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Research article

Resistance pattern of cephadroxil monohydrate and ceftriaxone sodium against different clinical isolates

Maqsood Ahmed Khan[1,2], Baqir .S. Naqvi[1], Mehwish Rizvi[1,2], Zeb-un-Nisa[1,2], Syed Imran Ali[1], Arif Sabah[3] , *Atta Abbas[3]

[1]Department of Pharmaceutics, Faculty of Pharmacy, University of Karachi, Karachi, Sindh, Pakistan.

[2]Department of Pharmaceutics, Faculty of Pharmacy, Ziauddin University, Karachi, Sindh, Pakistan.

[3]Department of Pharmacy Practice, Faculty of Pharmacy, Ziauddin University, Karachi, Sindh, Pakistan.

ABSTRACT

Resistance pattern of cephadroxil monohydrate and ceftriaxone sodium against different clinical isolates was the aim of the study and 90 clinical isolates comprising of *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella*, *Proteus* and *Pseudomonas aerogenosa* were collected from different local pathological laboratories and their resistant pattern against cephadroxil monohydrate and ceftriaxone sodium were studied using disc diffusion method. *Klebsiella*, (86.6% against cephadroxil monohydrate and 53.33% against ceftriaxone sodium) and Proteus (66.67% against cephadroxil monohydrate and 33.33% against ceftriaxone sodium). In case of *Staphylococcus aureus* and *Escherichia coli*, resistance found was 41.18% and 48% against ceftriaxone sodium,82.35% and 97.62% against cephadroxil monohydrate respectively and in case of *Pseudomonas aerogenosa* resistance found was 40% against ceftriaxone sodium and 90% against cephadroxil monohydrate. It is concluded from these figures that microbial resistance against these cephalosporins are increasing in the population which is alarming and therefore it is recommended to physicians to prescribe these antibiotics only if no other alternate is available in clinical practices.

Keywords: *Escherichia coli*, *Staphylococcus aureus*, *Klebsiella*, *Proteus*, cephalosporin.

INTRODUCTION

The extensive use of antibiotics for antibacterial therapy has started a fast progress and increase of antibiotic resistance in microorganisms, particularly in human pathogens. Moreover, a shift to an enlarge in number and severity of Gram-positive infections has been observed during last decade[1]. Antibiotic resistance occurs when bacteria alter in some way that it eliminates the usefulness of drugs, chemicals or other agents. Thus the bacteria endure and continue to increase causing more harm. Extensive and irregular use of antibiotics promotes the extent of antibiotic resistance. Bacterial susceptibility to antibacterial agents is achieved by determining the minimum inhibitory concentration[2]. Bacteria have developed many strategies to cope with antibiotics as some bacteria can survive antibiotic treatment by activating resistance mechanisms. The key mechanisms include active efflux of the antibiotic from the cell, transformation of the compound by specific enzymes and through alteration of its interaction site[3]. Human misuse of antibiotics plays a main role in resistance. This dilemma may occur when antibiotics are used in every disease. It is a common practice that many patients stop antibiotic

*** Corresponding author: Atta Abbas**

E-mail address: bg33bd@student.sunderlancd.ac.uk.

treatment as soon as they feel improved irrespective of the outcomes. These aborted treatments support drug resistance[4]. These conclusions provide evidence of the need for more rational use of antimicrobial agents all over the world. In order to slow-down the growth and distribution of resistant bacteria, restrictions on antibiotic prescribing are becoming more widespread[5].

Cephalosporin was first obtained from *Cephalosporium acremonium* in 1948 by Brotzu from the sea close to a sewer channel off the Sardinian coast. Crude filters from cultures of this fungus were originated to inhibit the in vitro growth of *Staphylococcus aureus*. Culture fluids in which the Sardinian fungus was cultured were found to have three distinct antibiotics, which were named cephalosporins P, N and C, 7-amino cephalosporinic acid, and with the adding up of side chain, it became possible to produce semisynthetic compound with antibacterial activity very much high than that of parent substance[6]. Cefadroxil is a 1st generation semi-synthetic cephalosporin with a broad antibacterial spectrum and a high chemotherapeutic potential when administered orally[7]. Ceftriaxone sodium is a cephalosporin with a prolonged serum half-life and a broad spectrum of antibacterial activity[8].

