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Review Article

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Management of Pseudomonas Aeruginosa Related Infection in Emergency Department

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Abstract

Pseudomonas aeruginosa relating infection has high mortality rate in health care setting. In particular, immunocompromised and critically ill patients. Recent studies suggested considering broad-spectrum antipseudomonal antibiotics for Gram-negative bacteria coverage in the emergency Department, especially for high-risk patients. A number of studies have been conducted to assess risk factors of resistance.

This review will evaluate the available antipseudomonal antibiotic along with its resistant pattern. Also it will discuss selected antipseudomonal agent in managing Multidrug resistant duo to Pseudomonas aeruginosa. The review will discuss the Drug selection approaches for patients with neutropenia, pneumonia, and urinary tract infections. The last part in the review will highlight the preferred empirical antipseudomonal antibiotic used at Emergency Department.

Keywords: Pseudomonas Aeruginosa, Multidrug Resistance, Emergency Department, Neutropenia, Pneumonia, and Urinary Tract Infections

Introduction

Pseudomonas aeruginosa (PA) is a Gram-negative, aerobic rod shaped bacterium, which belongs to the bacterial family Pseudomonadaceae [1]. In Emergency department (ED), Pseudomonas aeruginosa infection is expected with patient living in area with High prevalence of Pseudomonas infection, country with worm climate, or if the patient came to the ED with severe infection [2]. While Risk factors for with MDR Pseudomonas aeruginosa colonization in emergency department are: previous colonized, prolonged hospital stay, being bedridden or admission to ICU, on mechanical ventilation, malignant disease, and chronic illness such as obstructive pulmonary disease [3].

Several studies have shown that inappropriate empirical antimicrobial treatment is linked with poor results in individuals with varied types of infection. Specifically, delays in cure which increased mortality, morbidity and hospital cost [4-6].

The role of Emergency physician is to initiate therapy with broad-spectrum antimicrobials until full culture and susceptibility results are available [7, 8]. But, treatment of infections induced by P. aeruginosa could be difficult duo to high resistant of antipseudomonal agents available.

This review will evaluate the available antipseudomonal antibiotic along with its resistant pattern. Also, it will discuss selected antipseudomonal agent in managing Multidrug resistant duo to Pseudomonas aeruginosa. The review will discuss the Drug selection approaches for patients with neutropenia, pneumonia, and urinary tract infections. The last part in the review will highlight the preferred empirical antipseudomonal antibiotic used at Emergency Department.

Beta Lactams

When the local prevalence of PA multidrug resistant MDR is low, the recommendation from IDSA suggested that empirical PA coverage should include β-lactam plus either aminoglycoside or fluoroquinolone [9].

In meta-analysis, included 50 randomized studies comparing beta-lactams in treating febrile neutropenia; imipenem/cilastatin, piperacillin/tazobactam and meropenem had higher treatment success. While cefepime, cefozopran and Ceftazidime had lower treatment success [10]. Although we are favor for the use of meropenem over the use of imipenem/cilastatin at ED in patient history of seizure. As imipenem/cilastatin has higher neurologic adverse event compared to meropenem [11].

Both Carbapenem and Monobactam has lower cross-reactivity with penicillins and cephalosporins allergy [12, 13]. However, Aztreonam a monobactam has a cross reactivity with ceftazidime. Aztreonam can be a good choice in treating PA with patients who had IgE mediated hypersensitivity to penicillins or cephalosporins. But it has no activity against anaerobes, and that make meropenem or imipenem favored than aztreonam in treating patient with febrile

neutropenia and intra-abdominal infection.

We suggest in the absence of MDR, Meropenem followed by piperacillin/tazobactam then by cefepime then by ceftazidime in order will be the empirical drug therapy in patient with bacteremia, pneumonia and skin soft tissue infection.

Extended-spectrum β-lactamase (ESBL) production in PA is mostly common in Urinary tract and nosocomial infection [14, 15]. Risk factors for ESBL infection included previous receiving antibiotic within 90 days, presence of urinary or vascular catheters, Hemodialysis and prolonged hospital admission [16]. ESBLs hydrolyse penicillins and cephalosporins, and monobactam [17]. Carbapenem showed a great activity against ESBLs, although Ertapenem lac the activity against PA [17]. Imipenem is non-inferior to meropenem in managing ESBL. Although we prefer meropenem for its safety profile as we mentioned before.

Fluoroquinolones vs Aminoglycoside

Ciprofloxacin and Levofloxacin are the only Fluoroquinolones (FQ), which has activity against PA [9]. Although, it is not recommended as monotherapy in treating PA related infection [9, 18, 19]. Antipseudomonal FQ in combination to Antipseudomonal beta-lactams considered a good choice as empirical therapy treating infection related to PA [9, 18, 19].

Both levofloxacin and ciprofloxacin have equivalent Aera under the curve (AUC)/Minimum inhibitory concentration (MIC) ratios against PA [20]. Although, Ciprofloxacin has greater in-vitro activity than levofloxacin, while levofloxacin has a higher serum concentration level.

