Antimicrobial Stewardship in Institutions and Office Practices

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ABSTRACT

Medically inappropriate, ineffective and economically inefficient use of antimicrobials is commonly observed in the health care units throughout the world especially in the developing countries. Antimicrobial stewardship programs attempt to balance the demand for these life-saving drugs with the need to preserve their future efficacy. A comprehensive evidence-based stewardship program should include elements chosen from the recommendations based on local antimicrobials use and resistance problems and on available resources that may differ, depending on the size of the institution or clinical setting. For success of antibiotic stewardship it is essential to increase awareness amongst medical professionals. Discipline in antimicrobial prescribing is most vital in clinical settings. A careful assessment of the benefits of prescribing against the risk of non-prescribing of antibiotics should be considered. It should be an endeavor of every physician to justify antibiotic prescription in case of empirical use. Integration of advanced information technology into antimicrobial stewardship programs holds the potential to both reduce antimicrobial overuse and improve outcomes. **[Indian J Pediatr 2008; 75 (8) : 815-820]**
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Establishment of a judicial, rational antibiotic usage is an urgent need for better care of patients and combating antimicrobial resistance.[1] Antimicrobial stewardship programs attempt to balance the demand for these life-saving drugs with the need to preserve their future efficacy. The problem of rational antibiotic usage is complex,[2] and requires coordination of the activities of health care authorities, institutions, professional organisations and individual practitioners. Furthermore, on a community basis - requires restriction of non-human usage of antibiotics,[3] and awareness of society about both the useful and harmful effects of antibiotics. To be effective, we need to bring discipline in prescriptions of antibiotics in all settings – hospital, ambulatory including office practice and primary care.

Medically inappropriate, ineffective and economically inefficient use of antimicrobials is commonly observed in the health care system throughout the world especially in the developing countries. Although 50 percent or more of drug expenditures may be wasted through irrational prescribing; inappropriate prescribing often remain unnoticed by those who are involved in health sector decision making or delivery of health services.[4]

Obstacles in reducing inappropriate antibiotic prescribing in hospitals are due to: failure of healthcare workers to accept ownership of 'antibiotic resistance', difficulties in changing behavior, inadequate resourcing, 'process' (optimal interventions) not defined

Effective antimicrobial stewardship employs both knowledge of patient-level and ecologic effects of antimicrobials as well as the psychology of human behavior change. Strategies to influence prescribing patterns and improve antimicrobial use can be broadly divided into three approaches:

- Educate the prescriber to make the 'correct' choice at the time of prescribing (education and guideline strategies)
- Review antibiotic prescribing after the fact and attempt to persuade prescribers to change undesirable prescriptions (review and feedback strategies)
- Control prescribing options by dictating which antibiotics a clinician may or may not prescribe (formulary and restriction strategies and antibiotic cycling strategies)

People may have different perceptions and meanings regarding the term "rational drug use", however, the

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Conference of Experts on the Rational Use of Drugs, convened by the World Health Organisation WHO in Nairobi in 1985 defined that "Rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements for an adequate period of time, at the lowest cost to them and their community.[5] These requirements will be fulfilled if all the prescribers are disciplined and the process of prescribing is appropriately followed.[6] This will include following steps:

- Defining patient's problems (or diagnosis)
- Defining effective and safe treatments (drugs and non-drugs)
- Selecting appropriate drugs, dosage and duration
- Writing appropriate prescription
- Giving patients adequate information
- Planning to evaluate treatment responses.

A comprehensive evidence-based stewardship program to combat antimicrobial resistance should include elements chosen from the following recommendations(evidence level AI+AIII & BI+AIII)[7] based on local antimicrobial use and resistance problems and on available resources that may differ, depending on the size of the institution or clinical setting.

