REVIEW ARTICLE

ANTIBIOTIC STEWARDSHIP IN THE ICU- CHALLENGES AND STRATEGIES

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***Abstract**: Antibiotic stewardship in the Intensive Care Unit (ICU) is a pivotal challenge for intensivists, particularly within India's semi-open ICU systems. Inappropriate antibiotic use accelerates drug resistance, increases mortality, and raises treatment costs. This document summarizes core elements for successful stewardship programs, which rely on strong leadership, accountability, and multidisciplinary collaboration. Essential strategies involve antibiotic "time outs" after 48-hours, reassessment, prospective audits, and pharmacy-driven interventions such as dose optimization based on pharmacokinetic principles. Ultimately, these measures protect public health and ensure financial viability through reduced expenditures.*

***Keywords**: Antibiotic Stewardship, ICU (Intensive Care Unit), Antibiotic Resistance, Pharmacokinetics (PK/PD), Multidisciplinary Approach, Infection Control*

Antibiotic stewardship in the intensive care unit is of paramount importance and constitutes a major challenge for intensivists. Mostly ICUs in India are semi open systems, where antibiotic prescription authority is in multiple hands, right from primary consultants, anesthesiologists and physicians. An anesthesiologist–intensivist working in the ICU should possess sound knowledge of antimicrobial stewardship and awareness of local hospital infection patterns, with ready access to consultation from microbiologists and pharmacologists. Effective leadership in antibiotic management is essential and should be led by the

intensivist in charge of the ICU, supported by a multidisciplinary team comprising members from various specialties.

Patients who are unnecessarily exposed to antibiotics are placed at risk for serious adverse events with no clinical benefit. The misuse of antibiotics has also contributed to the growing problem of antibiotic resistance, which has become one of the most serious and growing threats to public health. Unlike other medications, the potential for spread of resistant organisms means that the misuse of antibiotics can adversely impact the health of patients who are not even exposed to them. The Centers for Disease Control and Prevention (CDC) estimates more than two million people are infected with antibiotic-resistant organisms.

Consequences of resistance

- Longer duration of illness
- Increased HAI
- Increased mortality
- Increased expense of treatment in ICU
- Patients act as reservoir of infection.

Improving the use of antibiotics is an important patient safety and public health issue as well as a national priority. The 2006 CDC guideline "Management of Multi-Drug Resistant Organisms in Healthcare Settings" stated that control of multi-drug resistant organisms in healthcare "must include attention to judicious antimicrobial use". In 2009, CDC launched the "Get Smart for Healthcare Campaign" to promote improved use of antibiotics in acute care hospitals and in 2013, the CDC highlighted the need to improve antibiotic use as one of four key strategies required to address the problem of antibiotic resistance in the US.

This document summarizes core elements of successful hospital Antibiotic Stewardship Programs. It complements existing guidelines on ASPs from organizations including the Infectious Diseases. There is no single template for a program to optimize antibiotic prescribing in hospitals. The complexity of medical decision-making surrounding antibiotic use and the variability in the size and types of hospitals require flexibility in implementation.

However, experience demonstrates that antibiotic stewardship programs can be implemented effectively in a wide variety of hospitals and that success is dependent on defined leadership and a coordinated multidisciplinary approach.

Core Elements of Hospital Antibiotic Stewardship Programs

Leadership Commitment: Leadership support is critical to the success of antibiotic stewardship programs and can take a number of forms, including:

- Formal statements that the facility supports efforts to improve and monitor antibiotic use.
- Including stewardship-related duties in job descriptions and annual performance reviews.
- Ensuring staff from relevant departments are given sufficient time to contribute to stewardship activities.
- Supporting training and education.
- Ensuring participation from the many groups that can support stewardship activities.

Financial support greatly augments the capacity and impact of a stewardship program and stewardship programs will often pay for themselves, both through savings in both antibiotic expenditures and indirect costs.

Accountability: Appointing a single leader responsible for program outcomes. Experience with successful programs show that a physician/intensivist leader is effective.

Drug Expertise: Appointing a single pharmacist leader responsible for working to improve antibiotic use.

Action: Implementing at least one recommended action, such as systemic evaluation of ongoing treatment need after a set period of initial treatment (i.e. “antibiotic time out” after 48 hours).

Tracking: Monitoring antibiotic prescribing and resistance patterns.

Reporting: Regular reporting information on antibiotic use and resistance to doctors, nurses and relevant staff.

Education: Educating clinicians about resistance and optimal prescribing.

