | 57.7% | 38.5% | 3.8% | 100.0% |
| Total | | Count | 31 | 25 | 9 | 65 |
| | | % within Group | 47.7% | 38.5% | 13.8% | 100.0% |

The positive cultures grew mainly gram negative bacilli (*Escherichia coli (E. coli*) and *Klebsiella*) and gram positive cocci (*Enterococcus faecalis* (*E. faecalis)* and *Streptococcus agalactiae* (*S. agalactiae*)). Post-procedure, the negative urine cultures were reduced from 59% to 20.5% for Group A; comparably from 57.7% to 23.1% in Group B. Therefore, the pre- and post-procedure urine culture results showed no advantages of one antibiotic over the other, since the pre- and post-procedure results are comparable as shown in Table 6.

**Table 6. The pre and post-procedure urine culture results of groups A&B.**

| Timing | Group A (Trometamol) | | Group B (Ciprofloxacin) | |
|---|---|---|---|---|
| | Growth | No growth | Growth | No growth |
| Pre-procedure | 41.0% | 59.0% | 43.3% | 57.7% |
| Post-procedure | 79.5% | 20.5% | 76.9% | 23.1% |

## Discussion

The need for prophylactic antibiotic coverage against UTI for patients undergoing invasive urodynamics studies is still controversial[1]. Here are no reliable Randomized Clinical Trials (RCTs) to form convincing evidence for or against the administration of antibiotics in this situation. In a major systematic review of antibiotic prophylaxis in urologic procedures, all previous RCTs on prophylactic antibiotics in urodynamics investigation were excluded due to the administration of antibiotics given after the intervention and not before, in addition to several other reasons[1].Even though the pre-procedural culture of urine shows no growth, this does not preclude the possibility of post-procedure UTI. In a previously published study[2], Quek and Tay reported a series of patients undergoing pressure flow studies (PFS), 25% developed irritative lower urinary tract symptoms (LUTS). Only 2/23 (2.1%) had positive urine cultures, therefore, symptoms were assumed not to be due to UTI. The majority of the patients in this study suffered detrusor over-activity (24/93) as the main indication for urodynamics study (UDS). Therefore, prophylactic antibiotics were deemed unnecessary for that center/study's population[2]. Kartal *et al*. concluded that UTI occurred in 14% in the control group of patients undergoing UDS, and that a single dose of ciprofloxacin prophylaxis was successful in reducing the incidence of UTI to 1%, therefore they recommended antibiotic prophylaxis for patients undergoing UDS[3]. A systemic review of effectiveness and safety supported the use of prophylactic antibiotics in urodynamics to reduce the risk of significant bacteriuria[4]. An earlier epidemiological report[5] revealed that there is seemingly a rapid increase in quinolone resistance among community acquired *E. coli* in some of the countries[5]. The same survey study indicated that some antimicrobial agents such as fosfomycin trometamol still exhibit low resistance, possibly due to their minimal or no use in hospitals and institutions. This was behind our choice for these 2 agents to be tested in the initial design of this current study. Fosfomycin trometamol has a wide spectrum of activity against

gram negative bacilli and gram positive cocci including staphylococci and *E. faecalis*[6]. A meta-analysis of 15 comparative study and two large comparative studies thereafter, showed an equivalent clinical and bacteriological efficacy and tolerance of fosfomycin trometanol 3 g as a single dose as the comparative drugs in the treatment of uncomplicated cystitis[6]. The infective organisms in this later case are presumably community-acquired, very different from those highly resistant micro-organisms seen in hospital acquired UTI that are expected to be the cause for post-procedure UTI that might occur following invasive UDS. However, till-date, oral quinolones are the first choice drugs used for antibiotic prophylaxis against UTI administered prior to UDS[7]. According to the results of this current study, both antibiotics were equally ineffective in the prophylaxis against UTI for patients undergoing invasive UDS when given at a single oral dose 3 hr before the procedure. Based on the present results, it's believed that whenever invasive UDS are indicated, patients with a significant urological disorder are at a high risk of developing UTI. Therefore, an effective dose of prophylactic antibiotic should be given till the final culture of the urine obtained from bladder catheterization is available. Subsequently, an appropriate course of suitable antibiotic is to be administered; should the culture shows bacterial growth and the sensitivity is known. Thus, a more suitable or a more potent antimicrobial agent, possibly of multi-dosage regime might be required if effective prophylaxis is desired.

