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Antibiotic stewardship in the ICU: Evaluating optimal therapy for sepsis patients

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Abstract
Sepsis necessitates rapid diagnosis and adequate treatment due to the high morbidity and fatality rates associated with the illness. While antibiotic treatment is essential for sepsis management, there are risks associated with antibiotic abuse and misuse, such as the development of antimicrobial resistance. In order to limit resistance while also ensuring that antibiotics are used optimally, antibiotic stewardship programs (ASPs) are crucial in the intensive care unit (ICU). This research looks at the range of action, dose, indications, and usage of both new and old antibiotics in the intensive care unit (ICU) for patients with sepsis. Antimicrobial de-escalation, the ideal scheduling of antibiotics, and the proper length of treatment are some of the important themes covered. The shift from empirical to targeted treatment and the development of rapid diagnostic tools for MROs are being prioritized as means to better results. Integrating ASPs into ICU procedures is crucial for promoting evidence-based, patient-centric care, according to the results. One way to improve sepsis care and slow the spread of antibiotic resistance is to adhere to stewardship guidelines, which include only administering antibiotics when absolutely necessary.

Keywords: Sepsis, antibiotic stewardship, Intensive care unit (ICU)

Introduction

Worldwide, sepsis is the top cause of death and morbidity in contemporary healthcare, especially in intensive care units (ICUs). To stop sepsis from becoming septic shock and eventually death, prompt and accurate medical treatment is necessary. Sepsis is a potentially fatal malfunction of organs brought on by an uncontrolled immune response to infection. Antibiotic treatment is essential for early diagnosis and management. The worldwide issue of antimicrobial resistance (AMR) has been worsened, however, by the improper use of medicines to patients who are severely sick. Critical care units are breeding grounds for multidrug-resistant organisms (MDROs), which the World Health Organization (WHO) has named one of the top 10 public health crises facing the world today. If we want to maximize treatment efficacy while minimizing resistance, we must establish antibiotic stewardship programs (ASPs). In the intensive care unit (ICU), antibiotic stewardship refers to a collection of interrelated practices that strive to provide the appropriate antibiotic to each patient for the appropriate amount of time. This method finds a happy medium between the immediate and critical need of treating illnesses like sepsis and the longer-term requirement of keeping antibiotics effective. The complexity and severity of critically sick patients, the urgency of starting empirical treatment and the limits of existing diagnostic technologies make establishing this balance in the ICU unique and challenging, despite its necessity. The concepts of antibiotic stewardship as they pertain to the intensive care unit (ICU) and sepsis treatment are examined in this paper. It draws attention to methods for improving antibiotic stewardship, difficulties encountered by critically sick people, and new resources that might improve these efforts. This study seeks to provide insights into improving patient outcomes and preventing AMR in intensive care unit settings by analyzing existing methods and innovations. (Mokrani *et al.*, 2023) [10] "

Overview of sepsis

The leading cause of death from infectious diseases globally is sepsis, which is characterized as a potentially fatal malfunction of organs brought on by an uncontrolled immune response to infection. Whether we are looking at incidence, prevalence, or fatality rates, the precise epidemiology of sepsis is still unclear and very varied. There are a number of variables that contribute to this, including a lack of specific and worldwide data, poorly organized records of various infectious diseases, and an oversimplified understanding of sepsis.

The diagnosis of a clinical condition is complicated when its symptoms are not easily identifiable. Approximately half of all sepsis cases in the United States are misclassified according to coding. Several screening techniques and biomarkers have been used in the absence of a universally accepted test for sepsis. The specificity of traditional individual sepsis indicators like C-reactive protein, total white cell count, and neutrophil count is inadequate to distinguish between individuals experiencing an inflammatory reaction to trauma or surgery and those with an infection, for instance. When it comes to identifying patients with invasive bacterial infections, procalcitonin has shown to be the most accurate.

The fatality rate of severe sepsis and septic shock remains high, even though there have been several treatment studies and the development of contemporary intensive care. Two therapies provide strong evidence of a mortality advantage when septic shock is treated early: prompt goal-directed treatment and suitable antimicrobial treatment. (José Alexis Pulido Álvarez *et al.*, 2023) [18]

Antibiotic stewardship

A collaborative endeavor by healthcare practitioners to practice safe antibiotic prescription is known as antibiotic stewardship, which is often called antimicrobial stewardship. Antibiotics should only be prescribed for diseases caused by bacteria and not viruses. The correct antibiotics should be prescribed based on the kind of infection, and the correct dosage and length of therapy should be determined, among other things.