Although medical practices are successful very fast in this era, yet many diseases at that needs appropriate agents to get cured. Due to rising resistance, many bacterial infections still today are not being treated effectively. If these infections are not treated suitably then they may become fatal threat in the future[4].

The objective of the present work was to find out the resistance pattern of clinical isolates belonging to *Escherichia coli, Staphylococcus Aureus, Klebsiella and Proteus* against cephadroxil monohydrate and ceftriaxone sodium which were chosen for their wider using disc diffusion method.

MATERIALS AND METHODS

The material and methods consisted of the following:

COLLECTION OF CLINICAL ISOLATES

Clinical isolates were collected from various pathological laboratories situated in Karachi. They were identified as *Escherichia coli* (N = 42), *Staphylococcus Aureus* (N = 17), *Klebsiella* (N = 15) , *Proteus* (N = 7). *Pseudomonas aerogenosa* (N =9). Zones of inhibition produced by antimicrobials against clinical by using disk diffusion (KirbyBauer) method. Isolates were determined by CLSI (formally NCCLS) and take reference as ≥ 18mm susceptible and ≤ 14(R) resistant for cephadroxil monohydrate 30 mcg that is the standard of cephalothin and we predict this value for the cephadroxil monohydrate.

ANTIMICROBIAL AGENTS

Standard discs cephadroxil monohydrate and ceftriaxone sodium were purchased from Oxoid, UK.

PREPARATION OF MEDIA

Mueller Hinton Agar and Mueller Hinton Broth were used during the study and they were prepared according to manufacturer's instructions (Merck).

PREPARATION OF MEDIA PLATES

Mueller Hinton Agar was poured into sterile Petri dish about 20-25 ml per plate. The plates were then place to one side on a flat surface and permitted to solidify for 15 minutes.

PREPARATION OF INOCULUM

The inoculation was prepared by touching the top of the colonies of the isolates with sterile wire loop and suspending in a tube containing 2-3 ml of broth. All work was carried out close to flame. The tubes are then incubated at 37°C for few hours till they reach to Macfarlan turbidity.

INOCULATION OF PLATES

A sterile swab was used for this reason. Sterile swab was dipped into a broth suspension of organism. Excess fluid was removed by pressing and revolving the swab against the side of tube above the level of suspension. The swab was then steak equally over the surface of the medium in three directions, revolving the plates approximately 60 degree to ensure even distribution.

PLACEMENT OF ANTIBIOTIC DISC

By using sterile forceps, the suitable antimicrobial discs of ceftriaxone sodium and cephadroxil monohydrate were positioned on the agar surface one by one side by side at about 25cm apart. Each disc was slightly pressed down to ensure its contacts with agar.

INCUBATION OF PLATES

Within 30 minutes of applying discs, the plates were inverted and incubated at 37°C for 24 hours, the plates were examined and zone of inhibition was measured.

RESULT

In the present study, resistant pattern of ninty (N = 90) clinical isolates of *Escherichia coli (*N = 42), *Staphylococcus aureus* (N = 17), *Proteus* (N = 6), *Psedumonas aerogenosa* (N = 10) and *Klebsiella* (N = 15) were studied using ceftriaxone sodium and cephadroxil monohydrate. The results are depicted in figures. 1 and 2 respectively. The results revealed that more than half (52.38%) of clinical isolates of *Escherichia coli*, almost half (41.18%) of *Staphylococcus aureus*, a third (33.33%) of *Proteus*, a fourth (40%) of *Pseudomonas aerogenosa* and more than half (53.33%) *Klebsiella* were resistant to ceftriaxone sodium.

