

ELORES: A NOVEL TREATMENT APPROACH IN ELECTRIC BURN PATIENT WITH BACTEREMIA AND VENTILATOR-ASSOCIATED PNEUMONIA: A CASE STUDY

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Received: 16 January 2016, Revised and Accepted: 22 January 2016

ABSTRACT

Rising challenge in treating nearly a million burn patients in India, with high mortality and morbidity attributed to nosocomial infections, is a serious concern. With cascades of reactions taking place in serious burn patients, there is a massive release of humoral factors, such as cytokines, prostaglandins, vasoactive prostanoids, and leukotrienes, along with multiple defects of cellular and humoral components of defense system. This immunocompromised state favors increased chances of nosocomial infections such as pneumonia and blood stream infections. The present case discusses a novel treatment approach with Elores (ceftriaxone, sulbactam, and adjuvant disodium edetate) in effectively treating burn patient with bacteremia and ventilator-associated pneumonia.

Keywords: Bacteremia, Elores, Electric burns, Ventilator-associated pneumonia.

INTRODUCTION

Infectious complications are a regular threat to burn patients during hospitalizations. Most of the infections that develop in burn patients are nosocomial and of pulmonary etiology [1]. In India, every year nearly 7 lakh burn patients are admitted to hospital, with a high percentage of morbidity and low survival. Estimated 75% of all deaths following burns are attributed to complications arising from nosocomial infections [2].

Thermal injury to the skin causes a massive release of humoral factors such as cytokines, prostaglandins, vasoactive prostanoids, and leukotrienes. Accumulation of these agents at the wound site consequences "spillover" into the systemic circulation, thereby causing immunosuppression [3]. The immunocompromised state of the burn patient is associated with multiple defects of humoral and cellular components defense system. The poor performing immune system markedly contribute to increased susceptibility to multi-drug resistant nosocomial infections such as pneumonia and blood stream infections (BSI) [4,5].

Further to this, burn trauma also affects the lower airways along with skin damage. Severely burnt patients who require mechanical ventilation even without inhalation injury, exhibit high pneumonia rates due to serious immunodepression after the burn trauma. The incidence of the pneumonia rate in burn patients was reported up to 31.3 episodes a 1,000 ventilation days [6]. Ventilator-associated pneumonia (VAP) in burn patients contributes to an increase in afflictions with the excess length of hospitalization and increased fatality [4]. The compromised host defense mechanism and ventilation support in burn patients create an ideal condition for Gram-negative bacterial infections [7].

Acinetobacter baumannii and *Pseudomonas aeruginosa* are major pathogen associated with burn patients. Multidrug resistant (MDR) nature of these pathogens elaborates inactivating enzymes such as extended spectrum beta-lactamases (ESBLs) and metallo-beta-lactamases (MBLs) that make beta-lactams and carbapenems ineffective, which cause 4-60% nosocomial infections in different parts of the world [8]. Burn infections caused by *P. aeruginosa* often deteriorate rapidly and lead to systemic spread and death within days or weeks [9]. Patients receiving ventilator assistance in the ICU have a 20-fold higher likelihood of developing pneumonia caused by *P. aeruginosa* [5].

Along with VAP, burn patients are more prone to BSI. In burn patients, BSI may occur as a result of seeding of the bloodstream from the burn wound, the respiratory tract or central venous catheters [5]. *A. baumannii* is commonly associated with bacteremia in burn patients along with *Staphylococcus aureus*, *P. aeruginosa*, and *Klebsiella pneumoniae* [10]. *Acinetobacter* sp., are actually part of the residential flora of the respiratory, skin, as well as gastrointestinal and genitourinary tracts [5].

In burn patients, complicated disease progress with more possibility of poly infections, high bacterial colonizations and emerging antibiotic resistance, leading to severe chronic infections [7]. Here, we present a challenging patient case with electric burn wounds with bacteremia due to *A. baumannii* and VAP caused by *P. aeruginosa*.

CASE REPORT

A 32-year male patient was transferred from a Government tertiary care hospital to our emergency department in a critical condition. The patient had sustained deep electric burns on left forearm, hand, back and left thigh, with electric ischemia on the left hand while working on a transformer. Fasciotomy of the forearm was performed at the government hospital. On examination, the patient was conscious, oriented, temperature of 36.9°C, pulse 84 beats/min, respiratory 22 cycles/min and blood pressure of 110/90 mm of Hg.