Maintaining an emphasis on antibiotic stewardship is important, according to the CDC:

- Improves treatment of bacterial infections
- Protects patients from unnecessary side effects

Reduces the likelihood of antibiotic resistance, sometimes known as "superbugs," due to excessive usage,

"The doctors who prescribe antibiotics do so out of a desire to help their patients, and the risk of side effects is minimal because antibiotics are generally safe and affordable," says Richard Harris, MD, an infectious disease specialist at Houston Methodist.

"You want to make sure you're not missing something, but you end up overtreating 50 [patients] for every one patient who actually needs to be treated," said Dr. Harris, who explains that the issue arises when the majority of patients you're treating don't necessarily need the care you're offering. (Rajar *et al.*, 2021) [14]

Antibiotic stewardship start

Antibiotic stewardship initiatives have emerged across to curb the excessive and needless prescription of these medications due to their overuse in both inpatient and outpatient settings. Dr. Harris claims the program was long overdue, and it's hard to pinpoint precisely when these programs made it into almost every big hospital and healthcare institution in the US (almost 85% of hospitals nationally were fulfilling CDC requirements as of 2018). In addition to other groups, the Society for Healthcare Epidemiology of America (SHEA) advocates for antimicrobial stewardship programs and equips healthcare providers with resources to put them into practice in both short- and long-term care settings throughout the nation. According to SHEA, these initiatives improve quality in several ways, including patient outcomes, antimicrobial resistance, healthcare-associated infections, and the usage of antimicrobials.

The gradual shift in focus onto antibiotic use is being attributed, according to Kathryn A. Boling, MD, a primary care provider with Mercy Medical Center in Baltimore, to a number of environmental factors, including the rise of resistant organisms and the necessity to use stronger intravenous antibiotics rather than the more common oral ones.

"People are urinating out small amounts of these drugs or flushing their antibiotics down the toilet, and it's contaminating the water we drink," she adds. "The medical community said 'uh-oh'" when all those elements were considered together.

The Centers for Disease Control and Prevention (CDC) started releasing detailed recommendations and guidelines for healthcare institutions (e.g., hospitals, clinics, and doctors' offices) to implement antibiotic stewardship programs in 2014. (Miller, 2017) [8]"

Secrets of antibiotics myths

Researchers from the ESCMID Study Group on Antibiotic Policies recruited interesting people from all around the world, including many different countries in Europe, the United States, Canada, and Australia. Colistin was not readily accessible in many nations, but cloxacillin and aztreonam were. Interestingly, when it came to the intravenous formulation of fosfomycin, only five out of thirty-eight nations possessed colistin. Because of their toxicity, limited spectrum, or commercial concerns, this class of medicines was previously ignored, according to the research. However, with the emergence of resistance, especially among GNB, there has been a renewed interest in their use. Even against microorganisms that have developed resistance to many treatments, these medications have a lengthy track record of success.

A number of drugs have shown efficacy against GNB, including fosfomycin, colistin, and cotrimoxazole. Despite the diversity of GPB activities, none of them inhibit anaerobe growth.

Aside from replacing nitrofurantoin or trimethoprim-sulfamethoxazole (TMP-SMX), fosfomycin does not seem to be helpful in treating uncomplicated cystitis caused by GNB-producing extended-spectrum beta-lactamases (ESBLs) or carbapenemases. Because K. *pneumoniae* and other Gram-negative pathogens often carry fosA hydrolase, an enzyme that renders the medicine inactive, it should only be administered when E. *coli* is the etiologic agent. It is not advised for the treatment of complex UTIs, bacteremia, or any other severe infectious disease that does not involve the urinary tract since it does not reach enough concentrations in the kidneys' parenchyma. However, because of the increase of germs that are resistant to many drugs, its use has increased, especially when combined with other treatments.