In case of cephadroxil monohydrate showed that 73.18% clinical isolates of *Escherichia coli, 58.82% Staphylococcus aureus,* 66.67% *Proteus 70% Psedumonas aerogenosa 66.67% Klebsiella* and were resistant to cephadroxil monohydrate. From these figures, it is clear that *Escherichia. coli, Staphylococcus aureus, Proteus spp Psedumonas aerogenosa, and Klebsiella spp* are more resistant against cephadroxil monohydrate as compared to ceftriaxone sodium. Table 1 illustrates the findings.

Table 1. Resistance pattern of isolates

Average diameter Zone of Inhibition (mm)		Number of clinical isolate resistant to cephadandroxil monohydrate and percentage of susceptibility.		Number of clinical isolates resistant to ceftrixone and percentage of susceptibility.		Name of organism	
Cephadroxil monohydrate	Ceftrixone	% of clinical isolates susceptible to cephadroxil monohydrate	Cephadroxil monohydrate	% of clinical isolates susceptible to ceftrixone	Ceftrixone	Total number of Clinical isolates	Name of Clinical isolates
8.7619 mm	17.262 mm	26.82	31	47.62	20	42	*Escherichia coli*
12.375 mm	12.823 mm	41.18	9	58.82	7	17	*Staphylococcus aureus*
6.9 mm	17.3 mm	30	7	60	4	10	*Pseudomonas aerogenosa*
9.1333 mm	13 mm	33.33	10	46.67	7	15	*Klebsilla spp*
16.5 mm	26.166mm	33.33	4	66.67	2	6	*Proteus spp*