• Core members of a multidisciplinary antimicrobial stewardship team include an infectious diseases physician and a clinical pharmacist with infectious diseases training (A-II) if available, a clinical microbiologist, an information system specialist, an infection control professional, and hospital epidemiologist (A-III). Because antimicrobial stewardship, an important component of patient safety, is considered to be a medical staff function, the program is usually directed by an infectious diseases physician or codirected by an infectious diseases physician and a clinical pharmacist with infectious diseases training (A-III).

• Collaboration between the antimicrobial stewardship team, the hospital infection control, pharmacy and therapeutics committees or their equivalents is essential (A-III).

• The support and collaboration of hospital administration, medical staff leadership, and local providers in the development and maintenance of antimicrobial stewardship programs is essential (A-III). It is desirable that antimicrobial stewardship programs function under the auspices of quality assurance and patient safety (A-III).

• The infectious diseases physician and the head of pharmacy, as appropriate, should negotiate with hospital administration to obtain adequate authority, compensation, and expected outcomes for the program (A-III).

• Hospital administrative support for the necessary infrastructure to measure antimicrobial use and to track use on an ongoing basis is essential (A-III).

• There are 2 core strategies, both proactive, that provide the foundation for an antimicrobial stewardship program. These strategies are not mutually exclusive.

(i) Prospective audit with intervention and feedback

Prospective audit of antimicrobial use with direct interaction and feedback to the prescriber, performed by either an infectious diseases physician or a clinical pharmacist with infectious diseases training, can result in reduced inappropriate use of antimicrobials (A-I).

(ii) Formulary restriction and preauthorization

Formulary restriction and preauthorization requirements can lead to immediate and significant reductions in antimicrobial use and cost (A-II) and may be beneficial as part of a multifaceted response to a nosocomial outbreak of infection (B-II)

• The following elements may be considered and prioritized as supplements to the core active antimicrobial stewardship strategies based on local practice patterns and resources.

- Education.
- Guidelines and clinical pathways.
- Antimicrobial cycling.
- Antimicrobial order forms.
- Combination therapy.
- Streamlining or de-escalation of therapy.
- Dose optimization.
- Parenteral to oral conversion.

• Health care information technology in the form of electronic medical records (A-III), computer physician order entry (B-II), and clinical decision support (B-II) can improve antimicrobial decisions through the incorporation of data on patient- specific microbiology cultures and susceptibilities, hepatic and renal function, drug-drug interactions, allergies, and cost.

• Computer-based surveillance can facilitate good stewardship by more efficient targeting of antimicrobial interventions, tracking of antimicrobial resistance patterns, and identification of nosocomial infections and adverse drug events (B-II).

• The clinical microbiology laboratory plays a critical role in antimicrobial stewardship by providing patient-specific culture and susceptibility data to optimize individual antimicrobial management and by assisting infection control efforts in the surveillance of resistant organisms and in the molecular epidemiologic investigation of outbreaks (A-III).

• Both, process measures (did the intervention result in the desired change in antimicrobial use?) and outcome measures (did the process implemented reduce or prevent

resistance or other unintended consequences of antimicrobial use?), are useful in determining the impact of antimicrobial stewardship on antimicrobial use and resistance patterns (B-III).

For success of antibiotic stewardship it is essential to increase awareness amongst medical professionals about need for rational prescribing practices. For proper implementation of such practices we need to have National, institutional, regional and primary care antibiotic policies.

NATIONAL ANTIBIOTIC POLICY

A national expert committee on antibiotic policies should be established. Professional organizations like IAP, API, Association of Microbiologists, Society for Infectious Diseases, Association of Preventive Medicine Specialists *etc* should take a lead. The committee should develop guidelines for creating and auditing antibiotic prescriptions as well as considerations of content.[5,8] They should consider both hospital and primary care settings as well as veterinary and agriculture use. Guidelines should be widely discussed through professional meetings of multidisciplinary groups, involving clinicians, microbiologists and pharmacologists/pharmacists.

