Review Article

Stop antibiotic resistance – A roller coaster ride through "antibiotic stewardship," "prescription auditing" and "AWaRe" assessment tool

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Abstract

The emergence of superbugs and highly resistant organisms like methicillin-resistant staphylococci, vancomycin-resistant enterococci, carbapenem-resistant enterobacteriaceae demands the monitoring of antibiotic prescription and usage in various domains. The impact of antibiotic resistance is huge that it increases mortality, morbidity, and economic costs. The issue has to be addressed at various levels and that is why regulatory bodies implement antibiotic stewardship programs. These programs give a list of guidelines like infection control, tracking antibiotic use, prescription auditing, and involvement of health professionals like pharmacists, nurses, etc., A comparison of the list of guidelines given by the Centre for Disease Control and Prevention and Indian Council of Medical Research gives an idea about the measures to be taken at various levels to reduce the burden of antibiotic resistance. Prescription auditing is one of the major components of antibiotic stewardship. The auditing can be done either prospectively or retrospectively using WHO core prescribing indicators and antibiotic-specific indicators. An AWaRe assessment tool was also used to evaluate antibiotic consumption in countries and hospitals. The antibiotics are classified into access, watch and reserve categories. The aim of implementing the AWaRe tool is to increase the rational use of access antibiotic and reduce the consumption of watch and reserve antibiotics. This review focuses on the importance of prescription auditing, AWaRe tool and antibiotic stewardship in decreasing the threat of antibiotic resistance.

Keywords: Antibiotic, auditing, AWaRe tool, prescription, stewardship

Introduction

As per WHO, antibiotic resistance is one of the top 10 global health problems, and almost 50% of the prescription, dispensing and sales of drugs are inappropriate.[1] The reported deaths due to antibiotic resistance is 7 million every year, which can increase to 10 million by 2050.[2,3] The major cause of antibiotic resistance includes inappropriate use of antibiotics, self-medication like misuse of antibiotics, using antibiotics in agriculture and livestock, and pollution of water sources by pharmaceutical companies.[4-6] The consequences of all these can result in postantibiotic era in which minor infections can kill patients.[7] It not only increases mortality and morbidity but also increases the economic burden of low- and middle-income countries.[8] Some examples of resistance in countries like India include fluoroquinolone resistance among enterbacteriaceace, methicillin-resistant *staphylococcus aureus*, carbapenem-resistant enterobacteriaceace. A study conducted by Sulis G *et al.* reported a high level of antibiotic prescription in primary care settings. The data were obtained from standardized patient–provider interaction-based studies in India, Kenya and China. The antibiotic prescription

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was observed in states like West Bengal, Delhi, Mumbai, and it was identified that the prescription of watch antibiotics like quinolones and macrolides was higher in primary care settings, and the reserve antibiotics were prescribed for diarrhoea in children.[9] In the South Indian Union territory, a prescription auditing study was conducted in nine primary health care centres and one tertiary care centre, and the study investigator found that upper respiratory infections were treated with antibiotics due to viral infections.[10] The primary health care centre is a health facility which treats most of the common self-limiting infections among the public, and it is high time that practicing physicians in primary health care centre understand the impact of irrational prescribing of antibiotics. These two recent studies indicate the need for awareness regarding the rational prescribing of antibiotics to primary care physicians. The methods to reduce the burden of antibiotic resistance include rational prescription of medicines, antibiotic stewardship programmes, educational interventions targeting various groups, improving the awareness about a local antibiogram and the resistance pattern among physicians. Centre for Disease Control and Prevention (CDC) in USA and ICMR in India proposed the two major antibiotic stewardship programmes. One of the components of the antibiotic stewardship programme is prescription auditing. This review focusses on prescription auditing and AWaRe (Access, Watch, Reserve) assessment tool which are considered to be important components.

Novelty

WHO introduced aWaRe assessment tool in 2019, but still many countries including India have not adopted AWaRe. This review sensitzes the need for AWaRe tool to ensure optimal use of antibiotics and to reduce antibiotic resistance.