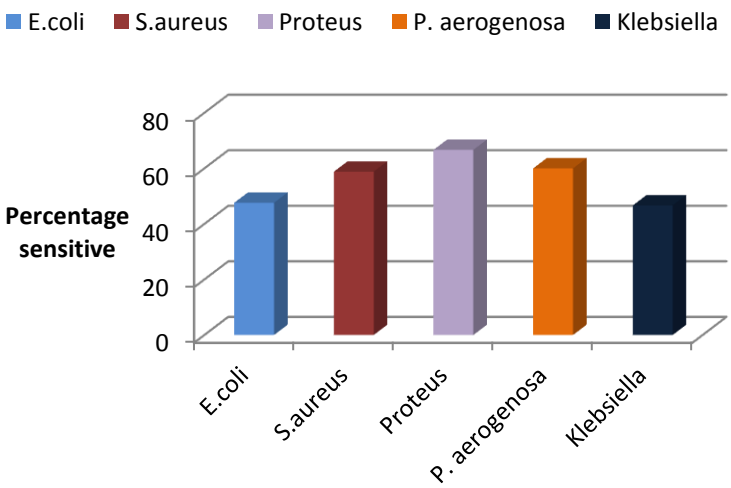

Figure l. Percentage of microrganism sensitive to ceftriaxone sodium

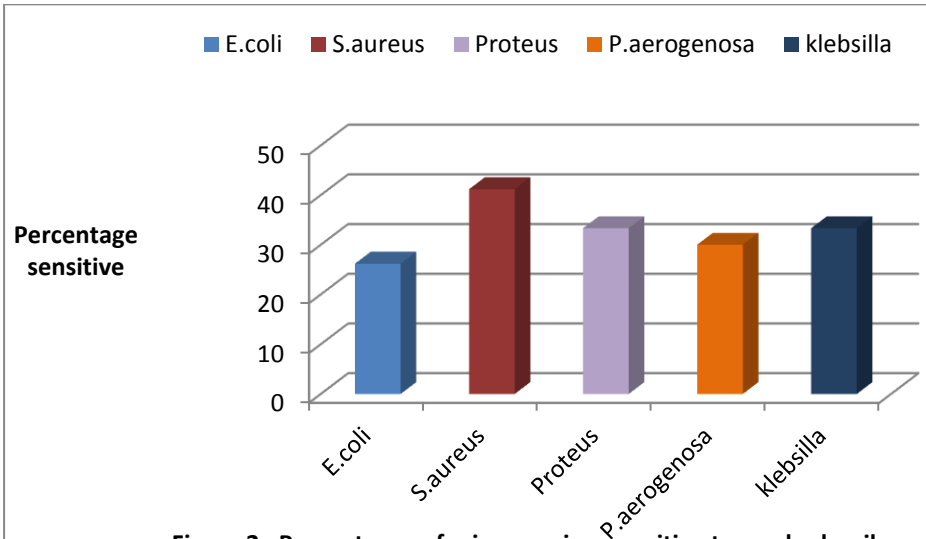

Figure 2. Percentage of microrganism sensitive to cephadroxil monohydrate

DISCUSSION

Antimicrobial resistance is now reported as global problem which was experienced for the first time in *Escherichia coli* in 1940. The primary factor responsible for the development and stretch of bacterial resistance is the careless use of antimicrobial agents[9]. Misuse of antimicrobial agents has optimistic the evolution of bacteria towards resistance that often outcome in therapeutic failure[4]. Antimicrobial stewardship is a key component of a versatile approach to preventing emergence of antimicrobial resistance. Good antimicrobial stewardship involves selecting a suitable drug and optimizing its dose and duration to heal an infection as minimizing toxicity and situation for selection of resistant bacteria strains[10]. Another study reported resistance *in P.aeruginosa* against ceftriaxone sodium and it was observed to be 67%[11]. *Enterobacteriaceae* group showed superior and statistically major resistance in the second study period against ceftriaxone sodium[12].

Ceftriaxone sodium is stable to beta-lactamases, mainly those produced by Gram-negative bacteria. It has high potency against all the microbes of family *Enterobacteriaceae*, *Haemophilus influenzae*, the *Nisseria* and nearly all Gram-positive cocci except *Enterococcal spp*[13] ceftriaxone sodium resistance rates in *Escherichia. coli* persistent to enhance[14], in another findings only 21% of different clinical isolates like *Psedomonas aerogenosa*, *E. coli*, and *Klebsiella* showed sensitivity to ceftriaxone sodium and the resistance against ceftriaxone sodium increases progressively[15]. The growing trends of resistance against cephalosporins were noticed with respect to *Acinetobacter* species, *Klebsiella* species and *Enterobacter* species for cefuroxime and ceftriaxone sodium[16]. This unnecessary use of cephalosporins in chemotherapy of hospitalized and outdoor patients has led to an amplify in resistance among *S. aureus*[17]. Nowadays, ceftriaxone sodium is the most commonly used antibiotic as a result bacteria are becoming more resistant to these broad-spectrum cephalosporins[18]. According to another study conducted in Indonesia which says that 71.4% of *Enterobacteriaceae* were resistant to ceftriaxone sodium[19].

Cefadroxil is a new semisynthetic cephalosporin with a broad antibacterial spectrum and a high chemotherapeutic potential when administered orally[20]. Cefadroxil is another 1st generation Cephalosporin having activity very much resemblance to cephalexin and 54% isolates of *Staphylococcus aureus* are resistant against cefadroxil[21]. Cefadroxil, the first generation orally active semisynthetic cephalosporin, available as monohydrate or trihydrate is highly active against Gram positive *cocci* and because of its mode of action has a slow bactericidal action to Gram negative *bacilli.*[22] In another study showed that more than 90% strains of *Staphylococcus aureus* are resistant to cefadroxil that clearly differentiate cephalexin and cefadroxil antibacterial spectra[6] in another study which confirm the high resistance of cephadroxil 93% against by *Staphylococcus aureus* and this study also confirm that *Klebsiella Pnumomoniae* of blood isolates, also shows 100%

resistance to ceftriaxone sodium.[23] The study also found resistance against cephadroxil monohydrate and ceftriaxone sodium and thus the study corroborates with the previous studies.[24,25,26]

CONCLUSION

In the population under investigation, bacterial strains are developing resistance against cephalosporin. It is suggested that physicians who prescribe cephalosporins prescribe with caution and rationality unless no other choice is available. A clinical pharmacist can come in handy in such scenarios; otherwise it seems that treatment of some infectious diseases may become impossible in the near future.

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