Broad interventions

Antibiotic Time-outs:- Antibiotics are often started empirically in hospitalized patients while diagnostic information is being obtained. However, providers often do not revisit the selection of the antibiotic after more clinical and laboratory data (including culture results) become available. An antibiotic "time out" prompts a reassessment of the continuing need and choice of antibiotics when the clinical picture is clearer and more diagnostic information is available.

Two blood culture samples from both hand is always preferable before putting iv access that is to be followed by all staffs in ICU.

Review: -All clinicians should perform a review of antibiotics 48 hours after antibiotics are initiated to answer these key questions:

1. Does this patient have an infection that will respond to antibiotics?
2. If so, is the patient on the right antibiotic(s), dose, and route of administration?
3. Can a more targeted antibiotic be used to treat the infection (de-escalate)?
4. How long should the patient receive the antibiotic(s)?

Prior authorization: - Some facilities restrict the use of certain antibiotics based on the spectrum of activity, cost, or associated toxicities to ensure that use is reviewed with an antibiotic expert before therapy is initiated. This intervention requires the availability of expertise in antibiotic use and infectious diseases and authorization needs to be completed in a timely manner.

Prospective audit and feedback: - External reviews of antibiotic therapy by an expert in antibiotic use have been highly effective in optimizing antibiotics in critically ill patients and in cases where broad spectrum or multiple antibiotics are being used. Prospective audit and feedback are different from an antibiotic" time out" because the audits are conducted by staff other than the treating team. Audit and feedback requires the availability of experts and some smaller facilities have shown success by engaging external experts to advise on case reviews.

Pharmacy-driven Interventions:- Automatic changes from intravenous to oral antibiotic therapy in appropriate situations and for antibiotics with good absorption (e.g., fluoroquinolones, trimethoprim-sulfamethoxazole, linezolid, etc.) which improves patient safety by reducing the need for intravenous access.

Dose adjustments in cases of organ dysfunction (e.g. renal adjustment).

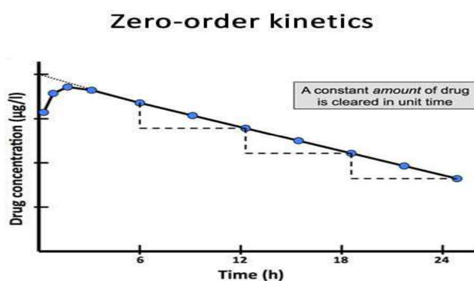
Dose optimization including dose adjustments based on therapeutic drug monitoring, optimizing therapy for highly drug-resistant bacteria, achieving central nervous system penetration, extended-infusion administration of beta-lactams, etc

Automatic alerts in situations where therapy might be unnecessarily duplicative including simultaneous use of multiple agents with overlapping spectra e.g. anaerobic activity, atypical activity, Gram-negative activity and resistant Gram-positive activity.

Time-sensitive automatic stop orders for specified antibiotic prescriptions, especially antibiotics administered for surgical prophylaxis.

Detection and prevention of antibiotic-related drug-drug interactions e.g. interactions between some orally administered fluoroquinolones and certain vitamins.

PK/PD:-Knowledge of pk/pd has an important role in prescribing antibiotics in an ICU.



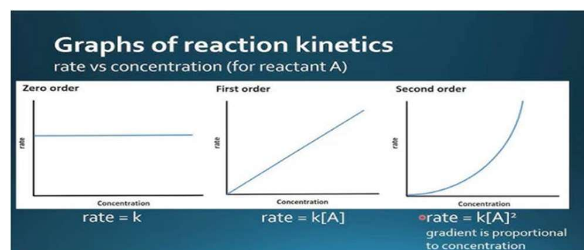


Fig: Different kinetics of drugs

Most antibiotics follows first order kinetics except few. Drugs which follow zero order kinetic are suitable for infusion whereas drugs following first order kinetics are suitable for interval doses.

Half-life and elimination:- Antibiotics those have long elimination half-life are suitable for single daily doses e.g, amikacin, fluoroqinolones etc. Other antibiotics are prescribed as intermittent bolus doses according to elimination half life's.

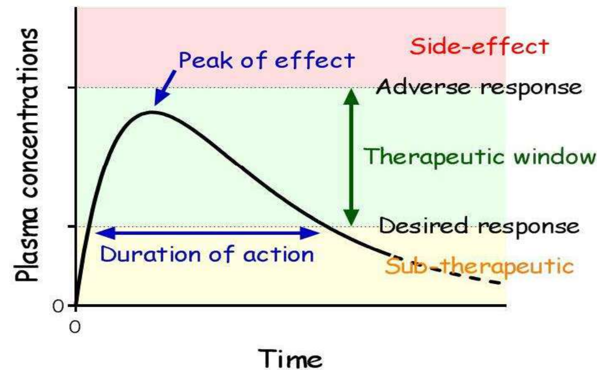


Fig- Dose response relationship

Piperacillin–tazobactam administered at 8-hourly intervals may result in subtherapeutic drug levels, as tazobactam has a shorter elimination half-life. Such inadequate concentrations fail to effectively eradicate target pathogens and may contribute to the development of antimicrobial resistance. A similar concern exists with imipenem–cilastatin; therefore, these antibiotics are preferably administered at 6-hourly intervals to maintain optimal therapeutic levels. Conversely, excessively high drug concentrations may exceed the therapeutic range and lead to toxicity, as seen with vancomycin in patients with renal impairment.