Local examination revealed, deep burns on left hand with cold extremities, loss of sensation on touch with signs of critical ischemia. Underlying muscles at the wrist and upper medial aspect of the left thigh appeared necrosed, along with underneath and surrounding necrosed skin. Wound on the left scapular region with necrosis of the underlying muscles and surrounding skin was noted. Superficial burns over back and scrotal edema was present.

The patient was admitted and immediately put on ventilator in surgical intensive care unit. All investigations were done and started with a broad spectrum antibiotic (cefepime), muscle relaxants, analgesics, and other supportive measures. Packed red blood cell transfusion was given. Debridement of the left hand, forearm, left scapular and left groin region was performed. Post 48 hrs of debridement and monitoring of finger circulation, the decision was taken for below elbow amputation due to diminished circulation and increasing necrosis. Patient

blood samples tested on the 13th day of postburn injuries revealed *A. baumannii* and accordingly antibiotics were stepped up. Ventilator tracheotomy was done as patient was on mechanical ventilation for longer duration of time. The patient started having fever (38.6°C) with increased tracheotomy secretions. Progressive infiltrate was identified on sequential daily chest X-ray. Samples of tracheotomy secretion were sent for culture and sensitivity, which revealed MDR *P. aeruginosa*, showing sensitivity to only Colistin and Elores. Patient was immediately put on Elores 3 g BD dose with 90 min infusion along with colistin. As tracheal secretions decreased and laboratory parameters stabilized, skin grafting left groin and right hand with major wound closure were done. With improving condition, the patient was weaned off from the ventilator, monitored closely and shifted toward for observation. Tracheal secretions decreased and showed a lower bacterial load of *P. aeruginosa*. The patient was continued on Elores 3 g BD dose for total of 15 days and colistin stopped after 7 days of administration. His fever spikes decreased and wound showed signs of granulation and healing. Patient was discharged on request and advised Elores 1.5 g BD with supportive medications and follow-up every 5 days. Patients condition showed marked improvement after 5 days of follow-up. Elores was stopped, and patient was put on oral antibiotic therapy and supportive medications.

DISCUSSION

Burns are one of the most common and devastating forms of trauma. They are at high risk of developing nosocomial infection because of low skin integrity, suppressed immune system, prolonged hospitalization and invasive therapeutic and diagnostic procedures [11]. The flora of burn wounds during hospitalization has been dominated by multi-drug resistant Gram-negative bacteria especially *P. aeruginosa* and *A. baumannii*.

A. baumannii is more frequently observed in the early stage of the burn injury especially in bacteremia. In the present case, *A. baumannii* clinical isolates were initially isolated in the blood samples after 13 days of burn injuries. It is similar to the study published by Lee *et al.*, where *A. baumannii* was reported mean 14.9 days after burn injury [12].

The incidence of VAP in burn patients requiring mechanical ventilation is high. In the present case, patient was identified MDR *P. aeruginosa* in tracheotomy secretions along with *A. baumannii* after 48 hrs of ventilation support. VAP further confirmed based on patient progressive infiltrate, fever and increased purulent tracheobronchial secretions. An increase in carbapenem-resistant bacteria has been continuously reported in burn patients. The majority of *P. aeruginosa*, an opportunistic human pathogen, isolates from burn patients were MDR in nature [11]. In the present case, patient was infected with *P. aeruginosa* which was sensitive only to colistin and Elores. Similarly, in a study by Lee *et al.*, reported 95.9% *P. aeruginosa* carbapenem-resistant clinical isolates in burn patients which were sensitive only to colistin [12]. In addition to this, in a study by, Brusselsaers *et al.*, the incidence of VAP in burn patients with inhalation injury is high: 55 episodes/1000 ventilation days [4].

It can be presumed that the presence of an inhalation injury contributes to the development of VAP in burn patients [4]. In patients with large burns VAP may be caused due to: increased capillary permeability occurring in remote organs like lungs, development of edema in respiratory mucosa caused by an inflammatory cascade, causing release of the proteolytic enzymes and oxidants which destroy the lung parenchyma and diminished surfactants, further accelerating edema formation, alveolar collapse, decreasing gas exchange, and consequently decrease in lung compliance [13].

