Impact of choice of Antibiotics on Antibiotic Resistance, Morbidity and Mortality in Critically Ill Patients

Essay

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Abstract

Introduction: The intensive care unit (ICU) is a place where patients with complex medical problems are crowded into a small area. The acute nature of critically ill patients necessitate the use of broad-spectrum antibiotics frequently. Fever in a patient in the ICU must be considered significant when the body temperature is >38.3°C (101°F) and a detailed evaluation must be carried out to ascertain whether infection is present or not. Fever is a sign of inflammation, not infection. Hence, non infectious causes of fever must be ruled out before subjecting the patient to a number of costly and invasive diagnostic procedures.

Aims: To review the current medical literature and recent guidelines for choice of antibiotics in critically ill patients and its effect on antibiotics resistance and rate of morbidity and mortality related to mis-prescription of antibiotics.

Summary: Antibiotic therapy must be initiated immediately in febrile patients with neutropenia, especially when criteria of severe sepsis are met. The antibiotics used for first-line therapy must be active against the most likely pathogens, as estimated based on the suspected source of infection. Suspicion of catheter-related infections or new pulmonary infiltrates are other indications of intravenous antibiotics administration.

Conclusion: Continuous infusions of beta-lactam antibiotics have been employed in an attempt to maximize the time that free drug concentrations exceed the bacterial MIC .Several studies have shown beneficial outcomes associated with continuous infusion piperacillin–tazobactam.

Several new drugs for severe infections have been approved within the past decade, but the pipeline of novel drugs to meet the challenge of MDR gram-negative pathogens remains limited.

Keywords: Choice of Antibiotics, Antibiotic Resistance, Morbidity and Mortality, Critically Ill Patients, Intensive care unit

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بسم الله الرحمن الرحيم

قالوا

سبحانك لا علم لنا

إلا ما علمتنا إنك أنت

العليم الحكيم

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List of Abbreviations

CLSI	: Clinical and Laboratory Standards Institutes
CPIS	: Clinical Pulmonary Infection Score
DRSP	: Drug-resistant Streptococcus pneumoniae
ESBLs	: Extended-spectrum B-lactamases
EUCAST	: European Committee on Antimicrobial Susceptibility Testing
FDA	: Food and Drug Administration
GNB	: Gram negative bacteria
HCAI	: Healthcare acquired infection
HAP	: Hospital acquired pneumonia
HRE	: Highly resistant enterobacteria
ICU	: Intensive care unit
IV	: Intravenous
MBL	: Metallo-B-lactamase
MDR	: Multidrug-Resistant Organisms
MDR-GNRs	: MDR gram-negative organisms
MIC	: Minimum inhibitory concentration
MRSA	: Methicillin resistant S aureus
PCTQ	: Procalcitonin

PD	: Pharmacodynamics
PK	: Pharmacokinetics
SIADH	: Syndrome of inappropriate antidiuretic hormone
UDP	: Uridine diphosphate
VAP	: Ventilator-associated pneumonia
VRE	: Vancomycin resistant enterococci

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Introduction

The intensive care unit (ICU) is a place where patients with complex medical problems are crowded into a small area. The acute nature of critically ill patients necessitate the use of broad-spectrum antibiotics frequently. Fever in a patient in the ICU must be considered significant when the body temperature is >38.3°C (101°F) and a detailed evaluation must be carried out to ascertain whether infection is present or not. Fever is a sign of inflammation, not infection. Hence, non infectious causes of fever must be ruled out before subjecting the patient to a number of costly and invasive diagnostic procedures ***(Sarin et al., 2015).***

Optimal antibiotic use is crucial in the critical care setting, especially in an era of rising antibiotic resistance and lack of new antimicrobial development. Study results indicate that 30% to 60% of antibiotics prescribed in ICUs are unnecessary, inappropriate, or suboptimal. Overprescribing and mis-prescribing antibiotics are undoubtedly contributing to the growing challenges posed by antibiotic-resistant bacteria, and epidemiological studies have clearly demonstrated direct relationships between antibiotic consumption and the emergence and dissemination of resistant strains in hospitals and ICUs ***(Luyt et al., 2014).***