Infection and syndrome specific interventions

The interventions below are intended to improve prescribing for specific syndromes; however, these should not interfere with prompt and effective treatment for severe infection or sepsis.

Community-acquired pneumonia:- Interventions for community-acquired pneumonia have focused on correcting recognized problems in therapy, including: improving diagnostic accuracy, tailoring of therapy to culture results and optimizing the duration of treatment to ensure compliance with guidelines.

Urinary tract infections (UTIs):- Many patients who get antibiotics for UTIs actually have asymptomatic bacteriuria and not infections. Interventions for UTIs focus on avoiding unnecessary urine cultures and treatment of patients who are asymptomatic and ensuring that patients receive appropriate therapy based on local susceptibilities and for the recommended duration.

Skin and soft tissue infections:- Interventions for skin and soft tissue infections have focused on ensuring patients do not get antibiotics with overly broad spectra and ensuring the correct duration of treatment.

Empiric coverage of Methicillin-resistant Staphylococcus aureus (MRSA) infections: - In many cases, therapy for MRSA can be stopped if the patient does not have an MRSA infection or changed to a beta-lactam if the cause is methicillin-sensitive *Staphylococcus aureus*.

Clostridium difficile infections: - Treatment guidelines for CDI urge providers to stop unnecessary antibiotics in all patients diagnosed with CDI, but this often does not occur. Reviewing antibiotics in patients with new diagnoses of CDI can identify opportunities to stop unnecessary antibiotics which improve the clinical response of CDI to treatment and reduces the risk of recurrence.

Treatment of culture proven invasive infections:- Invasive infections (e.g. blood stream infections) present good opportunities for interventions to improve antibiotic use because they are easily identified from microbiology results. The culture and susceptibility testing often provides information needed to tailor antibiotics or discontinue them due to growth of contaminants.

Checklist for Core Elements of Hospital Antibiotic Stewardship Programs

The following checklist is a companion to Core Elements of Hospital Antibiotic Stewardship Programs. This checklist should be used to systematically assess key elements and actions to ensure optimal antibiotic prescribing and limit overuse and misuse of antibiotics in hospitals. CDC recommends that all hospitals implement an Antibiotic Stewardship Program.

Facilities using this checklist should involve one or more knowledgeable staff to determine if the following principles and actions to improve antibiotic use are in place. The elements in this checklist have been shown

in previous studies to be helpful in improving antibiotic use though not all of the elements might be feasible in all hospitals.

LEADERSHIP SUPPORT	ESTABLISHED AT FACILITY	
A. Does your facility have a formal, written statement of support from leadership that supports efforts to improve antibiotic use (antibiotic stewardship)?	❑ Yes	❑ No
B. Does your facility receive any budgeted financial support for antibiotic stewardship activities (e.g., support for salary, training, or IT support)?	❑ Yes	❑ No
ACCOUNTABILITY		
A. Is there a physician leader responsible for program outcomes of stewardship activities at your facility?	❑ Yes	❑ No
DRUG EXPERTISE		
A. Is there a pharmacist leader responsible for working to improve antibiotic use at your facility?	❑ Yes	❑ No
KEY SUPPORT FOR THE ANTIBIOTIC STEWARDSHIP PROGRAM Does any of the staff below work with the stewardship leaders to improve antibiotic use?		
B. Clinicians	❑ Yes	❑ No
C. Infection Prevention and Healthcare Epidemiology	❑ Yes	❑ No
D. Quality Improvement	❑ Yes	❑ No
E. Microbiology (Laboratory)	❑ Yes	❑ No
F. Information Technology (IT)	❑ Yes	❑ No
G. Nursing	❑ Yes	❑ No
ACTIONS TO SUPPORT OPTIMAL ANTIBIOTIC USE POLICIES	POLICY ESTABLISHED	
A. Does your facility have a policy that requires prescribers to document in the medical record or during order entry a dose, duration, and indication for all antibiotic prescriptions?	❑ Yes	❑ No
B. Does your facility have facility-specific treatment recommendations, based on national guidelines and local susceptibility, to	❑ Yes	❑ No

assist with antibiotic selection for common clinical conditions?