Due to its narrow therapeutic index and known nephrotoxic potential, colistin is no longer recommended as a treatment for carbapenemase-producing GNB or Pseudomonas aeruginosa MDR by antibiotic therapy association schemes. This recommendation is based on the new BL-BLI and the increasing resistance to colistin as a result of its use in recent years. Current practice dictates that colistin is reserved for *Acinetobacter baumannii* infections and for usage in cases when the new BL-BLI is ineffective or too harsh.

The battle against ESBL-producing enterobacteriaceae and other carbapenem-resistant bacteria is aided by cotrimoxazole, which is effective in both easy and complicated UTIs. It works against common bacteria *Stenotrophomonas maltophilia* again, however it doesn't work against *Pseudomonas aeruginosa*. Instead of colistin, our ICU almost never suggests cefiderocol or a combination of ceftazidime/avibactam and aztreonam. (Rayaman, 2023) [15]

An appealing alternative for multidrug-resistant infections is tigecycline, thanks to its broad-spectrum action. Being a bacteriostatic antibiotic, however, it has been shown to cause treatment failure when administered alone in some cases.

Hence, in settings with a large percentage of MDR, these options should not be typically suggested for current empirical usage or in cases of septic shock.

While it is true that the number of *Staphylococcus aureus* infections has been on the rise worldwide, the number of

MRSA infections has been on the decline, it is important to remember that GPB cause more deaths in the US than emphysematous disease, Parkinson's disease, HIV/AIDS, homicides, and antimicrobial resistance surveillance in Europe (data from 2021 to 2023; Stockholm: European Center for Disease Prevention and Control and World Health Organization, 2023). Notable players in the fight against these infections include rifampicin, clindamycin, and TMP-SMX, a very inexpensive and highly sought-after medicine for sequential therapy. There are better options, such vancomycin, linezolid, and daptomycin, and none of these are recommended.

After demonstrating the germ's sensitivity to TMP-SMX, it seems to be reserved for long-term infections (such as nosocomial pneumonia and bacteremia).

For specific medical conditions like osteomyelitis, meningitis, necrotizing pneumonia, and endocarditis on the prosthetic valve (where rifampicin may have a stronger eradication effect), clindamycin and rifampicin should only be prescribed as a combination with first-line treatment.

Finally, when E. *faecium* develops resistance to vancomycin, linezolid, or daptomycin, quinupristin-dalfopristin may play a role as an alternate therapy option for infections caused by this bacterium. (Iskandar *et al.*, 2022) [6]

Concerning new antibiotics

In order to better combat multidrug-resistant bacteria, new antibiotics have been developed in the last several years. The Obama administration's 10 antibiotics by 2020 programs make it easier to patent novel antimicrobials, and their careful application increases the value of AMS programs.

It is beyond the scope of this study to provide a thorough analysis of newly developed antibiotics; nevertheless, there are excellent assessments available, both general and particular, in the literature. This is why, before delving into the detailed recommendations, we'll quickly go over some of the features of the new antibiotics. Given the current body of clinical evidence and the efficacy profile of ceftazidime/avibactam as an empirical therapy for patients with multidrug resistance, we will devote a little more space to this topic. Furthermore, we will briefly discuss some intriguing factors about ceftolozane/tazobactam and cefiderocol. (Hurst, Neemann and Chatterjee, 2022) [5] (Ling *et al.*, 2015) [7] "

Table 1: A Review of recent Antibiotics: Spectrum of action, dosage, and indications

