



## Case Report : Expanded-Spectrum Beta Lactamase-Producing *Klebsiella pneumoniae* in Burn Injury With Hospital Acquired Pneumonia

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### ABSTRAK

Angka kematian yang tinggi ditunjukkan pada pasien luka bakar berat yang disebabkan oleh infeksi *Klebsiella pneumoniae*. Belum banyak penelitian yang mengevaluasi efektifitas antibiotik pada pasien luka bakar dengan pneumonia yang disebabkan oleh *Klebsiella pneumoniae*. Laporan kasus ini mengevaluasi kombinasi meropenem dan levofloksasin untuk infeksi *Klebsiella pneumoniae* ESBL pada pasien luka bakar dengan pneumonia yang didapat di rumah sakit. Seorang pria berusia 52 tahun mengalami luka bakar pada bulan Agustus 2016 masuk rumah sakit dengan komplikasi Hospital Acquired Pneumonia (HAP). *Klebsiella pneumoniae* ESBL diisolasi dari kultur jaringan yang terbakar. Pada awalnya, pasien diterapi dengan antibiotik empiris meropenem dan levofloxacin selama satu minggu. Kemudian, *Acinetobacter baumannii* diisolasi dari jaringan dan ampicilin-sulbactam adalah satu-satunya antibiotik yang masih sensitif terhadap *Acinetobacter baumannii*. Akan tetapi, kombinasi meropenem dan levofloksacin tetap diberikan. Setelah pemberian antibiotik ini, terjadi perbaikan gejala klinis dengan tidak ditemukan sesak nafas, demam, batuk, dan infiltrat paru juga membaik. Kombinasi meropenem dan levofloksacin dapat menjadi pilihan terapi untuk pengatasan pneumonia yang didapat di rumah sakit terkait dengan *Klebsiella pneumoniae* ESBL dan juga *Acinetobacter baumannii*. Dikarenakan bakteri tersebut tergolong MDR patogen, kombinasi antibiotik antipseudomonal harus diberikan. Penelitian lebih lanjut diperlukan untuk mengklarifikasi efektivitas meropenem dan levofloksasin untuk mengobati infeksi *Klebsiella pneumoniae* ESBL pada pasien luka bakar.

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### Keywords:

Acinetobacter baumannii ;  
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Klebsiella pneumoniae ESBL  
Levofloxacin ;  
Meropenem

### ABSTRACT

Patients with severe burn are significantly higher mortality than in mild burns, especially complicated by *Klebsiella pneumoniae* infection. This case report assessed the combination efficacy of meropenem and levofloxacin to treat *Klebsiella pneumoniae* ESBL on the scald-burn injury with hospital-acquired pneumonia. A 52-year-old male had scald burn on August, 2016 with late onset of Hospital Acquired Pneumonia (HAP). *Klebsiella pneumoniae* ESBL was isolated from tissue burned culture. Initially, the patient was treated with meropenem and levofloxacin injection for a week. Then, *Acinetobacter baumannii* was isolated from tissue burned infection and ampicilin-sulbactam was the only antibiotic which still susceptible to this pathogen. By the the clinical judgment, the combination of these antibiotics was still continued. After administration of these antibiotics, rapid clinical improvement with signs such as dyspnea, fever, and cough were not observed and the lung infiltrate was improved. The combination of meropenem and levofloxacin may be a useful treatment option for hospital-acquired pneumonia related to *Klebsiella pneumoniae* ESBL and *Acinetobacter baumannii*. Further research is needed to clarify the effectiveness of meropenem and levofloxacin to treat *Klebsiella pneumoniae* ESBL infection in patients

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## 1. Introduction

*Klebsiella pneumoniae* is a pathogenic bacteria that is usually found in burns. Some of this bacteria produces Extended-spectrum beta-lactamase (ESBL) enzyme which resistance to many beta lactam antibiotics<sup>1</sup>. Infections caused by multidrug-resistant Gram negative bacteria that produce extended-spectrum beta-lactamase (ESBL) enzyme are associated with higher morbidity and mortality than non caused by ESBL<sup>2,3</sup>. Hospital-acquired pneumonia (HAP) is most difficult problem in patients who admitted in the hospital for a long time. Burn injury especially in severe burn with total body surface area (TBSA) more than 20% is very high risk to hospital acquired pneumonia (HAP)<sup>4</sup>. Because of high resistance to several antibiotics, treatment of ESBL sometimes difficult. (ESBLs) are enzymes that hydrolyze cephalosporins groups, such as ceftazidime and ceftriaxone and several antibiotics that have the beta-lactam rings<sup>5</sup>. Burn patients, especially in full thickness burns are more at risk of infection due to ESBL-producing *K. pneumoniae* with greater severity than infections that are not caused by *K. pneumoniae*. Furthermore, infections caused by ESBL-producing *K. pneumoniae* can predict of death when it occurs in older patients with severe burns <sup>6</sup>. A recent study in patients with severe burns showed that significantly higher mortality with *K. pneumoniae* ESBL infection than that of with *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, and methicillin-resistant *Staphylococcus aureus* (MRSA)<sup>7</sup>. Because ESBL bacteria show a high level resistance to a number of antibiotics, carbapenems are an option to treat infection due to ESBL. Carbapenem can be used immediately when a patient is suspected of having an ESBL infection while waiting for the results of an antibiotic sensitivity test <sup>8</sup>. In Indonesia, study on ESBL that evaluated the efficacy of antibiotics to treat ESBL infection, especially in burn patients is still rare.

