

TREATMENT WITH CSE-1034 (ELORES™) FOR UROSEPSIS DUE TO MULTI-DRUG RESISTANT *PSEUDOMONAS AERUGINOSA*

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ABSTRACT

Urosepsis is a type of sepsis caused by infection of urogenital tract and characterized with an inflammatory response. Ability of *Pseudomonas aeruginosa* to develop a resistance to various antibiotics presents as a therapeutic challenge for the physician. In the present case report, we discuss a case of 70-year-old male patient suffering with urosepsis due to multi-drug resistant (MDR) *P. aeruginosa* pathogen. This patient was treated with a novel antibiotic adjuvant entity Elores™ (ceftriaxone / sulbactam / disodium edetate). The present case shows Elores™ to be safe and efficacious in the treatment of urosepsis due to MDR *P. aeruginosa*. Elores™ can be considered as drug of choice in the treatment of MDR *P. aeruginosa* infections.

Keywords: Elores™, *Pseudomonas aeruginosa*, Antibiotic resistance, Urosepsis, Complicated urinary tract infection, Disodium edetate.

INTRODUCTION

Urosepsis is defined as sepsis caused by infection of urogenital tract and characterized with inflammatory response. Urosepsis accounts for 25% of total sepsis cases [1]. About 40% cases of nosocomial infections are of urinary tract infections (UTIs) [2]. Obstruction of urine is a frequent reason for sepsis. Complicated UTI (cUTI) is the common cause of urosepsis [2]. Gram-negative bacteria are commonly responsible for urosepsis. Among these Gram-negative bacteria, *Escherichia coli* is responsible for 50% of cases while *Proteus* spp., *Enterobacter* and *Klebsiella* spp. Collectively comprises 30% of cases. *Pseudomonas aeruginosa* causes 5% of total urosepsis cases infected with Gram-negative bacteria [2]. The ability of *P. aeruginosa* to develop the resistance to various antibiotics poses a therapeutic challenge for the physician [3,4].

In the present case report, we discuss a case of 70-years-old male suffering from urosepsis due to multi-drug resistant (MDR) *P. aeruginosa* which was successfully treated with Elores™.

CASE REPORT

A 70-year-old male patient was admitted to hospital with complaints of pain, weakness, burning micturition, and renal calculi. He was operated 52 days before, for renal calculi with bilateral percutaneous nephrolithotomy under spinal anesthesia. He presented with complaints of general weakness and had vitals as follow: (a) Body temperature of 98.4°F, (b) blood pressure of 130/70 mmHg, (c) pulse rate of 76/minute, (d) SPO₂ 99% on room air, and (e) respiratory rate of 21 breaths/minute. Systemic examination showed cardiovascular system: S1, S2 normal, chest: Bilateral equal air entry, abdomen: Soft and nontender and central nervous system: conscious and oriented. He was presumptively diagnosed with urosepsis, chronic kidney disease, and obstructive uropathy.

The treatment was started empirically with intravenous piperacillin/tazobactam 4.5 g every 12 hrs. Hemogram showed total leukocyte count (TLC) to be 16,500/cumm. Urine sample was sent for culture and susceptibility test. Based on diagnostic criteria for sepsis, clinical and laboratory examinations patient was diagnosed with urosepsis. Urine culture and sensitivity report showed the presence of pathogen *P. aeruginosa*, which was resistant to most of antibiotics as listed in Table 1. As *P. aeruginosa* was resistant to piperacillin/tazobactam so piperacillin/tazobactam was discontinued. Elores™ 3 g every 12 hrs was administered by intravenously for an infusion time of 90 minutes for 7 days. TLC normalized after 7 days (8500/cumm).

DISCUSSION

P. aeruginosa causes various hospital acquired infections characterized by substantial morbidity and mortality. *P. aeruginosa* pathogen presents a serious challenge for the treatment of urosepsis because of its ability to develop resistance to antibiotics. Thus, selection of antibiotic should be done very judiciously [5]. In the present case study, culture and sensitivity report revealed the resistance of *P. aeruginosa* to piperacillin/tazobactam, so this antibiotic was discontinued. *P. aeruginosa* was susceptible to colistin in culture and susceptibility test. However, colistin was not used because of nephrotoxicity and neurotoxicity concerns [6,7]. cUTI and urosepsis are not approved indications for tigecycline [8]. Elores™ is safe and efficacious in *Pseudomonas* infection. Moreover, this antibiotic combination is eliminated (Ceftriaxone: 50-60%; Sulbactam: 70-80%) mainly in urine [9]. Elores™ had 4-5 fold lower minimum inhibitor concentration as compared to ceftriaxone and sulbactam [10].

Elores™ is highly potent and efficacious in the treatment of metallo-β-lactamases (MBL) producing *P. aeruginosa* [5]. A study published in 2013 showed susceptibility of 515 isolated (extended-spectrum-β-lactamases [ESBL]: 45.63%, MBL: 16.89%, ESBL + MBL: 14.36%) of *P. aeruginosa* to antibiotics. Isolates with MBL and ESBL + MBL genes were resistant to meropenem, imipenem, ceftazidime, cefepime,

Table 1: Culture and susceptibility profile of urine sample

Antibiotic	<i>P. aeruginosa</i>
Carbapenem	Resistant
Gentamicin	Resistant
Piperacillin/tazobactam	Resistant
Cefoperazone + sulbactam	Resistant
Cefepime	Resistant
Cefotaxime	Resistant
Ceftazidime	Resistant
Ceftriaxone	Resistant
Ciprofloxacin	Resistant
Levofloxacin	Resistant
Norfloxacin	Resistant
Oflxacin	Resistant
Azteonam	Resistant
Nitrofurantoin	Resistant
Amikacin	Intermediate
Tobramycin	Intermediate
Elores™	Sensitive

P. aeruginosa: Pseudomonas aeruginosa

piperacilline + tazobactam antibiotics and susceptibility to Elores™ was 97.3% and 95.1% and for doripenem was 11.3% and 19.5% for MBL and ESBL + MBL, respectively [5].

All the three components of Elores™ have synergistic effect against microbial infection. Ceftriaxone acts as antibiotic while sulbactam is irreversible β lactamase inhibitor. Disodium edetate chelates zinc ions (required for MBL activity), enhances the membrane permeation, and inhibits efflux pump [9,10]. A Phase III clinical trials results showed 83.33% cure rate in UTIs [4]. That's why in this case after discontinuation of piperacillin/tazobactam, Elores™ was given. In the present case, we observed therapeutic efficacy of Elores™ in *P. aeruginosa* infection. Clinical cure justifies the use of Elores™ as an antibiotic therapy.

CONCLUSION

The present case shows Elores™ to be safe and efficacious in the treatment of urosepsis due to MDR *P. aeruginosa*. Elores™ can be considered as drug of choice in the treatment of MDR *P. aeruginosa* infections.

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