Drug	Usual Dosing Regimen in Sepsis	Indication	Activity > 80%
Ceftaroline	600 mg q8 h IV	CAP, cSSTI	MRSA
Ceftobiprole	500 mg q8 h IV	HAP, CAP	MRSA
Ceftazidime/avibactam	2 g/0.5 g q8 h IV	BSI, HAP, VAP, cIAI, UTI	ESBL, Amp C, KPC
Ceftolozane/tazobactam	1.5 g q8 h/3 g q8 h (VAP) IV	BSI, UTI, cIAI, HAP, VAP	ESBL, Amp C
Aztreonam/avibactam (ATM/AVI)	6500 mg ATM/2000 mg AVI q24 h on day 1; 6000 mg ATM/2000 mg AVI q24 h IV	HAP, VAP, BSI, UTI, cSSTI, cIAI	ESBL, Amp C, KPC, Metallo-β, Stenotrophomonas
Meropenem/vaborbactam	2 g/2 g q8 h IV	UTI, cIAI, HAP, VAP	ESBL, Amp C, KPC
Cefiderocol	2 g q8 h IV	BSI, HAP, VAP, cIAI, UTI	ESBL, Amp C, KPC, Metallo-β, OXA-48, Pseudomonas, Stenotrophomonas
Imipenem/relebactam	500 mg/250 mg q6 h IV	BSI, HAP, VAP, cIAI, UTI	ESBL, Amp C, KPC, Pseudomonas
Eravacycline	1 mg/kg q12 h IV	cIAI	ESBL, Amp C, KPC, Metallo-β, OXA-48, Acinetobacter, Stenotrophomonas
Plazomicin	15 mg/kg q24 h IV	In combination for BSI, UTI, HAP, VAP	ESBL, Amp C, KPC, OXA-48
Tedizolid	200 mg q24 h IV, oral	cSSTI, HAP	MRSA
Cefepime/taniborbactam	2 g/0.5 g q8 h IV	UTI, HAP, VAP	ESBL, Amp C, KPC, OXA-48, Stenotrophomonas
Cefepime/enmetazobactam	2 g/0.5 g (phase 3 studies)	UTI (phase 3 studies)	ESBL, Amp C, KPC, OXA-48
Cefepime/zidebactam	2 g/0.5 g (phase 3 studies)	Phase 3 studies	ESBL, Amp C, KPC, OXA-48, Acinetobacter, Stenotrophomonas
Temocilin	2 g/8 h IV (phase 3 studies)	Phase 3 studies	ESBL, Amp C, KPC

Optimal timing of antibiotics in patients with sepsis"

According to the recommendations of the Surviving Sepsis Campaign, individuals experiencing septic shock or sepsis should be given empirical, broad-spectrum antibiotics no later than one hour after triage. When faced with patients who are very likely to have a serious illness, this suggestion may lead doctors, particularly residents, to adopt a "administer antibiotics first and ask questions later" mentality. Nevertheless, considering the present global rise in AMR, the idea that delaying antibiotic delivery by one hour increases mortality must be reevaluated, Misuse and overuse of antibiotics worsens the problems associated with antimicrobial resistance. Diagnostic accuracy has dropped significantly as a result of a quality improvement program's goal of shortening the time it takes to treat community-acquired pneumonia from 8 hours to 4 hours. Although there is some evidence that delayed antibiotic delivery may increase mortality, it is mostly based on findings from retrospective studies of data that were originally collected for other reasons, thus the evidence is not conclusive. Information such as the location of the illness, the correct medication to use, the dosage, and the method of infection management is missing from these records. An American research found that 18% of individuals treated for sepsis in the ER turned out to be completely healthy. In addition, out of 2,579 patients brought to two intensive care units in the Netherlands for suspected sepsis, 13% had no infection after further testing, and 30% were found to have just a high suspicion of having sepsis. Instead, regardless of the appropriateness of empirical antibiotics, 28-day mortality increased from 26.7% to 42.9% due to initial inadequate source control. (Moss and Prescott, 2019) [11]

An analysis of 17,990 patients from the Surviving Sepsis Campaign database showed that there was no change in true mortality even after delaying antibiotic administration by as long as five hours. The mortality rate increased 7.5% linearly with each hour of antibiotic delay after controlling for characteristics such as the site of sepsis diagnosis, location, infection source, hypotension, mechanical ventilation, and other organ failures. Such complex and nuanced aspects cannot be adequately represented by large-scale modifications based on the population. In most circumstances, the window of opportunity between the onset of infection or organ malfunction (time zero) and the presentation or diagnosis of sepsis may range from a few hours to several days. Thus, it's questionable if a linear hourly rise in death risk corresponding to antibiotic delivery delays following sepsis discovery or presentation is a valid predictor. It was first observed by Kumar *et al*. that there is a linear increase in mortality risk with delayed antibiotic delivery in intensive care unit patients experiencing shock. Delaying the delivery of an effective antibiotic for more than 36 hours greatly raises the chance of death. It is difficult to provide antibiotic susceptibility results within 36 hours in practice, and many studies have shown no difference in death rates among patients treated with incorrect empirical antibiotics. Factors pertaining to the patient or the condition are more likely to influence the likelihood of death.