INSTITUTIONAL ANTIBIOTIC POLICY

Each health-care institution should have a therapeutics committee (TC), which should develop a local antibiotic policy based on national recommendations. This committee should be multidisciplinary so that the policy is acceptable to all sections of the institution. It should monitor the implementation of the policy, receive feedback information, assess the outcome and discuss it with the doctors.[1, 8, 9, 10, 11] The policy should be revised each year, based on the experience of prescribers and the susceptibility reports of the microbiology laboratory. Audit targets should be set both for the antibiotic prescriptions and the TC itself.[12,13]

The TC should consist of experts in pediatrics, infectious diseases, internal medicine, surgery, Ob/Gy, clinical microbiology, pharmacology and hospital pharmacy.

Three levels for antibiotic prescribing are generally recommended:

- First choice antibiotics, to be prescribed by all doctors;
- Restricted choice – for multiply-resistant pathogens, polymicrobial infections, some patient conditions that need special attention and/or more expensive antibiotics, to be prescribed after discussion with head of department or TC representative;
- Reserve antibiotics:
  - Reserved for life-threatening infections and/or antibiotics known to select more resistance
  - To be used after permission from a TC member.

Antibiotic policy should be discussed with all hospital staff, before becoming an official hospital policy. Some hospitals have computerized prescribing of antibiotics,[4] (which in the future, should become more commonplace[14]. This and other innovations such as the antibiotic order form and automatic stop form can be useful to control antibiotic usage[9,13] and improve the quality of prescription. Good collaboration between clinicians, the clinical microbiology laboratory, the committee for infection control and the pharmacy is necessary for achieving all the goals of a RAP[11] and a multi-disciplinary antibiotic team (MAT) should be formed to ensure this.[1]

PRIMARY CARE SETTING ANTIBIOTIC POLICY

A similar or identical TC should elaborate complementary Antibiotic Policy guidelines for office practice and general practice and should also oversee their implementation and audit as suggested in Europian stretegy for controlling antibiotic resistance.[11, 15] Such TCs are often developed through area prescribing committees in collaboration with local microbiologists, pediatricians and general practitioners (GPs).[16] An appropriate system for audit and feedback enables the health authority to follow changes over time and target individual practices whose prescription appears inappropriate.

Patient education is also important, especially about the hazards of misuse and over-use of antibiotics (as in self medication and/or OTC purchase) leading to treatment failure, chronic infection, suppression of normal flora and selection of resistant bacteria.[17] The importance of patient's compliance should be emphasized, especially for long course therapy, such as for tuberculosis.[11] Finally, encouraging vaccination is important in preventing morbidity and mortality.[16]

ANTIMICROBIAL PRESCRIPTION IN CLINICAL SETTINGS

Discipline in antimicrobial prescription is most vital in this area.[10] Prescribing antibiotics should be done under strict indications. Therapeutic decisions are best made depending upon the clinical situations:

- Reserved for life-threatening infections and/or antibiotics known to select more resistance
- The urgent situation - in severely ill patients *e.g.*,

septic shock, endocarditis, meningitis, neonatal sepsis, NEC, osteomyelitis need immediate therapy.
- Moderately ill patients with focal infection *e.g.*, pneumonia, urinary, biliary tract infection, where therapy should be administered within 2 hours.
- Minor bacterial infection, which is not self-limiting but where therapy can wait laboratory confirmation.
- Prophylaxis upon specified medical and surgical indications.

A careful assessment of the benefits of prescribing against the risk of non-prescribing of antibiotics should be considered including:

- Patient cure/improvement against failure/mortality
- Development of resistance in pathogens infecting the patient
- Risk of spread of resistance to other patients, family-society members.
- Suppression of normal flora
- Development of resistance in normal flora
- Risk for super-infection

Factors other than antibiotics which can help to overcome should be considered: *e.g.*, drainage of abscess,[1] catheter replacement, immuno-stimulation or reduced immuno-suppression, vaccination, reduced duration of ventilatory assistance, minimizing the use of central venous catheters, patient isolation.[1]

