SUSCEPTIBILITY OF *PSEUDOMONAS AERUGINOSA* TO THIRD GENERATION CEPHALOSPORINS

By

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ABSTRACT

Pseudomonas aeruginosa (*Ps. aeruginosa*) is a nosocomial pathogen distributed worldwide. The organism is known as the causative agent of many diseases. The aim of this study was to determine susceptibility of *Ps. aeruginosa* to third generation cephalosporins (Ceftazidime, Ceftriaxone, Cefotaxime, cefoprazone).

Clinical specimens (n=293) were collected from patients in different hospitals, including Khartoum Teaching Hospital, Ear Nose Throat Hospital, Military Hospital and National Health Laboratory. The patients including 55% males and 45% females aging lees than1 to 88 years. *Ps. aeruginosa* was recovered and identified by conventional methods.

A total of 68 strains of *Ps. aeruginosa* were isolated from infected wounds 36 (53%), infected ears 24 (35%), and urine 8 (12%). The study showed that ceftazidime was the most effective (91%) followed by cefoperazone (47%), ceftriaxone (7%) and cefotaxime (3%).

The results indicated no significant differences between isolates recovered from males or females (P>0.05).

KEY WORDS: Third generation cephalosporins, *Ps. aeruginosa*, susceptibility test.

الملخص:

الزائفة الزنجارية من الممرضات داخل المستشفيات، وتتوزع في جميع أنحاء العالم، وهي معروفة كمسبب لعدد من الأمراض. تناولت الدراسة تقييم فاعلية الجيل الثالث من مضادات السفالوسبورينات (سفتازديم ، السفتريكسون، السفوتاكسيم والسفوبيرازون).

جمعت العينات السريرية (العدد 293) من مرضى بمستشفيات مختلفة شملت مستشفى الخرطوم و مستشفى الأذن والانف والحنجرة ومستشفى السلاح الطبي والمعمل القومي الصحي. كان المرضى 55% ذكور و 45% إناث، وتراوحت أعمارهم بين أقل من سنة و 88 سنة. تم عزل وتحديد نوع والزائفة الزنجارية بالطرق البكتريولوجية المعروفة. مجموع 68 سلالة من الزائفة الزنجارية تم عزلها ، مثلت باكتيريا الزائفة الزنجارية المعزولة من مسحات الجروح الملتهبة 36 (53%) سلالة ، و من مسحات الآذان الملتهبة 24 (35%) سلالة ، ومن عينات البول 8 (12%) سلالات.

أظهرت الدراسة أن السيفتازديم هو أكثر المضادات الحيوية كفاءة (91%) يتبعه السيفوبيرازون (47%) ، السيفترايكسون (7%) أخيراً السيفوتاكسيم (3%). أشارت النتائج إلى عدم وجود إختلافات إحصائية في نشاط المضادات الحيوية تحت الإختبار ضد الميكروب المعزول من الذكور والإناث (P>0.05).

INTRODUCTION

The naturally occurring cephalosporins were first isolated from *Cephalosporium* sp. in 1945 (Boyd and Hoerl, 1991). It is a β-lactam compound with a nucleus 7-aminocephalosporanic acid (Brooks, *et al*., 1995), which consist of β-lactam rings fused to dihydrothiazin ring. Various substitutions at the 3 and 7 position alter their antibacterial activity and pharmacokinetic properties (Balows, *et al*., 1991). The mechanism of action of cephalosporins is analogous to that of penicillins, binding to specific penicillin binding proteins that serve as drug receptor on bacteria, inhibiting cell wall synthesis by blocking the transpeptidation of peptidoglycan and activating autolytic enzymes in the cell wall that can produce lesions resulting in bacterial death (Brooks, *et al*., 1995).

Third generation cephalosporins have little activity against Gram positive cocci, *staphylococci* and *enterococci*. A major advantage of third generation drug is their enhanced activity against Gram-negative rods. Another important distinguishing feature of several third generation drugs (except cefoperazone) is the ability to reach central nervous system and to appear in the spinal fluid in sufficient concentration to treat meningitis caused by Gram-negative rod (Brooks, *et al*., 1995).

Third generation cephalosporins broad spectrum against gram-negative bacteria is due to their stability to β-lactamase and their ability to penetrate through the outer cell envelope of Gram-negative bacilli. There are two sub group among these agents: those with potent activity against *Ps. aeruginosa* (ceftazidime and cefoperazone) and those without such activity (ceftizoxime, cefotaxime, ceftriaxone and moxalactam) (Balows, *et al.*, 1991).

This study was designed to determine the susceptibility of *Ps. aeruginosa* isolated from clinical specimens in Sudan to third generation cephalosporins.

MATERIALS AND METHODS

This study was performed on specimens collected from Khartoum Teaching Hospital, Ear Nose Throat Hospital, Military Hospital and National health Laboratory in Khartoum State. Patients aged 1-88 years and were suffering from wound, ear, and urinary tract infections were enrolled.

Different types of culture media were used for primary isolation, purification, biochemical tests and sensitivity testing of *Ps. aeruginosa*. These include blood agar, nutrient agar, Simmon's citrate agar, urea agar, peptone water and Mueller-Hinton agar (MAST Diagnostic, England"). The media were prepared and sterilized according to manufacturer. The identification of the isolates depended on cultural characteristics, Gram's stain, and biochemical tests (Barrow and Filtham, 2003).