Although delaying antibiotic administration in patients with severe bacterial infections can increase the risk of mortality, it is equally harmful to expose patients needlessly to antibiotics, whether for non-bacterial infections or for prolonged periods of time. High death rates have been linked to lengthier treatment periods and increased overuse of antibiotics, according to many research. The risks associated with antibiotics are well-known and include infections caused by *Clostridioides difficile*, kidney failure, drug-induced hepatitis, inhibition of bone marrow function, severe rash, and acquired MDRO. Less well understood, however, are potential negative impacts on the microbiota or mitochondrial toxicity. (Pradipta *et al.*, 2013) [13]

Distinguishing between sepsis and septic shock is important. There is a lack of clear evidence for sepsis patients who do not have shock, but for patients with septic shock, the timing of successful antibiotic delivery is important. Patients with septic shock had a significantly higher risk of mortality when antibiotics were delayed, compared to patients with sepsis without shock, according to two retrospective studies; however, the validity of these findings is debatable due to the ongoing controversy surrounding statistical adjustments. In addition, a randomized trial comparing the mortality rates of 2,672 patients suspected of having sepsis found no difference between the groups treated with antibiotics in out-of-hospital settings versus those treated in the emergency room, even though the median time between the two groups was 96 minutes. Patients with infections but no sepsis or shock made up 95% of the subjects in that research. Hence, it's important to carefully collect reliable data before deciding whether to provide antibiotics to individuals with sepsis who do not have shock.

Patients suspected of having sepsis or septic shock need a methodical approach to treatment. The severity of the illness and a correct diagnosis should determine whether patients need rapid and aggressive therapy or not. If a patient suspected of illness rapidly goes into shock, antibiotics must be administered immediately. Antibiotics should be discontinued without delay in cases when shock or fast worsening is not caused by a bacterial infection, since this occurs in a large number of patients. In addition, it is important to carefully consider laboratory, radiographic, and microbiological data when deciding whether or not to provide antibiotics to a patient without shock and low infection likelihood. (Schinkel *et al.*, 2020) [16]

The treatment of sepsis involves lowering the antibiotic dose

Antimicrobial de-escalation (ADE) is the process of switching from broad-spectrum to narrow-spectrum antibiotics, or from drugs with a high ecological effect to those with a lower one, or from antibiotics used in combination to none at all. As an example, ADE may need the transition from combination treatment to immunotherapy in order to achieve double coverage of certain bacteria or the cessation of empirical antibiotics in cases where a culture test has not shown a positive result. When treating patients with severe infections in the ICU, it is important to examine ADE, a portion of the ASP with a larger range, in relation to antibiotic treatment, among other considerations. Previous research on ADE in the intensive care unit mostly consisted of observational studies published by hospitals and other medical facilities with an interest in ASPs. It is anticipated that ADE will have different effects when compared to broad-spectrum antibiotics used in empirical antimicrobial treatment. To start, methods to lessen MDRO (33) may be aided by ADE. One factor that leads to the rise of MDRO is the extended use of broad-spectrum antibiotics as an empirical therapy. Second, ADE has the potential to lessen the side effects of broad-spectrum antibiotics. C. diff infections and superimposed infections caused by MDRO or fungus are common adverse responses. Finally, by lowering total antibiotic usage and expenditure, ADE may help reduce medical expenses and hospital stays. The ASP approach should prioritize minimizing antibiotic exposure, since the cumulative dosage of antibiotics is connected to AMR independent of the drug range. This is why it is important to examine ADE through the lens of current research from the ASP point of view. “

Mortality rates were similar in a randomized clinical trial that compared patients who had their pivotal or main antibiotics de-escalated to those who kept taking the antibiotics, even though the de-escalation group used fewer broad-spectrum antibiotics. Nevertheless, the de-escalation group had a higher duration of stay in the intensive care unit (15.2 ± 15 days compared to 11.8 ± 12.6 days). While meta-analyses have linked ADE to decreased death rates, this finding is based on observational research, which might be biased. Patients who exhibited signs of clinical improvement were the ones most often given ADE. After taking into account any confounding factors, more research is required. (Niederman *et al.*, 2021) [12]