Steps for rational prescribing by Indian council of medical research (ICMR)

ICMR mentions a 30% rule with regard to antibiotics in India, and it includes the following:

- 30% of the antibiotics are not prescribed appropriately,
- 30% of the surgical prophylaxis is not appropriate,
- 30% of the pharmacy cost is spent on antibiotics
- 30% of the inpatient prescription contain antibiotics
- 30% of the amount spent on antibiotics can be reduced by antibiotic stewardship programme.[11]

One of the major reasons for the increase in the burden of antibiotic resistance is an irrational prescription of antibiotics. ICMR has listed certain steps to guide prescribers regarding the rational prescription of drugs. They include identifying a proper clinical diagnosis, restricting the empirical therapy to a selected group of patients, identifying the possible microorganisms responsible for the infection, choice of the appropriate antibiotic, de-escalation of drugs/therapy when needed, identifying the time to stop the antibiotics, limiting the duration of therapy and optimizing of pharmacokinetic, pharmacodynamics parameters.[12]

Comparison of antibiotic stewardship activities proposed by CDC and ICMR

The organization CDC proposed the core elements of the Antibiotic Stewardship program as an assessment tool to guide the hospitals to monitor antibiotic stewardship activities in the year 2019.[13] ICMR also issued a document containing the antibiotic stewardship guidelines in the year 2018. The components of both these recommendations have distinctive features and targets, as listed in Table 1.

Prospective prescription auditing

A prospective audit is a component of the antibiotic stewardship guidelines by ICMR. In this audit antibiotic stewardship, personnel will review the case. The team comprises infectious disease physician, nurse and pharmacist. The two types of the method in prospective audit and retrospective audit include one-step and two-step methods. The one-step method is the one in which the infectious disease physicians directly review the case and give feedback regarding antibiotic use. In the two-step process, the first review of the case will be by the nurse or pharmacist followed by a presentation to the physician who gives his valuable feedback. The review includes the switch to oral from parenteral therapy on day 1, assessing the appropriateness based on the microbiological cultures on day 4, and reviewing the duration of therapy on day 7.

The advantage of a prospective audit is the freedom for the physicians to accept or deny the recommendation suggested by the antibiotic stewardship program team (ASP) team. This approach facilitates learning among physicians, and individualization of drugs for patients improves the health care outcome. The disadvantages of this method are that it is costly to implement and requires manpower. The manpower also needs adequate training before conducting the audit.[14]

Retrospective prescription auditing

The retrospective auditing of antibiotic prescriptions is done using WHO prescribing indicators in many studies.[15,16] The prescriptions will be collected, and the following parameters will be analysed.

WHO prescribing indicators

1. Average number of drugs per prescription
2. % of prescriptions with drugs from the essential medicine list
3. % of prescriptions with antibiotics
4. % of prescriptions with drugs with generic name
5. % of prescriptions with injection prescribed[17]

Other than the WHO prescribing indicators, the other parameters measured specifically for antibiotic prescriptions include

1) Distribution of diagnosis for which the antibiotic is prescription
2) % of prescription based on lab diagnosis
3) % of the most commonly prescribed antibiotics
4) % of the prescriptions with inappropriate use (like dose, frequency, duration of antibiotic use not mentioned)[18]

5) Completeness of prescription like patient details[19]
6) Legibility and rationality of the prescription

Many studies were conducted in hospitals and pharmacies based on the WHO prescribing indicators, and these studies are listed in Table 2.

From the above-mentioned studies, only in few studies, it is understood that the inpatient use of antibiotics is higher than the outpatient and the most common group of antibiotics include amoxicillin (penicillin group), and macrolides in the outpatient department. The most common antibiotics used in inpatient settings include amoxicillin (access group) and cephalosporin (watch) group of antibiotics.

AWaRe assessment tool

AWaRe is an assessment tool introduced in the year 2017 by WHO, and this tool supports antibiotic stewardship programme. The tool

Table 1: List of guidelines for antibiotic stewardship by CDC and ICMR

Antibiotic stewardship assessment tool CDC (2019)	Antibiotic stewardship guidelines by ICMR (2018)
Hospital leadership commitment. 1. Time 2. Resources 3. Regular meeting to discuss the report and outcomes 4. Integration of stewardship activities with patient safety and quality improvement.	Appropriate use of microbiology lab 1. Prescription of antibiotics after culture results.
Accountability 1. Responsibility for stewardship program activities and outcome.	Infection control Maintaining sanitary precautions
Pharmacy expertise 1. Involvement of pharmacist to implement the program and monitor the outcome. 2. Adequate training and experience	Streamlining/de-escalation 1. Stopping antibiotics in the case of noninfectious/viral causes 2. Switching over from broad spectrum to narrow spectrum based on the culture results 3. Changing combination therapy to single medication 4. Switching over from parenteral to oral drug therapy.
Action: Implement interventions to improve antibiotic use Prospective audit and feedback Preauthorization	Formulary restriction and preauthorization 1. Restricting the antibiotics in the formulary 2. Preapproval by antibiotic stewardship team before prescribing antibiotics
Tracking antibiotic use and outcome	Prospective audit and feedback
Conducting review meetings on antibiotic selection among prescribers	Audit by the infectious disease physician to review the optimal use of antibiotics
Reporting antibiotic use and outcome Antibiogram to the prescribers	Right drug, dose, duration and dosing schedule