Once pneumonia occurs, early adequate antibiotic therapy is essential to optimize the chance of survival. Inappropriate empiric therapy, not covering the causative organism, has been associated with an increased casualty rate [4]. Studies show that a delay in the initiation of appropriate antibiotic therapy for patients with VAP (early or late

in onset) has association with increased obliteration, the cost of care and fatality [13]. Antibiotic prophylaxis reduces mortality, bacteremia, and VAP among patients in intensive care units (ICUs) [14]. However, due to the high endemic levels of antibiotic resistance, the benefits of prophylactic antibiotics for VAP have been considerably low in ICUs [13].

In the present case, prophylactic antibiotics initiated with a broad spectrum antibiotic (cefepime) by considering the risk of deep electric burns, signs of critical ischemia and possibility of developing gangrene. However, the patient condition was not improved even after prophylactic antibiotic therapy, he further developed superinfections like bacteremia due to *A. baumannii* and VAP caused by *P. aeruginosa*. Therapy with novel antibiotic adjuvant entity Elores was initiated in the current case by discontinuing cefepime to optimize the chance of survival after super-infection with MDR pathogens was identified which were susceptible to Elores and colistin. Elores was chosen based on the strong literature evidence, culture sensitivity reports and ample evidence against ESBL and MBL producing MDR *P. aeruginosa* and *A. baumannii*.

Elores has established safety, efficacy and broad-spectrum activity against ESBL/MBL producing *A. baumannii* and *P. aeruginosa* pathogens. *In vitro* study on Elores, has shown enhanced susceptibility to MDR Gram-negative bacteria by its synergistic effect and action on multiple resistant mechanisms of bacteria [15]. In a microbial surveillance study by Chaudhary *et al.*, Elores showed 93-96% susceptibility on carbapenemase-producing *A. baumannii* [16]. In a recent study, on Antibiotic susceptibility pattern of Gram-negative pathogens from ICU patients in an Indian hospital Elores demonstrated high susceptibility compared to imipenem-cilastatin, meropenem, cefoperazone-sulbactam and piperacillin-tazobactam [17]. Similarly, phase-III clinical studies published on Elores showed 80.33% and 91.3% clinical cure rates in patients including skin and skin structure infections and lower respiratory tract infections respectively [18]. Likewise, a case study by Arpit Jain on acute lung abscess caused by MDR *P. aeruginosa* was successfully treated with Elores [19].

According to the study by Chaudhary and Payasi [15] enhanced sensitivity of Elores to MDR *P. aeruginosa* could be due to: synergistic activity of ceftriaxone, sulbactam and disodium edetate which enhances bacterial cell permeability, chelation of divalent ions present in MBL enzymes for activation, ATP concentration in Gram-negative bacteria controls the rate of rRNA transcription initiation in protein synthesis or down-regulation of protein expression responsible for MexA-MexB-OprM efflux pump overexpression [15].

Studies published on Elores, report excellent efficacy on carbapenem-resistant pathogens [20,21]. Goyal [22] recently published a case study on pneumonia caused by ESBL producing pathogen, showing resistance to carbapenems and successfully treated with Elores. Similarly, a case study by Gupta [23] Gupta, patient with ESBL producing nosocomial infection and hypersensitive to Meropenem and Colistin was successfully treated with Elores.

In our case, the patient responded well after Elores and colistin antibiotic therapy. Hence, selection of an efficient antibiotic therapy regimen in burn patients should be based on the ability of drug sensitive to bacteria isolated from burn wound, periodic bacterial cultures and monitoring the nosocomial infections in the burn wards.

CONCLUSION

Burn patients are ideal hosts for opportunistic infections during hospitalization because of their higher degree of immunosuppression. The compromised immune state of the burned patient favor increased susceptibility to MDR nosocomial infections causing pneumonia and BSI. The present case study shows Elores to be a safe and effective choice in treating MDR nosocomial infections in critical burn patients with colistin.