Antibiotic duration is unaffected by ADE. The ADE group used antibiotics for a considerably longer period (14.1 ± 13.4 days compared to 9.9 ± 6.6 days) in one randomized controlled study that was connected to ADE. Superinfection was thought to be possible in the ADE group due to the overall longer antibiotic treatment. When additional research compared the two groups based on median values and non-parametric statistics for antibiotic usage duration (9 vs. 8 days; P = 0.11), they found no statistically significant difference. Possible misunderstandings about the total amount of time antibiotics are used have also been put forth as reasons for the extended usage of these drugs. Another theory is that narrow-spectrum antibiotics might be safer. It is possible to misinterpret the shortening of the antibiotic usage term and the early discontinuation of all medicines as being associated with antibiotic-related adverse events (ADEs) when these factors are used in the analysis of ADEs.

There is no clear correlation between ADE and ecological impact in intensive care unit patients, despite the fact that ADE has been implemented as a successful technique for lowering AMR. Prior ADE research that used intensive care unit patients as endpoints for MDRO collection failed to find a statistically meaningful correlation between the two. In the near term, the ecological impact has been reduced by using empirical broad-spectrum antibiotics, which have minimal impacts on antimicrobial resistance (AMR). Discontinuing or switching from broad-spectrum to narrow-spectrum antibiotics may not be as beneficial in ADE, according to a recent research that found AMR to arise early on in antibiotic therapy, within the first two or three days. Substituting a narrow-spectrum antibiotic for an empirical broad-spectrum antibiotic may increase the patient's exposure to antibiotics, which might be detrimental. For instance, the cumulative ecological effect can be higher when levofloxacin is used in lieu of meropenem, an empirical broad-spectrum antibiotic, since the patient is exposed to two antibiotic spectrums in a short amount of time. Due to the limitations of retrospective and observational research, there has been a lack of adequate evidence to assess the effects of ADE on AMR to date. Additional large-scale prospective studies are required.

The post-prescription review procedure, which includes ADE, has been shown to be more successful in lowering antibiotic usage compared to prior authorization, the other important component of evidence-based ASP intervention. To prevent patients' microbiomes from being repeatedly altered by using various antibiotics in a sequential fashion, it may be helpful to keep the current medications for a short period (≤5 days) if an empirical antibiotic is suitable. (Mohaideen, Vaani and Hemalatha, 2023) [9]

Antibiotic treatment duration for sepsis patients

ICU patients with bacteremia, UTIs, severe intra-abdominal infections, ventilator-associated pneumonia, community-acquired pneumonia, and other forms of bacteremia may safely and effectively undergo short-term (5–7 days) antibiotic treatment. A previous trial with sepsis patients shown that a method based on procalcitonin (PCT) to reduce the duration of antibiotics was both effective and safe. Nevertheless, a recent trial comparing PCT-based therapy to traditional treatment found no reduction in antibiotic duration in individuals with lower respiratory tract infections. Reduce the total length of antibiotic therapy; short-term treatment is indicated for pneumonia, urinary tract infection, and intra-abdominal infection, according to recommendations in numerous countries and worldwide treatment guidelines. Recent investigations have shown antibiotic administrations that are overly protracted, thus increasing the requirement for ASPs, despite such advice. (Vishalashi, Gupta and Verma, 2021) [17]"

Pathophysiology and diagnosis of sepsis

Overview of sepsis and progression to septic shock

A dysregulated immune response to infection results in organ failure and sepsis, a potentially fatal illness. In response to microbial invasion, it starts with the activation of inflammatory pathways, which may result in coagulopathy, decreased oxygen supply, and extensive endothelial damage. Sepsis escalates to septic shock if treatment is not received, which is marked by tissue hypoperfusion, chronic hypotension, and metabolic abnormalities and greatly raises the chance of death. (Dunkel and Corley, 2015) [3]

Role of biomarkers in diagnosis

Biomarkers play a critical role in diagnosing sepsis and guiding treatment.

Procalcitonin (PCT): Elevated in bacterial infections; used to differentiate bacterial from viral causes and guide antibiotic therapy.

C-reactive protein (CRP): Indicates systemic inflammation but lacks specificity; often used in conjunction with other markers.

These biomarkers help assess disease severity and response to therapy.

