Cefaclor Therapy in Uncomplicated Cystitis

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Abstract

Thirty patients with acute urinary tract infection were treated orally with 500 mg of cefaclor three times a day for 7 days. Urine cultures were made before treatment and after therapy. In 97 per cent (29/30) of these patients clinical success was achieved and in 90 per cent (27/30) of them, pathogens were eradicated. Our study showed that cefaclor was still active against most Enterobacteriaceae, such as *Escherichia coli* and *Klebsiella* species, the principle pathogens of urinary tract infection. No adverse effects of cefaclor were observed in this study.

Oral cephalosporin antibiotic regimen has received much attention in clinical settings where there are opportunities for easy compliance, unnecessary hospital stay and financial savings. This applies particularly to patients with acute uncomplicated UTIs (UTI). A large number of trials have supported the benefits of such a treatment strategy(1,2).

Cefaclor is an orally absorbed cephalosporin with a chemical structure similar to that of cephalexin. The substitution of a chloro group for the methyl group on the beta-lactam ring has markedly improved the *in vitro* antibacterial activity and has resulted in substantially greater activity *in vitro* than that of cephalexin against most cephalosporin-sensitive enterobacteriaceae(3).

Previous studies(4) which have compared cefaclor, a semisynthetic orally administered cephalosporin with cotrimoxazole in a course of 10 days' duration have suggested that both were effective while cefaclor caused fewer side effects and resulted in rapid resolution of symptoms.

We present the results of a study which demonstrated the efficacies and adverse profiles of a conventional 7 days course of cefaclor in the treatment of 30 patients with acute uncomplicated UTIs.

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MATERIAL AND METHOD

Study Design

Two general practicioners in Ramathibodi Medical School, Mahidol University Medical Center entered 27 famales and 3 males patients aged between 15 and 59 years with symptoms suggestive of acute uncomplicated lower UTI (and specifically frequency and dysuria) into this prospective study.

Patients were excluded for any of the following reasons : pregnancy, lactation, and history of hypersensitivity to the study drugs, evidence of blood dyscrasia, hepatic or renal impairment, antimicrobial therapy during the 7 days proceeding entry into the trial, previous enrollment in this trial, signs and/or symptoms consistent with of upper UTI, or concurrent medication which might interact with the study cefaclor drug.

On enrollment, a clean-catch mid stream urine specimen was obtained from each patient and analyzed in the trial laboratory. Patients were then assigned to receive 500 mg cefaclor every 8 hours for 7 days regimen.

Clinical Assessment

The initial follow-up assessment was performed on day 7 when a relevant history and repeat clean-catch mid stream urine were obtained from all patients who attended.

Clinical Response was assessed in terms of the following definitions :

Cure : Elimination of signs and symptoms of infection with no recurrence within the post-therapy period.

Failure : Signs and symptoms did not subside or improve during therapy.

Relapse : Worsening of signs and symptoms of infection following initial improvement.

Improvement : Significant but incomplete resolution of signs or symptoms of infection.

Unable to evaluate : Unable to evaluate symptomatic response due to extenuating circumstances.

Patients who met the criteria for clinical study and who were shown to have a bacteriologically confirmed UTI (defined as 10^5 cfu of pathogenic organisms/ml in the clean-catch MSU) continued in the study, while patients who did not have significant bacteriuria were withdrawn.

Further follow-up assessments were made at day 7 and day 14 when patients were questionnaired about their symptoms and repeat clean-catch MSU were obtained. Only the patients who were classified as clinical and bacteriological successes were followed-up after the assessment and on day 7th and day 14th.

All patients were considered evaluable for safety and the first follow-up visit information about adverse events.

RESULT

34 patients were initially recruited into the trial. All these 34 patients were assigned to receive 500 mg of cefaclor 3 times a day for 7 days.

4 patients were withdrawn from the study at the time of the first follow-up visit. The principle reasons for exclusion were violated criteria (1 patient), failure to attend for follow-up (2 patients), a missing initial clean-catch MSU (1 patient).

Of the remaining patients, 30 were shown to have significant bacteriuria and were therefore evaluable for efficacy. The pathogens isolated from the patients are shown in Table 1. Predictably, *Escherichia coli* was the commonest isolate of the patients treated with cefaclor, none of which were strains resistant to cefaclor.