The aim of this case report is to describe a case of ESBL producing - *Klebsiella pneumoniae* in a patient with scald burn injury – hospital acquired pneumonia who successfully treated with combination of meropenem and levofloxacin.

## 2. Result and Discussion

Mr.S, a-52 year old male sustained scald burn in a hot steam coal plant in August 2016. Patient was conservatively managed including debridement at twice in a private hospital. When first admitted to the hospital, the patient condition was in full awareness and the blood pressure was 127/87 mmHg, pulse rate of 104 beats per minute, respiratory rate of 30 times per minute, and temperature of 36,9°C. On local examination, he was diagnosed as 26,5% second degree burns present in regimen facialis, thoracolumbal, extrimitas superior dextra and sinistra, extrimitas inferior dextra and sinistra.

At the emergency departement, the patient underwent a number of laboratory examinations, such as blood chemistry, complete blood count, and blood gas analysis and then the patient was hospitalized in the burn unit. The results of blood chemistry test demonstrated normal ALT and AST, ureum and creatinin levels were in the normal range, trombocytopenia, anemic, hypoalbuminemia, neutrophilia and the result of blood gas analysis showed blood pH was normal as shown in **table 1**. Further the patient confirmed as Systemic Inflammatory Response Syndrome (SIRS). By the chest X-ray examination at the five days after admission, the lung showed infiltrate with a white patch, which indicated that pneumonia is confirmed.

**Table 1.** Results of laboratory work up

Variables	References	Value
Hb (g/dL)	13,3 – 14,7	9,6
WBC (x10 <sup>3</sup> / µl)	3,37 – 10,0	26,7
Platelet (x10 <sup>3</sup> / µl)	150 - 450	128
RBC (x10 <sup>6</sup> / µl)	3,69 – 5,46	3,40
Neutrophil (%)	39,8 – 70,5	93,6
Albumin (g/dL)	3,4 – 5,0	2,57
ALT (U/L)	0 – 50	41
AST (U/L)	0 – 50	32
BUN (mg/dL)	10 - 20	20
Creatinin (mg/dL)	0,6 – 1,3	0,65
Na (mEq/L)	136 – 145	140
K (mEq/L)	3,5 – 5,1	4,4
Cl (mEq/L)	98 – 107	110
Blood gas analysis		
pH	7,35-7,45	7,5
pCO2 (mmHg)	35 – 45	32
pO2 (mmHg)	80 – 100	61
HCO3 (mmol/L)	22,0 – 26,0	25
Base Excess (BE) (mmol/L)	-3,50 – 2,00	1,8
O2 Saturated (%)	94 – 98	93

Shortly after admission to the hospital, tissue burned infection was taken aseptically and processed by microbiological procedures. *Klebsiella pneumoniae* ESBL was isolated from this culture and the resistance data was shown in **Table 2**. The patient was isolated and treated with injection IV meropenem one gram three times daily and levofloxacin 750 mg once daily. The patient totally completed thirteen days of meropenem and seventeen days of levofloxacin. The blood culture positives for *Bacillus cereus*.

**Table 2.** Results of culture and resistance test of the tissue burned

<b>Isolates : <i>Klebsiella pneumoniae</i> ESBL</b>			
Amikacin	S	Gentamycin	R
Cotrimoxazole	S	Aztreonam	R
Ciprofloxacin	S	Amoxicilin-clavulanic acid	R
Levofloxacin	S	Ampicilin	R
		Ampicilin-sulbactam	R
		Cephazolin	R
		Ceftazidime	R
		Cefotaxime	R
		Ceftriaxone	R
		Tetracyclin	R
		Chloramphenicol	R
		Fosfomycin	R
		Ertapenem	R

A week after admission, tissue burned infection was taken again and *Acinetobacter baumannii* was isolated from this culture and the resistance was shown in **Table 3**. After the completion of meropenem and levofloxacin, patient's condition improved and the infection was finally controlled. Patient was discharged after 25 days of hospitalization.