Importance of early detection and empirical therapy

Early recognition of sepsis is crucial to prevent progression to organ failure and septic shock. Empirical broad-spectrum antibiotic therapy, initiated within the first hour of diagnosis, improves survival by targeting likely pathogens. Rapid diagnostics and early intervention are essential components of effective sepsis management. (Font, Thyagarajan and Khanna, 2020) [4]

Principles of antibiotic stewardship

Definition and Goals of Antibiotic Stewardship Programs (ASPs)

Antibiotic Stewardship Programs (ASPs) are coordinated efforts aimed at optimizing the use of antimicrobial agents to achieve the best clinical outcomes while minimizing adverse effects, including antimicrobial resistance (AMR). The goals of ASPs include improving patient outcomes, reducing healthcare costs, and preserving the efficacy of antibiotics for future generations. (Anwar *et al.*, 2023) [1]

Core strategies

Right Drug, Dose, and Duration

- Selection of the appropriate antibiotic based on the likely pathogen, site of infection, and patient factors.
- Administering the correct dose to achieve optimal therapeutic levels while minimizing toxicity.
- Prescribing for the shortest effective duration to reduce resistance risk without compromising treatment efficacy.

De-escalation based on culture and sensitivity results

- Empirical broad-spectrum antibiotics are started early but should be narrowed once culture and sensitivity results are available.
- Reducing the spectrum helps lower the risk of resistance and avoids unnecessary exposure to broad-spectrum agents.

Avoidance of unnecessary combination therapies

- Limiting the use of multiple antibiotics unless clinically justified (e.g., polymicrobial infections or specific resistance concerns).
- Prevents increased risk of adverse effects and resistance development.

Multidisciplinary approach in ICUs

- Collaboration among infectious disease specialists, intensivists, pharmacists, microbiologists, and nursing staff.
- Regular audits and feedback sessions to improve prescribing practices.
- Integration of rapid diagnostics and decision-support systems for timely and informed antibiotic use.

By adhering to these principles, ASPs play a vital role in balancing the need for effective treatment in critically ill patients with the responsibility to mitigate antimicrobial resistance.

Empirical Vs Targeted therapy

Importance of empirical antibiotic therapy in the "Golden Hour"

It is crucial to start empirical antibiotic treatment as soon as possible after detecting sepsis, during the "golden hour," when the chances of survival are highest. Because infections and organ damage proceed so quickly, deaths are dramatically increased when antibiotics are not started immediately. Based on the infection's presumed origin and local resistance trends, empirical treatment prescribes broad-spectrum antibiotics to cover all possible bacteria.

Transitioning to targeted Therapy: Role of microbiological testing

Once microbiological testing results, such as blood cultures and sensitivity profiles, are available, transitioning to targeted therapy is essential. This approach narrows antibiotic coverage to the specific pathogen and minimizes unnecessary exposure to broad-spectrum agents, reducing the risk of antimicrobial resistance and adverse drug reactions.(Cui *et al.*, 2017) [2]

Balancing early broad-spectrum use with De-Escalation strategies

While broad-spectrum antibiotics are vital for initial management, prolonged use can lead to resistance and harm the patient’s microbiome. De-escalation strategies involve:

- Reducing the spectrum of antibiotics based on culture results.
- Discontinuing unnecessary antibiotics as clinical status improves.
- Reassessing therapy daily to ensure continued appropriateness.

This balance ensures effective treatment during the critical early phase while preserving antibiotic efficacy and minimizing resistance development.

Conclusion

In order to optimize sepsis therapy and minimize risks related to antibiotic resistance, antibiotic stewardship in the intensive care unit is essential. It is possible to greatly enhance patient outcomes in sepsis with the prompt administration of suitable antibiotic treatment and de-escalation tactics. The selection of antibiotics, whether they are new or old, should be guided by the spectrum of action, the patient's condition, and local resistance trends. Both types of antibiotics play significant roles. To improve treatment efficacy, it is necessary to go from empirical to targeted therapy, which requires rapid diagnostic tools for finding MDR-organisms. Striking a balance between the requirement for quick response and the avoidance of long-term antimicrobial resistance may be achieved via the implementation of strong antibiotic stewardship programs in the intensive care unit. Antibiotic effectiveness is preserved for future generations, healthcare expenses are lowered, and patient survival rates are increased via these efforts. The future of sepsis management in intensive care units is on the constant assessment of antibiotic treatment regimens and improvements in diagnostic tools.

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