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A literature review of Pseudomonas aeruginosa infection and the appropriate regimen of antibiotics whether Combination antibiotic therapy or monotherapy.

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Abstract: Pseudomonas aeruginosa is a common cause of gram-negative infection, especially in patients with compromised host defense mechanisms. It is the most common pathogen isolated from patients who have been hospitalized longer than 1 week, and it is a frequent cause of nosocomial infections. Pseudomonas infections are complicated and can be life-threatening. The choice of antibiotic monotherapy or combination therapy to treat Pseudomonas aeruginosa bacteremia is controversial. The aim of this review is to discuss the infection by pseudomonas with its characteristics and to compare both types of therapy to determine which delivers the best outcome for P. aeruginosa bacteremia. Neither combination therapy nor monotherapy treatment appears to have a significant effect on mortality rates in patients with P. aeruginosa bacteremia. Further studies evaluating the effects of combination therapy or monotherapy in more specialized cases, such as when encountering a multidrug-resistant organism, are necessary.

Key words: Pseudomonas aeruginosa, Drug resistance, monotherapy, gram negative infection

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1. Introduction

Pseudomonas aeruginosa is a common pathogen that is implicated in a wide variety of nosocomial infections. Hospital mortality rates associated with P. aeruginosa bacteremia is reported to be >20% in recent studies. Inappropriate use of empirical antibiotic therapy has been identified as an independent contributor to the high hospital mortality rate of P. aeruginosa bacteremia.

Combination empirical antimicrobial therapy directed against Gram-negative bacteria may be a more treatment of P. aeruginosa bacteremia can be minimized by using combination treatment until final susceptibility results are known. Utilizing two antipseudomonal drugs of different classes helps to guarantee pathogen coverage until final sensitivities are determined.

Previous studies involving potential treatments for P. aeruginosa bacteremia have varied in their approaches to definitive antimicrobial therapy. Moreover, studies have not specifically examined the effect of administering combination antimicrobial agents [9,10]. Despite the theoretical advantages of combination empirical therapy, there is no evidence to support the use of combination therapy over monotherapy for the treatment of P. aeruginosa infection. [13]

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2.Signs and symptoms

Pseudomonas infections frequently involves the following parts of the body, with corresponding symptoms and signs:

Endocarditis: Fever, murmur, and positive blood culture findings; peripheral stigmata such as Roth spots, Jane way lesions, Osler nodes, splinter hemorrhages, and splenomegaly

Bacteremia: Fever, tachypnea, and tachycardia; hypotension and shock; jaundice. Pseudomonas bacteremia produces distinctive skin lesions known as etyma gangrenous. Though bacteremia can be caused by a multitude of mechanisms, some more frequent causes are urinary tract infections and users of intravenous narcotics.

Skin and soft tissue infections: Hemorrhagic and necrotic lesions, with surrounding erythema; subcutaneous nodules, deep abscesses, cellulitis, and fasciitis; in burns, black or violaceous discoloration or eschar. [4]

Ecthyma gangrenosum lesions are hemorrhagic and necrotic, with surrounding erythema. These characteristic lesions are almost always caused by Pseudomonas infection and usually are found in the axilla, groin, or perianal area but may involve any part of body.

Pseudomonas also has emerged as an important source of burn wound sepsis. Invasive burn wound sepsis is defined as the bacterial proliferation of 100,000 organisms per gram of tissue, with subjacent involvement of subjacent unburned tissue. [2]

Pseudomonal burn wound infections appear black or as a violaceous discoloration or eschar. Systemic manifestations of burn wound sepsis may include fever or hypothermia, disorientation, hypotension, oliguria, ileus, and leukopenia.

The organism also flourishes on moist skin. Pseudomonas is a common cause of hot tub or swimming pool folliculitis. Patients present with pruritic follicular, maculopapular, vesicular, or pustular lesions on any part of the body that was immersed in water. Addtionally, green nail syndrome is a paronychia infection that can develop in individuals whose hands are frequently submerged in water.

Secondary wound infections occur in patients with decubiti, eczema, and tinea pedals. These infections may have a characteristic blue-green exudate with a fruity odor. [3]

Pseudomonas skin and soft tissue infections can be destructive and can cause massive necrosis and gangrene. [6]

Skeletal infections: Local tenderness and a decreased range of motion; neurologic deficits

The most common sites of involvement are the vertebral column, the pelvis, and the sternoclavicular joint. These sites are usually infected due to secondary seeding (eg. Bacteremia or UTI).

Along with bacteremia seeding, the infection may be contiguous. This infectious mechanism is usually related to penetrating trauma, surgery, or overlying soft tissue infections. Patients at higher risk for pseudomonas bone and joint infections include those with puncture wounds to the foot, peripheral vascular disease, intravenous drug abuse, or diabetes mellitus.

Patients with pyoarthrosis present with swelling and pain in the affected joint. Patients are persistently febrile. [1]

Vertebral osteomyelitis may involve the cervical spine, and patients present with neck or back pain lasting weeks to months. Occasionally, patients with complicated UTI may develop lumbosacral vertebral osteomyelitis.

3. Risk factors for infection with resistant P aeruginosa include the following:

Intensive care unit (ICU) stay

Bedridden status

Prior use of certain antibiotics, including broad¬-spectrum cephalosporins, aminoglycosides, carbapenems, and fluoroquinolones

Presence of invasive devices

Diabetes mellitus

Undergoing surgery [6]

4.Laboratory Studies

A CBC count may reveal leukocytosis with a left shift and bandemia. In patients with hematologic malignancy or status post chemotherapy, leukopenia with neutropenia is expected. Leukopenia is a poor prognostic indicator.