REFERENCES

- Huzar TF, Cross JM. Ventilator-associated pneumonia in burn patients: A cause or consequence of critical illness? *Expert Rev Respir Med* 2011;5(5):663-73.
- Fouzia B, Damle AS, Maher G. Changing patterns of burn infections. *IOSR J Dent Med Sci* 2013;5(4):11-4.
- Mayhall CG. The epidemiology of burn wound infections: Then and now. *Clin Infect Dis* 2003;37(4):543-50.
- Brusselsaers N, Logie D, Vogelaers D, Monstrey S, Blot S. Burns, inhalation injury and ventilator-associated pneumonia: Value of routine surveillance cultures. *Burns* 2012;38(3):364-70.
- Jeschke MG, Kamolz LP, Sjöberg F, Wolf SE. *Handbook of Burns: Acute Burn Care*. Vol. 1. New York: Springer Wien; 2012. p. 227.
- de La Cal MA, Cerdá E, García-Hierro P, Lorente L, Sánchez-Concheiro M, Díaz C, *et al*. Pneumonia in patients with severe burns: A classification according to the concept of the carrier state. *Chest* 2001;119(4):1160-5.
- Anvarinejad M, Japoni A, Razaftpour N, Mardaneh J, Abbasi P, Amin Shahidi M, *et al*. Burn patients infected with metallo-beta-lactamase-producing *Pseudomonas aeruginosa*: Multidrug-resistant strains. *Arch Trauma Res* 2014;3(2):e18182.
- Biswal I, Arora BS, Kasana D, Neetushree. Incidence of multidrug resistant *Pseudomonas aeruginosa* isolated from burn patients and environment of teaching institution. *J Clin Diagn Res* 2014;8(5):DC26-9.
- Turner KH, Everett J, Trivedi U, Rumbaugh KP, Whiteley M. Requirements for *Pseudomonas aeruginosa* acute burn and chronic surgical wound infection. *PLoS Genet* 2014;10(7):e1004518.
- D'Avignon LC, Murray CK. Fever in the burn patient. *Infect Dis Antimicrob Agents*. Available from: <http://www.antimicrobe.org/e44.asp>.
- Azimi L, Motevallian A, Ebrahimzadeh Namvar A, Asghari B, Lari AR. Nosocomial infections in burned patients in Motahari hospital, Tehran, Iran. *Dermatol Res Pract* 2011;2011:436952.
- Lee HG, Jang J, Choi JE, Chung DC, Han JW, Woo H, *et al*. Blood stream infections in patients in the burn intensive care unit. *Infect Chemother* 2013;45(2):194-201.
- Luo J, Guo GH. Interpretation for practice guidelines for prevention, diagnosis, and treatment of ventilator-associated pneumonia in burn patients by American burn association. *Burns Trauma* 2015;3:11.
- Avni T, Levcovich A, Ad-El DD, Leibovici L, Paul M. Prophylactic antibiotics for burns patients: Systematic review and meta-analysis. *BMJ* 2010;340:c241.
- Chaudhary M, Payasi A. Ethylenediaminetetraacetic acid: A non-antibiotic adjuvant enhancing *Pseudomonas aeruginosa* susceptibility. *Afr J Microbiol Res* 2012;6(39):6799-804.
- Chaudhary M, Payasi A. Incidence, prevalence and control of multidrug resistant (MDR) carbapenemase producing *Acinetobacter baumannii* in Indian intensive care units. *J Pharm Res* 2013;7(2):175-80.
- Arora S, Munshi N. Comparative assessment of antibiotic susceptibility pattern of Gram-negative pathogens isolated from intensive care unit patients in Pune. *Br Microbiol Res J* 2015;10(2):1-9.
- Chaudhary M, Payasi A. Clinical, microbial efficacy and tolerability of Elores, a novel antibiotic adjuvant entity in ESBL producing pathogens: Prospective randomized controlled clinical trial. *J Pharm Res* 2013;7(4):275-80.
- Jain A. Acute left lung abscess caused by multidrug-resistant *Pseudomonas aeruginosa* treated with Elores: A case study. *Int J Adv Res* 2015;3(7):173-6.
- Chaudhary M, Payasi A. Susceptibility trend of drugs among metallo β -lactamase producing strains of *Escherichia coli*, *Klebsiella pneumoniae*, *Acinetobacter baumannii* and *Pseudomonas aeruginosa* in India. *Int J Adv Pharm Biol Chem* 2015;4(2):303-12.
- Chaudhary M, Payasi A. Inhibition of metallo beta-lactamases by Elores. *J Antimicrob Photonics* 2013;128:177-82.
- Goyal S. Management of pneumonia with multiloculated left pleural effusion caused by extended spectrum beta-lactamases producing *Klebsiella pneumoniae*. *Int J Clin Biomed Res* 2015;1(4):73-6.
- Gupta N. A case study: Viral pneumonia induced acute respiratory distress syndrome with super infection of ESBL producing *Klebsiella pneumoniae* treated with antibiotic adjuvant entity: Elores. *Int J Adv Res* 2015;3(8):136-9.