Before starting antibiotic treatment, appropriate specimen needs to be taken, wherever possible, from the patient and sent for relevant laboratory examination including culture, species identification of probable pathogens and sensitivity of organism. The results obtained should be used to guide/adjust the antibiotic therapy[3]. In urgent clinical situations helpful information to guide empiric therapy includes data about, localization and source of infection nosocomial/community acquired, prior antibiotic therapy, prior invasive procedures, prior cultures, current relevant resistance patterns. While making a decision about starting antibiotic, we should question[17]:

- What is my rational in prescribing an antibiotic to this patient - does he really need it?
- Is it empiric or for prophylaxis?
- If there is confirmation of a bacterial infection, what is the causative organism and probable susceptibility?
- How ill is the patient, how quickly do treatment need to be given and what route is appropriate?

Other factors, relevant to be considered are:

- *In vitro* susceptibility
- Antibiotic spectrum and the need for combination therapy
- Antibiotic activity, bactericidal/ bacteriostatic
- Site of infection and achievable antibiotic concentrations
- Dosage regimen and modern pharmaco-dynamic principles
- Dosing regimen and host factors (age, weight, immunosuppression, underlying disease, renal/ hepatic dysfunction, allergy).
- Cost/effectiveness ratio
- Adverse events, including drug interactions and those due to poor absorption of many oral agents

Empiric antibiotics

Empirical use of antibiotics may be scientifically acceptable if few prerequisites are judiciously met with. It should be an endeavor of every physician to justify antibiotic prescription in case of empirical use[11].

When one should start ?

- High probability of bacterial infection while waiting for laboratory results

In case of clinically suspected sepsis or fever in an infant < 3 months of age, it is important not to delay antibiotic therapy for fear of complications and hence empirical antibiotic therapy is rational but only after necessary laboratory tests are sent out.

- High probability of bacterial infection where waiting is dangerous

Situations like sick neonate, undiagnosed fever in an immunocompromised host or child in ICU with invasive interventions justify empirical antibiotic therapy. Continued attempt must be made to diagnose infection with proper laboratory tests for ideal treatment.

- High probability of bacterial infection in spite of absence of proof of infection

Diagnosis difficult to prove and may be fatal, justifies empirical antibiotic therapy. Failure of symptomatic treatment of chronic respiratory problems such as bronchiectesis or sinusitis deserve antibiotic therapy even in absence of clinical or laboratory proof of bacterial infection. Persistent cardiac failure in spite of proper treatment or unaccounted fever in heart defect may be due to bacterial endocarditis.

- Suspected viral infection with atypical progress

If fever persists beyond the anticipated period in a viral infection, bacterial complications are likely and empirical antibiotic is rational while search for bacterial infection to be continued.

- Uncomplicated near-certain bacterial infections

Conditions like acute lymphadenitis, acute onset of otitis media with pus discharge in age <2 years, green foul smelling nasal discharge and acute dysentery with blood / mucus in stools are classical presentations of bacterial infection in office practice and short course of an antibiotic is rational even without further proof of bacterial

infection. However a recurrence of such infection necessitates further investigations and not just repeat antibiotic therapy.

What empirical antibiotic[10]

• Community acquired infections are most common in office practice and usually drug resistance is not an issue except in conditions such as typhoid fever or recurrent bacterial infections. Hence choice of antibiotic for common office practice infections should be any simple first line single oral drug. Parenteral antibiotic is rarely necessary in office practice. One may choose low resistance potential antibiotic such as amoxycillin for routine use.

• Patients requiring hospitalization for complicated or serious community acquired infections such as typhoid fever, pneumonia or dysentery, should also be treated with first line drugs based on local epidemiology. It is best to use single antibiotic One may ideally choose antibiotic with both parenteral and oral formulations so that same antibiotic can be continued orally after reasonable control of infection following initial parenteral therapy.

• Vulnerable host with community acquired bacterial infection may justify hospitalization and treatment with two antibiotics with broad cover till specific bacteriological diagnosis is available.