Strain of *Ps. aeruginosa*, ATCC 27853, USA was included in the study as control.

Susceptibility tests: The following discs were used to test the activity of the third generation cephalosporins:

ceftazidime (CAZ)30mg, Abtek Biological Ltd., UK; cefoperazone (CFP) 30 mg, Oxoid, UK; cefotaxime (CTX) 30 mg, Abtek Biological Ltd, UK; and ceftriaxone (CRO) 30 mg Bioanalyse, UK.

The test was performed using modified Kirby-Bauer disc diffusion technique. The procedure was carried out in accordance to the National Committee for Clinical Laboratory Standards (NCCLS) (WHO, 1997).

The inoculums turbidity was adjusted to McFarland standard turbidity.

Reading and Interpretation: The diameter of each zone of inhibition (including diameter of the disc) was measured by a ruler, and interpreted according to Table 2 of NCCLS for test organisms and Table (3) of NCCLS for the standard strain of *Ps. aeruginosa* ATCC 27853.

RESULTS

Two hundred and ninety three specimens were collected from patients. The majority of specimens (38%) were obtained from KTH. The age of the patients (males 55% and females 45%) range from less than one year to 88 years. The patients were suffering from different bacterial disorders. The specimens include wound swabs, ear swabs and urine samples. Cultivation of these specimens on blood, CLED and MacConkey's agar showed that 248 (85%) of the specimens yielded significant bacterial growth and the rest 45 (15%) showed no bacterial growth and thus excluded from this study.

The 68 Ps. aeruginosa isolates were tested against the selected 4 cephalosporins by used disc diffusion method. The antibiotic susceptibility rates of Ps. aeruginosa were: ceftazidime, 91%, cefoperazone 47%, cefotaxime 3% and ceftriaxone 7% (Table 1).

Table 2 summarizes the antimicrobial susceptibility pattern of Ps. aeruginosa according to the site of infection.

Table 1: Susceptibility of *Ps. aeruginosa* (n=68) to ceftazidime, cefoperazone, cefotaxime and ceftriaxone

Activity	ceftazidime	cefoperazone	cefotaxime	ceftriaxone
Sensitive	91%	47%	3%	7%
Resistance	7%	32%	50%	69%
Intermediate	2%	21%	47%	24%

Key: S= Susceptible; R= Resistant; I= Intermediate.

Table 2. Susceptibility pattern of *Ps. aeruginosa* according to the site of infection.

Site of infection	ceftazidime			cefoperazone			cefotaxime			ceftriaxone		
	S	R	I	S	R	I	S	R	I	S	R	I
Wound	97	3	00	55	28	17	00	47	53	3	67	31
Ear	96	00	4	46	21	33	8	42	50	12	67	31
Urinary tract	50	50	00	12	88	00	11	87	13	13	87	00

Key: S= Susceptible; R= Resistant; I= Intermediate.

DISCUSSION

This study was conducted to evaluate the activity of four members of the third generation cephalosporins against *Ps. aeruginosa* in clinical specimens. The majority of the isolates (n=36) were recovered from infected wounds. This result is in agreement with Masaad (2005).

Ps. aeruginosa isolates were more among males 37(54%) than females 31(46%). This result confirmed the results obtained by Masaad (2005) who

found *Ps. aeruginosa* among males and females were 74% and 26% respectively. This may be due to the fact that males were more exposed to accidental wound infection than females. Isolation of *Ps. aeruginosa* from different sites: wounds (53%), ear swabs (35%) and urine samples (12%) were found to be similar to those obtained by Masaad (2005).

The result showed that Khartoum Teaching Hospital (KTH) had the highest rate of *Ps. aeruginosa* isolates 33(49%) followed by Ear, Nose and Throat Hospital 23(34%) followed by National Health Laboratory 7(10%) and then Military Hospital 5(7%). This may be due to the large number of specimens collected from KTH. The age group 16-30 years was the most exposed group to *Ps. aeruginosa* infection 22(32%). The age group less than one year was least exposed group to infection 2(3%).

In vitro activities of some third generation cephalosporins (ceftazidime, cefoperazone, cefotaxime and ceftriaxone) were tested using 68 isolates of *Ps. aeruginosa*. Of the tested isolates 62(91%) were sensitive to ceftazidime, while sensitivity of these isolates to cefoperazone was 32(47%). The other two antibiotics cefotaxime and ceftriaxone were less active against *Ps. aeruginosa*, and their activities were 2(3%) and 5(7%) respectively. These results confirm the finding of Masaad (2005) who found the activity of ceftazidime on *Ps. aeruginosa* was 87%. Similar results (91%) and (89%) were obtained by Kechrid and Ben Hassan, (2000) and Qadri, *et al.*, (1991) respectively. The activity of cefoperazone in the present study was found similar to the result obtained by Sarver, *et al.*, (1981) and Lee *et al.*, (1990).

On the other hand, our findings on cefotaxime agree with those of Bonomo *et al.*, (2003) who reported that cefotaxime resistance was 46%. This result was significantly different from that obtained by Tayseer (1997). Moreover, Watankunakorn (1983) reported that the majority of *Ps. aeruginosa* were resistance to cefotaxime. The two studies were confirmed by the finding of the present study.

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