Furthermore, fluoroquinolones are not often active against PA that are resistant to antipseudomonal β-lactams [9]. Aminoglycosides exhibit potent in vitro activity against PA [9]. Aminoglycoside is alternative to FQ in combination to beta-lactams in treating infection related to PA [9, 18, 19]. Aminoglycoside resistance among gram-negative organisms is common [21]. Also Organisms resistant to other antimicrobials (such as ESBLs), are often resistant to most aminoglycosides due to the presence of aminoglycoside-modifying enzymes [21]. Thus Aminoglycoside should not use as monotherapy in treating PA [9]. Both tobramycin and amikacin offer in vitro advantages over gentamicin against PA [22]. However, amikacin tobramycin and are equally effective in the treatment PA infections and have similar safety profile [23].

In a retrospective cohort, comparing aminoglycoside to FQ in treating PA. The study showed no significant difference in the odds of clinical cure between FQ & Aminoglycoside (adjusted odds ratio 2.4, 95% confidence interval [CI] 0.7–9.0). There was no significant difference in 28-day mortality in patients who received FQ or an aminoglycoside combination (22% vs. 18%, adjusted hazard ratio 0.82, 95% CI 0.29–2.28) [24]. Suggested equivalency in both clinical cure and mortality between FQ or aminoglycoside when combined to beta lactams in treating PA [25].

We are favor of FQ in ED rather than aminoglycoside for patient with renal impairment. Even if the patient has cardiac problem, Loading dose should be given and routine QT readings should be monitored. When QT prolongation reached 500 then aminoglycoside is preferred.

Multi-Drug-Resistant (MDR)

When PA MDR is high prevalence, ceftolozane-tazobactam was preferred over polymyxins or aminoglycosides, result from retrospective, multicenter, observational cohort study [26]. Ceftolozane-tazobactam was non-inferior to meropenem in terms of both 28-day all-cause mortality and clinical cure [27]. High-dose ceftolozane-tazobactam is an efficacious and well tolerated treatment for Gram-negative nosocomial pneumonia [27]. Ceftazidime-avibactam is another alternative to carbapenems when PA MDR suspected [28]. Also Ceftazidime-avibactam has a good activity against ESBL producing PA [29].

In conclusion, we suggest empirical therapy in ED when MDR prevalence is high, ceftolozane-tazobactam will be the drug of choice, flowed by Ceftazidime-avibactam in treating patient with bacteremia and pneumonia. While adding metronidazole to the regimen when treating patient with Intraabdominal infection. We recommend Fosfomycin in combination to Meropenem in treating patient with urinary tract infection as first line empirical therapy.

Carbapenem Resistant

Carbapenem resistance is the most serious resistant strain facing the health care professionals when treating infection caused by PA [30, 31]. Some β-lactam inhibitors, such as clavulanic acid and sulbactam has a good activity against PA resistant strain [29]. In one study, aztreonam-ceftazidime-avibactam combination was shown to be potent in Carbapenem resistant to PA [32]. Another study showed both aztreonam-ceftazidime-avibactam and aztreonam-amoxicillin-clavulanate were found to be equal in susceptibility against PA [33].

Although the addition of vaborbactam extends the spectrum of meropenem to include some carbapenem-resistant organisms. Meropenem-vaborbactam highly active against many carbapenem-resistant Enterobacteriaceae. but unfortunately, it does not expand its coverage to carbapenem-resistant against PA [34].

In conclusion, carbapenem resistance is serious infection. Empirically antibiotic is not routinely initiated at ED. A sensitivity culture should perform to select the appropriate broad-spectrum antibiotic. Unless the was known to have carbapenem resistance, thus we recommend initiating aztreonam-ceftazidime-avibactam followed by aztreonam-amoxicillin-clavulanate.

Inhaled Pseudomonas Pneumonia

In treating PA pneumonia with patient with Cystic fibrosis, inhaled antipseudomonal is recommended as prophylactic therapy [9]. Thus the use of inhaled antipseudomonal antibiotic is rarely used at ED.

Both nebulization and intravenous infusion of ceftazidime and amikacin had equal efficiency for treating ventilator-associated pneumonia caused by PA [35, 36]. When comparing Inhaled antibiotic against PA the first-line choice will be tobramycin as many studies supported its efficacy and safety [36, 37]. However, there are no studies comparing inhaled tobramycin with inhaled aztreonam in patients who are naïve to both drugs or who have been receiving chronic aztreonam but not tobramycin.

Unfortunately, Duo to low supporting data for the use of inhaled colistin, colistin should prescribe only for those patients do not respond well or cannot tolerate tobramycin and/or aztreonam [38]. Although a prospective, centrally randomized, phase III, open-label

study comparing Inhaled colistin and tobramycin in treating cystic fibrosis, the results showed that colistin demonstrated efficacy by virtue of non-inferiority to tobramycin in lung function after 24 weeks of treatment [38]. And it was well tolerated in term of adverse effect and PA resistant. Although, the use of inhaled antibiotic against PA is not commonly used at ED.

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