In Vitro Activity and Clinical Evaluation of Cefixime in Urinary Tract Infection

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Abstract

Thirty-five women with uncomplicated acute lower urinary tract infections proven by significant pre-treatment bacteriuria ($\geq 10^5$CFU/ml) were treated with an oral dose of 100 mg cefixime twice a day for seven days.

Thirty five patients included in this study were checked for response to treatment on the last day of therapy, 7-14 days and 4 weeks post therapy. The clinical response and bacterial eradication rate for cefixime were 91.4 per cent (32/35). The infecting organisms, *E. coli* and *Proteus mirabilis*, were inhibited at MIC_{90}= 0.5 and $\leq$ 0.03 μg/ml, and MBC = 1 and 0.06 μg/ml respectively. No adverse events were found in this study.

Cefixime, a newly oral third generation cephalosporin, is characterized by excellent *in vitro* activity against a broad spectrum of micro-organisms,[1-3] and superior pharmacokinetic properties[4,5]. It has a bioavailability of 50 per cent after oral administration and it is highly stable in the presence of ß - lactamase and has a long elimination half life (3 hours) compared with other cephalosporin. This long elimination half-life of cefixime has made possible twice-daily administration with potential added benefit of improved patient compliance[6]. In the present study the efficacy and tolerance of twice a day, 100 mg oral doses of cefixime in non-pregnant women with acute uncomplicated lower UTI is reported.

MATERIAL AND METHOD

Female patients aged between 19 and 60 years, attending the Department of Family Medicine and Infectious Disease & Host Defence Unit, Department of Medicine, with acute UTIs were included. Pregnant women, patients with known or suspected hypersensitivity to penicillin or cephalosporin, with a history of central vascular acci-

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Table 1. *In vitro* activity of cefixime against pathogens isolated from UTI.

Pathogens	MIC_{50}	MIC_{90}	MBC (μg/ml)
E. coli (30)	0.25	0.5	1
Proteus mirabilis (3)	≤ 0.03	≤ 0.03	0.06
Streptococcus group D (1)	ND	ND	ND
Streptococcus nonhemo.not enterococci (1)	ND	ND	ND

dent, with renal impairment or liver disease or with other disease which could interfere with the evaluation of the therapeutic effect of the trial, were excluded.

Patients who presented with clinical signs of cystitis characterized by dysuria, frequency, suprapubic pain and significant bacteriuria (≥ 10^5 CFU/ml, midstream urine) were asked to participate in the study. Seventy per cent of the patients had symptoms for ≥ 7 days, suggesting a 7 day regimen[7]. Two urine cultures, obtained by the clean voided midstream method were examined within 48 hours prior to starting therapy. Only patients with significant bacteriuria in both urine specimens were included in the study. Patients in the study had a thorough medical and physical examination. In addition, a complete blood count and serum chemistry including liver and kidney function tests were carried out. Treatment consisted of oral administration of a 7 day course of 100 mg bid dose of cefixime. The clinical response was assessed on the last day of therapy, 7-14 days and 4 weeks post therapy and defined as cured, improved and failed based on the resolution of patients' symptoms and pyuria. Bacteriological response was characterized as follows : (I) eradication (initial pathogen eradicated), (ii) superinfection (isolation of a new pathogen) and (iii) persistence (isolation of original pathogen).

RESULTS

Thirty - five patients, suffering from acute UTI proven by significant bacteriuria (≥ 10^5 CFU/ml), were initially included in the study. Thirty-two patients had negative culture in midstream urine specimens, examined on the last day of therapy, 7-14 days and 4 weeks after treatment. None showed clinical signs of cystitis at follow-up, except 2 patients who still showed pyuria and one of them was suffering from CA Cervix.

Table 2. Results of cefixime therapy of UTI.

Clinical Responses	Bacteriological evaluations		
	eradication	persistence	superinfection
cured	30(85.71%)	-	-
improved	2(5.71%)	-	-
failed	-	3(8.57%)	-

Therapy failed in 3 patients, two were infected by *E. coli* and one with an initial infection due to *Proteus mirabilis* showed persistence in the following urine specimen and recurrence with the same *Proteus mirabilis* and from IVP study showed calcification at the right renal area, however, all of three pathogens were sensitive to cefixime. Thirty-five pathogens were isolated, which were 30 *E. coli*, 3 *Proteus mirabilis*, 1 *Streptococcus* group D and 1 *Streptococcus* nonhemo. not enterococci. *E. coli* and *Proteus mirabilis* were inhibited by cefixime at MIC_{90}= 0.5 and ≤0.03 μg/ml, MBC = 1 and 0.06 μg/ml respectively (Table 1). Clinical cure was achieved in 91.4 per cent (30 cured and 2 improved) and bacteriological rate was 91.4 per cent (Table 2). No significant changes in the blood parameters or laboratory values were recorded in any of the patients. None of the patients experienced severe adverse reactions.

DISCUSSION

Cefixime, like other cephalosporins, exhibited *in vitro* broad spectrum antimicrobial activity. Gram-negative pathogens, the main cause of genitourinary tract infections are especially susceptible to this antimicrobial agent[1,2,4]. Consequently, good results can be anticipated in the

treatment of UTIs. In the study, women suffering from bacteriologically confirmed acute uncomplicated lower UTIs received a 7 day course of bid dose 100 mg of cefixime since most of our patients (70%) had suffered UTI for more than or 7 days[6]. Of the 35 patients evaluable for assessment 32 patients had negative urine culture and almost all the patients (91.4%) were clinically asymptomatic at the time of follow-up. This is a good response rate, confirming the results reported by other investigators[1,2].

In conclusion, cefixime given as a seven day course of twice a day dose of 100 mg cefixime (200 mg/day) was an effective therapy in women with bacteriologically confirmed acute uncomplicated lower UTIs.

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การศึกษาฤทธิ์ของยาในหลอดทดลองและการประเมินผลการรักษาทางคลินิกของยาเซฟิกไซม์ ในผู้ป่วยติดเชื้อในระบบทางเดินปัสสาวะ

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ผู้ป่วยหญิง 35 ราย ที่ได้รับการวินิจฉัยว่า เป็นโรคติดเชื้อในระบบทางเดินปัสสาวะ และผลการเพาะเชื้อพบว่ามีเชื้อก่อโรค $\geq 10^5$ โคโลนี/มิลลิลิตร ในปัสสาวะ จะได้รับการรักษาด้วยยา cefixime ในขนาด 200 มิลลิกรัมต่อวัน เป็นเวลา 7 วัน จากนั้นจะติดตามการรักษาในวันที่ 7, 14, และ 28 หลังได้รับยา

จากการศึกษาพบว่าผู้ป่วยตอบสนองต่อการรักษาโดยยา cefixime เท่ากับ 91.4% (32 ใน 35 ราย) และอัตราการกำจัดเชื้อเท่ากับ 91.4% เช่นกัน เชื้อที่เป็นสาเหตุก่อโรค ได้แก่ *E.coli* และ *Proteus mirabilis* ซึ่งจะถูกยับยั้งการเจริญเติบโตที่ MIC_{90} เท่ากับ 0.5 และ $\leq$ 0.03 ไมโครกรัมต่อมิลลิลิตร ตามลำดับ และ cefixime สามารถฆ่าเชื้อทั้งสองชนิดได้ที่ MBC_{90} เท่ากับ 1 และ 0.06 ไมโครกรัมต่อมิลลิลิตร และในการศึกษานี้ไม่พบผลข้างเคียงที่เกิดจากการใช้ยา cefixime ในผู้ป่วยทั้ง 35 ราย

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