SPECIFIC INTERVENTIONS TO IMPROVE ANTIBIOTIC USE

Are the following actions to improve antibiotic prescribing conducted in your facility?

BROAD INTERVENTIONS	ACTION PERFORMED	
C. Is there a formal procedure for all clinicians to review the appropriateness of all antibiotics 48 hours after the initial orders (e.g. antibiotic time out)?	❑ Yes	❑ No
D. Do specified antibiotic agents need to be approved by a physician or pharmacist prior to dispensing (i.e., pre-authorization) at your facility?	❑ Yes	❑ No
E. Does a physician or pharmacist review courses of therapy for specified antibiotic agents (i.e., prospective audit with feedback) at your facility?	❑ Yes	❑ No
PHARMACY-DRIVEN INTERVENTIONS Are the following actions implemented in your facility?	ACTION PERFORMED	
F. Automatic changes from intravenous to oral antibiotic therapy in appropriate situations?	❑ Yes	❑ No
G. Dose adjustments in cases of organ dysfunction?	❑ Yes	❑ No
H. Dose optimization (pharmacokinetics/pharmacodynamics) to optimize the treatment of organisms with reduced susceptibility?	❑ Yes	❑ No
I. Automatic alerts in situations where therapy might be unnecessarily duplicative?	❑ Yes	❑ No
J. Time-sensitive automatic stop orders for specified antibiotic prescriptions?	❑ Yes	❑ No
DIAGNOSIS AND INFECTIONS SPECIFIC INTERVENTIONS Does your facility have specific interventions in place to ensure optimal use of antibiotics to treat the following common infections?	ACTION PERFORMED	
K. Community-acquired pneumonia	❑ Yes	❑ No
L. Urinary tract infection	❑ Yes	❑ No
M. Skin and soft tissue infections	❑ Yes	❑ No
N. Surgical prophylaxis	❑ Yes	❑ No

O. Empiric treatment of Methicillin-resistant Staphylococcus aureus (MRSA)	❑ Yes	❑ No
P. Non-C. Difficile infection (CDI) antibiotics in new cases of CDI	❑ Yes	❑ No
Q. Culture-proven invasive (e.g., blood stream) infections	❑ Yes	❑ No

TRACKING: MONITORING ANTIBIOTIC PRESCRIBING, USE, AND RESISTANCE

PROCESS MEASURES	MEASURE PERFORMED	
A. Does your stewardship program monitor adherence to a documentation policy (dose, duration, and indication)?	❑ Yes	❑ No
B. Does your stewardship program monitor adherence to facility-specific treatment recommendations?	❑ Yes	❑ No
C. Does your stewardship program monitor compliance with one of more of the specific interventions in place?	❑ Yes	❑ No
ANTIBIOTIC USE AND OUTCOME MEASURES	MEASURE PERFORMED	
D. Does your facility track rates of C. difficile infection?	❑ Yes	❑ No
E. Does your facility produce an antibiogram (cumulative antibiotic susceptibility report?	❑ Yes	❑ No
Does your facility monitor antibiotic use (consumption) at the unit and/or facility wide level by one of the following metrics:	MEASURE PERFORMED	
F. By counts of antibiotic(s) administered to patients per day (Days of Therapy; DOT)?	❑ Yes	❑ No
G. By number of grams of antibiotics used (Defined Daily Dose, DDD)?	❑ Yes	❑ No
H. By direct expenditure for antibiotics (purchasing costs)?	❑ Yes	❑ No

REPORTING INFORMATION TO STAFF ON IMPROVING ANTIBIOTIC USE AND RESISTANCE

A. Does your stewardship program share facility-specific reports on antibiotic use with prescribers?	❑ Yes	❑ No
B. Has a current antibiogram been distributed to prescribers at your facility?	❑ Yes	❑ No
C. Do prescribers ever receive direct, personalized communication about how they can improve their antibiotic prescribing?	❑ Yes	❑ No

EDUCATION		
A. Does your stewardship program provide education to clinicians and other relevant staff on improving antibiotic prescribing?	❑ Yes	❑ No

Conclusion

Antimicrobial stewardship programs (ASPs) adopt a multidisciplinary approach with strong leadership and continuous monitoring, aimed at safeguarding public health. Education and training of support staff form a cornerstone of these programs. Adequate financial support significantly enhances the capacity and effectiveness of stewardship initiatives, and such programs often prove to be cost-effective by reducing antibiotic expenditure as well as indirect healthcare costs.

Suggested readings

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