• Situations of suspected nosocomial infection justify second line antibiotics or combination of antibiotics selected on the basis of local epidemiology.

During the treatment we have to consider the relevance of:

- Bacterial identification/susceptibility
- Appropriateness of dose, route, duration
- Adverse effects,
- Patient status, improvement/failure

Finally evaluation should be performed with respect to:

- Therapeutic response: improvement, failure, death (analyze the reason)
- Any specific event to note: adverse effect, resistance during therapy, reinfection, super infection

For clinicians involved in prophylaxis, similar questions should be[1]:

- What is the need to give antibiotic prophylaxis in this patient?
- Which organism has to be covered with prophylaxis?
- Which antibiotic to be given?
- When to start the antibiotic?
- What should be the dose?
- How long should antibiotic prophylaxis last?
- The need to repeat the dose in surgical prophylaxis eg. if the operation is prolonged.
- Is there any evidence for bacterial infection after the patient has been operated?

Unfortunately, in the real world, prescribing patterns many a times do not conform to these criteria and can be termed as inappropriate or irrational or non disciplined prescribing. Regular irrational prescribing may be regarded as "pathological"[6].

Common patterns of irrational prescribing may manifest in the following forms:

- The use of drugs when no drug therapy is indicated, e.g. antibiotics for viral upper respiratory infections
- The use of the wrong drug for a specific conditions requiring drug therapy, *e.g.,* tetracycline or aminoglycosides in childhood diarrhea requiring ORS,
- The use of drugs with doubtful/unproven efficacy, *e.g.* the use of antimotility agents in acute diarrhea.
- The use of drugs of uncertain safety status, *e.g.* use of dipyrone (Baralgan, *etc.*)
- The use of correct drugs with incorrect administration, dosages, and duration, *e.g.* the use of IV paracetamol when suppositories or oral formulations would be appropriate.
- The use of unnecessarily expensive drugs, *e.g.* the use of a third generation, broad-spectrum antimicrobial when a first-line, narrow spectrum agent is indicated.

IMPACT OF NON-DISCIPLINED PRESCRIPTION PRACTICES

Non-disciplined prescription practices leads to inappropriate use of antimicrobials. The impact of this irrational use of drugs can be seen in many ways[10]:

- Reduction in the quality of drug therapy leading to increased morbidity and mortality
- Waste of resources leading to reduced availability of other vital drugs and increased costs,
- Increased risk of unwanted affects such as adverse drug reactions and the emergence of drug resistance, *e.g.* MDR malaria, MDR tuberculosis, MDR enteric fever
- Psychosocial impacts such as when patients come to believe that there is 'a pill for every ill'. This may cause an apparent increased demand for drugs.

In summary, antibiotics should ideally be prescribed for treating bacterial infections. They are also used for prophylaxis of bacterial infections in selective situations. However in clinical practice, antibiotics are often used empirically. Empirical use is based on personal observation and practical experience. Empirical use of antibiotics may be scientifically acceptable if few prerequisites are judiciously met with. Therefore it should be an endeavor of every physician to justify antibiotic prescription in general and specially in case of empirical use with documented reasoning. Potential risk of

empirical antibiotic therapy should always be weighed against probable benefits. Unfortunately overuse of antibiotics has led to many multy-resistant organisms. Several interventions to optimise antibiotic prescribing can improve the therapy of hospital inpatients (with improvements in clinical or microbiological outcome).

Comprehensive antibiotic stewardship program is essential in these situations. Superiority of multiple interventions over single interventions not confirmed, but it is likely that multiple interventions will be implemented. Restrictive interventions are more effective than educational interventions, at least in the short term. Integration of advanced information technology into antimicrobial stewardship programs holds the potential to both reduce antimicrobial overuse and improve outcomes, benefiting both the patient being treated and future patients relying on the effectiveness of our antimicrobial armamentarium.

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