Obtain at least 2 sets of blood cultures (2 aerobic, 2 anaerobic bottles) from different sites.Positive results on blood culture in the absence of extra cardiac sites of infection may indicate pseudomonal endocarditis. However, bacteremia may complicate intravenous catheter infections, urinary tract instrumentation, trauma, and surgery in the absence of endocarditis.

In UTI, urinalysis is helpful in determining a diagnosis. Culture confirms the diagnosis and provides information concerning antibiotic susceptibility.

Obtain wound and burn cultures and cultures from other body fluids and secretions according to the clinical scenario. To aid in diagnosis, obtaining burn wound biopsies with quantitative bacterial cultures is recommended. A bacterial count of greater than 105 organisms per gram of tissue is diagnostic of a burn wound infection. Obtain Gram stain and culture of cerebrospinal fluid if meningitis is suspected.

Triphasic bone scans or MRI may be useful in patients with suspected skeletal infection. Brain CT scan or MRI allows for evaluation of patients suspected of having a pseudomonas brain abscess.[4]

5.Management

Pseudomonal infections are showing increasing resistance to antibiotics. Resistance can be acquired during the course of therapy. [7] Current recommendations are for two agents from different classes to be used when the risk of antibiotic resistance is high (eg, in severe sepsis, septicemia, and inpatient neutropenia). [9]

Pseudomonas infection can be treated with a combination of an antipseudomonal beta-lactam (eg, penicillin or cephalosporin) and an aminoglycoside. Carbapenems (eg, imipenem, meropenem) with antipseudomonal quinolones may be used in conjunction with an aminoglycoside. With the exception of cases involving febrile patients with neutropenia, in whom monotherapy with ceftazidime or a carbapenem (eg, imipenem, meropenem) is used, a 2-drug regimen is recommended. [10]

No advantage for using combination therapy was found for all-cause mortality or treatment failures in the subgroup of patients with P. aeruginosa infections. In contrast, a related meta-analysis focused on the relationship between combination therapy and reduced mortality rates in patients with Gram-negative bacteraemia, revealing a significantly reduced mortality after combination therapy in a subgroup analysis of P. aeruginosa bacteraemia. However, owing to the poor quality and heterogeneity of the studies included in these meta-analyses, convincing clinical data are sparse, and studies often vary in their findings. The most recent meta- analysis examined the use of a - lactam plus an aminoglycoside

or fluoroquinolone combination versus -lactam monotherapy for P. aeruginosa infections. As previously shown, a subgroup analysis (five studies) of

P. aeruginosa bacteraemia showed no significant differences in mortality rates between monotherapy and combination therapy [13].

Antibiotics Class Summary

Empiric antimicrobial therapy must be comprehensive and should cover all likely pathogens in the context of the clinical setting.

Gentamicin: aminoglycoside antibiotic for gram-negative coverage. Used in combination with both an agent against gram-positive organisms and one that covers anaerobes. Not the drug of choice, but consider this if penicillins or other less toxic drugs are contraindicated. Gentamicin is additionally used in mixed infections caused by susceptible staphylococci and gram-negative organisms. Dosing regimens are numerous. Adjust dose based on CrCl and changes in volume of distribution. May be administered IV/IM.

Piperacillin-Tazobactam (Zosyn): antipseudomonal penicillin plus beta-lactamase inhibitor. Inhibits biosynthesis of cell wall and is effective during stage of active multiplication.

Aztreonam (Azactam): monobactam that inhibits cell wall synthesis during bacterial growth. Active against gram-negative bacilli but very limited gram-positive activity and not useful for anaerobes. Lacks cross-sensitivity with beta-lactam antibiotics. May be used in patients allergic to penicillins or cephalosporins.

Ciprofloxacin (Cipro): Exerts bactericidal effect against both actively dividing and dormant bacteria. Fluoroquinolone effective against pseudomonads, streptococci, some MRSA, Staphylococcus epidermidis, and most gram-negative organisms but no activity against anaerobes. Inhibits bacterial DNA synthesis and, consequently, growth. Continue treatment for at least 2 d (7-14 d typical) after signs and symptoms disappear.

Cefepime (Maxipime): a fourth-generation cephalosporin for the treatment of Pseudomonas infections. Gram-negative coverage comparable to ceftazidime but has better gram-positive coverage. Cefepime is a zwitterion that rapidly penetrates gram-negative cells. Best beta-lactam for IM administration. Poor capacity to cross blood-brain barrier precludes use for treatment of meningitis.

Ceftazidime (Fortaz): A third-generation cephalosporin with high activity against Pseudomonas. Arrests bacterial growth by binding to 1 or more penicillin-binding proteins.

Tobramycin: obtained from Streptomyces tenebrarius; two to four times more active against pseudomonal organisms as compared to gentamicin.

Meropenem (Merrem): ultra–broad-spectrum beta-lactam semisynthetic carbapenem antibiotic that inhibits bacterial cell wall synthesis.

Doripenem (Doribax): binds to several of penicillin-binding proteins, which in turn inhibit bacterial cell wall synthesis. Bacteria eventually lyse due to ongoing cell wall autolytic enzymes. [8]

Inpatient & Outpatient Medications: aminoglycosides in combination with beta-lactam agents with good antipseudomonal activity may be prescribed on an inpatient or outpatient basis. [12]

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