Table 1. Causative agents in 30 patients

Isolates	MIC (ug/ml)		
	n	MIC_{50}	MIC_{90}
Escherichia coli	23	1.6	10.7*
Klebsiella pneumoniae	3	2	10@
Gardnerella spp.	1	ND	ND
Staphylococcus saprophyticus	5	2.5	2.5
Total	32#		

#Some cases had 2 causative agents.
* MIC<1-2 = 13 strains, MIC 4 = 4 strains, MIC 8 = 2 strains, MIC 16 = 4 strains.
@ MIC 1 = 1 strain, MIC 4 = 1 strain, MIC 16 = 1 strain, ND = Not done

Table 2. Clinical and bacteriological responses.

Bacterilogical responses	Clinical responses			Total
	Cured	Improved	Failure	
Eradication	23	3	1	27 (90%)
Relapse	1	1	-	2 (6.7%)
Failure	-	1	-	1 (3.3%)
	24 (80%)	5 (16.7%)	1 (3.3%)	30

Of the patients who were evaluable for efficacy, almost 100 per cent of patients who received cefaclor reported at the first following visit that they had taken all of the cefaclor medication.

Clinical Response

The clinical response rates for evaluable patients are shown in Table 2, at the follow-up assessment.

A successful outcome was recorded in 29 of 30 patients (97%), (good success 24, improved 5 and clinical failure 1). Only patients who attended for follow-up assessment were classified as having responded to treatment. The mean time of resolution of dysuria was 3 days after the cefaclor treatment. Adverse reactions related to cefaclor were not observed in any of the patients.

Bacteriological Respone

The bacteriological response rate for these patients who were eligible for eradication are shown in Table 2. Eradication of causative pathogens occurred in 90 per cent (27/30). One strain of *E. coli* was not eradicated, but for *in vitro* susceptibility test, this strain was susceptible to cefaclor at MIC 4.

DISCUSSION

Cefaclor is an semisynthetic orally administered cephalosporin whose chemical structure is similar to that of cephalexin. This drug has a wide spectrum of activity against common causative pathogens. It also appears to have a requisite spectrum of activity against the common gram-negative pathogens.

In this study, cefaclor resulted in a success rate of 97 per cent in uncomplicated cystitis and is active against most enterobacteriaceae such as *Escherichia coli, Proteus mirabilis* and *Klebsiella species*(3,5,6), the main pathogens of UTIs (UTI), and against *Staphylococcus saprophyticus* which is occasionally present and pathogenic in UTIs.

Cefaclor as used in this study appeared to be successful on a 3 times a day dosage schedule and is a safe and effective antibiotic for the treatment of UTIs.

(Received for publication on May 16, 1997)

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การศึกษาประสิทธิภาพของเซฟาคลอร์ ในการรักษาผู้ป่วยติดเชื้อทางเดินปัสสาวะ

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Cefaclor เป็นยาปฏิชีวนะกลุ่ม เซฟาโลสปอริน ชนิดรับประทานที่ถูกดูดซึมได้ดี โดยมีสูตรโครงสร้างคล้าย Cephalexin การแทนที่ Methyl group ด้วย Chloro group บน ß-lactam ring ยังผลเพิ่มฤทธิ์ต้านเชื้อต่อกลุ่ม Enterobacteriaceae ที่ไวต่อยาเซฟาโลสปอริน

ในการศึกษานี้ผู้ป่วย 30 รายที่มีอาการติดเชื้อทางเดินปัสสาวะ ได้รับยา Cefaclor ขนาด 500 มิลลิกรัม วันละ 3 เวลา นาน 7 วัน ได้ทำการตรวจวิเคราะห์เชื้อจากตัวอย่างปัสสาวะของผู้ป่วยแต่ละรายทั้งก่อนและหลังได้รับยาเพื่อยืนยันผลการรักษา ผลปรากฏว่า ผู้ป่วยร้อยละ 97 (29/30) ตอบสนองต่อยาได้ดีเยี่ยม อัตราขจัดเชื้อสาเหตุสูงถึงร้อยละ 90 ไม่พบผลข้างเคียงใด ๆ ในผู้ป่วยที่ได้รับยา Cefaclor

โดยสรุปการศึกษานี้แสดงว่า Cefaclor ยังคงประสิทธิภาพสูงในการต้านเชื้อกลุ่ม *Enterobacteriaceae* ส่วนใหญ่ได้แก่ *Escherichia coli* และ *Klebsiella species* ซึ่งเป็นเชื้อหลักของโรคทางเดินปัสสาวะอักเสบ

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