## Conclusions

The findings of this prospective randomized trial support the believe that patients with a urological disorders/diseases, significant enough to indicate an invasive urodynamics study, are at a high risk for developing post-procedure nosocomial or hospital acquired UTI. Thus, a single dose of either fosfomycin trometamol or ciprofloxacin was equally ineffective in the prophylaxis against UTI in those patients. A single dose of either agents may very well be effective in the treatment of community acquired uncomplicated cystitis. More studies are needed to identify the optimal antibiotic and the proper dosing to effectively produce prophylaxis from UTI, in patients undergoing invasive UDS in a hospital-based setting.

## Acknowledgment

Fosfomycin trometamol used in this study was supplied to us free of charge as a donation from Zambon Company S.P.A., Bresso, Italy through a local agent.

### References

[1] **Bootsma AM, Laguna Pes MP, Geerlings SE, Goossens** A. Antibiotic prophylaxis in urologic procedures: a systematic review. *Eur Urol* 2008, **54**(6): 1270-1286.

[2] **Quek P, Tay LH.** Morbidity and significant bacteriuria after urodynamics studies. *Ann Acad Med Singapore* 2004; **33**(6): 754-755.

[3] **Kartal ED, Yenilmez A, Kiremitci A, Meric H, Kale M, Usluer G**. Effectiveness of ciprofloxacin prophylaxis in preventing bacteriuria caused by urodynamics study: a blind, randomized study of 192 patients. *Urology* 2006; **67**(6): 1149-1153.

[4] **Latthe PM, Foon R, Toozs-Hobson P.** Prophylactic antibiotics in urodynamics: a systemic review of effectiveness and safety. *Neurourol Urodyn* 2008; **27**(3): 167-173.

[5] **Kahlmeter G.** The ECO.SENS Project: a prospective, multinational, multicenter epidemiological survey of the prevalence and antimicrobial susceptibility of urinary tract pathogens-interim report. *J Antimicrob Chemother* 2000; **46** Suppl 1: 15-22.

[6] **Naber KG, Schito G, Botto H, Palou J, Mazzei T.** Surveillance study in Europe and Brazil on clinical aspects and Antimicrobial Resistance Epidemiology in Females with Cystitis (ARESC): implications for empiric therapy. *Eur Urol* 2008; **54**(5): 1164-1178.

[7] **Wolf JS Jr, Bennett CJ, Dmochowski RR, Hollenbeck BK, Pearle MS, Schaeffer AJ; Urologic Surgery Antimicrobial Prophylaxis Best Practice Policy Panel.** Best practice policy statement on urologic surgery antimicrobial prophylaxis. *J Urol* 2008; **179**(4): 1379-1390.

# دراسة سريرية مستقبلية مزدوجة الإعماء لمقارنة جرعة وحيدة من كل من فسفوماسين ترومیتامول و سبروفلوكساسين للوقاية من خمج البول عند المرضى المزمع إخضاعهم لدراسة حركية التبول

**هشام أحمد موصلي، وحسن محمد علي فارسي، وطه أبو المجد عبد المجيد، وعبد الملك محمد سعيد طيب، وأحمد جلال الصياد ، ومحمد ممدوح رزق، وعادل خلف الطويرقي ، ومحمد هاني عبدالوهاب**

*قسم المسالك البولية، كلية الطب، جامعة الملك عبدالعزيز*

*جدة – المملكة العربية السعودية*

*المستخلص.* هدفنا إلى اختبار فعالية جرعة وحيدة من عقار الفسفوترومیتامول مقارنة بالسبروفلوكساسين في الوقاية من خمج البول عند المرضى المزمع خضوعهم لدراسة حركية التبول.في دراسة سريرية مستقبلية مزدوجة الإعماء قُسم المرضى بطريقة عشوائية إلى مجموعتين أ ، ب . حيث أعطيت المجموعة (أ) عقار الفوسفوترومیتامول وأعطيت المجموعة (ب) السبروفلوكساسين.المجموع الكلي٦٥ مريضاً منهم ٤٥ أنثى و ٢٠ ذكراً وتراوح العمر من ١٠ إلى ٧٢ سنوات بمتوسط ٣٢،٥٠±٥،١٣ سنوات.أظهرت تحاليل البول زيادة الخلايا الصديدية في المجموعة أ عن المجموعة ب ، وقلت نسبة العينات الموجبة لتزريع الجراثم في البول من ٥٠٪ الى ٥،٢٠٪ في المجموعة ا مقارنة بـ٧،٥٧٪ الى ١،٢٣٪ في المجموعة ب. ظهر لنا أن كلا العقارين متساويين في قلة

الفعالية في الوقاية من خمج البول عند المرضى المزمع خضوعهم لدراسة حركية التبول.