Most published observational data suggest that the time to appropriate antibiotic administration is a major outcome determinant for ICU patients with severe bacterial infections. Indeed, each hour of delay in administering effective antibiotics for septic shock is associated with measurably increased mortality. Thus, as strongly recommended by all guidelines, obtaining biological specimens should not postpone timely antibiotic administration to patients with severe sepsis or septic shock ***(Luyt et al., 2014).***

Antimicrobial stewardship programs are aimed at optimizing antimicrobial selection, dosing, route, and duration of therapy to maximize clinical cure or prevention of infection while limiting the unintended consequences such as the emergence of resistance, adverse drug events and cost ***(Dellit et al., 2014).***

Resistance is a measure of decreased ability of an antimicrobial agent to kill or inhibit the growth of a microbial organism. In practice, this is determined by testing a patient isolate against an antimicrobial in an in vitro assay system ***(Fraimow and Tsigrelis, 2011).***

Antimicrobial resistance has emerged as an important determinant of mortality for patients in the intensive care unit. This is largely due to the increasing presence of pathogenic microorganisms with resistance to existing antimicrobial agents, resulting in the administration of inappropriate treatment ***(Kollef et al., 2013)***.

Effective strategies for the prevention of antimicrobial resistance within intensive care units are available and should be aggressively implemented. These strategies can be divided into non-pharmacologic infection control strategies (e.g., routine hand hygiene, implementation of infection-specific prevention protocols) and antibiotic management strategies (e.g., shorter courses of appropriate antibiotic treatment, narrowing of antimicrobial spectrum based on culture Results). Increasing current efforts aimed at the prevention of antimicrobial resistance is especially important given the limited availability of new antimicrobial drug classes for the foreseeable future ***(Kollef et al., 2013).***

Aim of the Work

To review the current medical literature and recent guidelines for choice of antibiotics in critically ill patients and its effect on antibiotics resistance and rate of morbidity and mortality related to mis-prescription of antibiotics.

Classification and Pharmacology of Antibiotics

Definition

Antibiotics may be informally defined as the subgroup of anti-infectives that are used to treat bacterial infections. Other classes of drugs, most notably the sulfonamides, may be effective antibacterials. Similarly, some antibiotics may have secondary uses, such as the use of demeclocycline (Declomycin, a tetracycline derivative) to treat the syndrome of inappropriate antidiuretic hormone (SIADH) secretion. Other antibiotics may be useful in treating protozoal infections ***(Kim et al., 2011)***.

Classifications

Although there are several classification schemes for antibiotics, based on bacterial spectrum (broad versus narrow) or route of administration (injectable versus oral versus topical), or type of activity (bactericidal. versus bacteriostatic), the most useful is based on chemical structure. Antibiotics within a structural class will generally show similar patterns of effectiveness, toxicity, and allergic potential ***(Garg et al., 2014).***

1-Penicillins

The penicillins are the oldest class of antibiotics and have a common chemical structure which they share with the cephalopsorins. The two groups are classed as the β-lactam antibiotics, ,which kill bacteria rather than inhibiting growth ***(Silva et al., 2011).***

The penicillins can be further subdivided. The natural pencillins are based on the original penicillin G structure; penicillinase-resistant penicillins, notably methicillin and oxacillin, are active even in the presence of the bacterial enzyme that inactivates most natural penicillins. Aminopenicillins such as ampicillin and amoxicillin have an extended spectrum of action compared with the natural penicillins; extended spectrum penicillins are effective against a wider range of bacteria. These generally include coverage for Pseudomonas aeruginaosa and may provide the penicillin in combination with a penicillinase inhibitor ***(Khosa et al., 2013).***