**Table 3.** Results of culture and resistance test of the tissue burned

<b>Isolates : <i>Acinetobacter baumannii</i></b>			
Ampicilin-sulbactam	S	Gentamycin	R
		Aztreonam	R
		Amoxicilin-clavulanic acid	R
		Tobramycin	R
		Amikacin	R
		Cephazolin	R
		Ceftazidime	R
		Cefotaxime	R
		Ceftriaxone	R
		Tetracyclin	R
		Chloramphenicol	R
		Fosfomycin	R
		Ertapenem	R
		Imipenem	R
		Meropenem	R
		Levofloxacin	R
		Cefoperazone-sulbactam	R

ESBL-producing *K. pneumoniae* is the most pathogenic gram negative bacteria that causes severe infection, especially in burn patients. Infections in burn patients due to ESBL-producing *K. pneumoniae* are more difficult to treat, this is because the bacteria are not only resistant to beta lactam antibiotics, but also most of them showed resistant to the fluroquinolones and aminoglycosides antibiotics<sup>9</sup>. Hospital-acquired pneumonia (HAP) is a pneumonia that occurs when patients undergo treatment at the hospital, usually occurs when a patient hospitalized more than two days as early onset HAP and late onset HAP if more than five days after admission<sup>10</sup>. It has been associated that patient with late onset HAP are related to nosocomial pathogen, multi-drug resistant bacteria and mortality rates were higher than patients without HAP<sup>11</sup>. The most frequent bacteria for HAP are gram negative pathogens. In late onset HAP, bacteria that usually found in bronchoalveolar lavage or blood culture were classified as high resistant, such as *Klebsiella pneumoniae*, *Enterobacteriaceae*, *Pseudomonas aeruginosa*, and Methicillin-resistant *Staphylococcus aureus*<sup>12</sup>.

Our findings also similar that *Klebsiella pneumoniae* and *Acinetobacter baumannii* was found in tissue burned culture. Our patient was diagnosed as late onset hospital acquired pneumonia. Previously, the patient had been hospitalized for 4 days and received cephalosporin antibiotics, Ceftriaxone. American Thoracic Society (ATS) reported that patients who previously admitted to the hospital for two or more at 90 days before, are high risk factors for multi-resistant pathogenic bacteria that cause hospital acquired pneumonia<sup>13</sup>. Without waiting for culture results, our patient was given empiric treatment of meropenem and levofloxacin. The patient was administered meropenem one gram three times daily and levofloxacin 750 mg once daily. Based on algorithm of HAP therapy, patient was divided in group 3 or at risk of pathogenic resistant infection, and the combination of meropenem and levofloxacin met the criteria to be given to our patient. For patients suspected to late-onset hospital pneumonia, or patients with susceptible for multidrug-resistant bacteria, the combination of antibiotics should be taken with high activity for pseudomonas such as meropenem, piperacilin-tazobactam, cefepime plus amikacin or ciprofloxacin and levofloxacin<sup>14</sup>.

Meropenem is a carbapenem class antibiotic that is effective for ESBL-producing *K. pneumoniae* and for Carbapenem Resistant - *Acinetobacter baumannii* (CRAB)<sup>15</sup>. Carbapenem is resistant to attack by ESBL enzymes, and its small molecular size makes it easy to penetrate bacterial cell walls<sup>16</sup>. Our study was similar to the study by Shoja et al that showed as much as 92,5% of A.

*baumanii* isolated from burn patients and highly resistant to carbapenems<sup>17</sup>. The use of quinolones was effective for the treatment of infections caused by ESBL producing bacteria in several animal model studies. However, rare plasmids containing the ESBL gene also show genes that are resistant to quinolones. A study reported that there was a relationship between ESBL producing bacteria and ciprofloxacin resistance. Cross resistance case in *Pseudomonas spp.* has been identified as a risk factor to imipenem, formerly used a class of fluoroquinolone, and a recent study reported that imipenem-resistant to *Pseudomonas spp.* Isolates also showed resistance to ciprofloxacin or levofloxacin, signifying that cross resistance is occurred for imipenem<sup>18</sup>.

A week after admission, *Acinetobacter baumannii* was found in tissue burned culture, and ampicillin-sulbactam was the only one antibiotic which sensitive to this pathogen. Eventhough *Acinetobacter baumannii* was resistant to meropenem and levofloxacin, these antibiotics were still given to our patient. The patient showed clinical and laboratory improved. There were no dyspnea, cough, fever, leukocytes in normal range, and no infiltrate in lung. In patients with hospital acquired pneumonia caused by *Acinetobacter* bacteria, treatment with carbapenem or ampicillin and sulbactam if the isolate is sensitive to these antibiotics, is still recommended. The evidence showed that the ampicillin-sulbactam, carbapenem and colistin were as effective for acinetobacter therapy as determined by antimicrobial sensitivity. The guideline showed that the ampicillin-sulbactam and carbapenems are still preferred because of fewer side effects, and colistin is only be used to treat *Acinetobacter* that is still sensitive to colistin due to the high risk of nephrotoxicity<sup>19</sup>.

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