Table 2: A list of studies on auditing on antibiotic prescriptions

S. no	Type of study and place of study	Sample size	Results
1.	Retrospective audit of outpatient prescriptions Eastern region, Ghana (2016)	1600 prescriptions	19.1% prescription of antibiotics Antibiotic most common prescribed: amoxicillin, metronidazole[15]
2.	Prospective audit cross sectional Triage area tertiary hospital Northern India (2018)	517 patients	58% were prescribed antimicrobials Most common – ceftriaxone, amoxicillin clavulanic acid, metronidazole[18]
3.	Prospective study tertiary hospital Kolanchery Kerala (2017)	610 records	Most commonly prescribed antibiotics- penicillins and macrolides[20] Most commonly prescribed antibiotics- penicillins and macrolides[20]
4.	Prospective cross-sectional study at Anantapur AP paediatric population	845	Percentage of encounters with antibiotics is 50% which is higher compared with WHO value Most commonly prescribed antibiotics – cephalosporins[21]
5	Prospective cross-sectional study at inpatient departments in Jaipur	300	Ceftriaxone + sulbactam is the most commonly prescribed drug[22]
6.	Cross-sectional retrospective study at Asmara Eritr Inpatient-based study (2018)	100	79% of the hospitalized patients had an antibiotic in their prescription. Ampicillin was the most commonly prescribed antibiotic.[23]
7.	Retrospective study among paediatric patients at Abudhabi	419	The percentage of cases with antibiotic prescription is 43% (higher than WHO-prescribing indicator) Most commonly prescribed antibiotic is cefaclor (31.1%) followed by co amoxiclav (24.6%)[16]
8.	Retrospective study in Indonesia Comparing two hospitals: Hospital A and B A- With well-defined antibiotic protocols B- No protocols	A-499 B-500	A higher proportion of inpatients treated with antibiotics (84%)[24]

Table 3: List of access watch and reserve antibiotics as per WHO classification

S. no	Type	Description	Drugs as recommended by WHO
1.	Access	This group of antibiotics has a lesser resistance potential Effective against a broad range of commonly encountered organisms in clinical practice Drugs to be prescribed for the 25 most common infections. These drugs should be at good quality, affordable and available at all times, The goal of AWaRe is to achieve a country level target of 60% of the access antibiotics in prescriptions.	Sulfonamide-trimethoprim penicillin-ampicillin, amoxicillin First generation cephalosporins aminoglycosides-amikacin, gentamicin
2.	Watch	Major target group of monitoring and antibiotic stewardship programme	Second generation cephalosporins like cefaclor, cefamandole Third-generation cephalosporins Fluoroquinolones like ciprofloxacin, Levofloxacin Glycopeptides like vancomycin Macrolides like azithromycin, Erythromycin Pencillins like carbencillin
3.	Reserve	The group of antibiotics that are reserved for the treatment of infections due to multi-drug-resistant organisms Preferred in highly specific patients and settings Active against "High priority" or critical priority in the priority pathogens list Ex: Carbapenem-resistant enterobacteriaceae.	Monobactams, carbapenams, fifth-generation cephalosporins, polymyxin (colistin), tigecycline

promotes the rational use of antibiotics by guiding the countries. It is given as an excel sheet in which antibiotics are classified into access watch and reserve group of antibiotics [Table 3].[25]

The goal of AWaRe tool is to reduce the utilization of watch and reserve antibiotics and to increase access to antibiotics in the required clinical conditions.

Application of WHO AWaRe tool in research

AWaRe assessment tool was used to assess the antibiotic use in 56 countries, and it was identified that there was a wide variation in the percentage of access, watch and reserve antibiotics among hospitalized patients. The usage of access antibiotic usage was the highest in Singapore and the lowest in China. The percentage of prescription of watch was high in Iran and low in Finland. The prescription of reserve antibiotics was low in all countries.[26]

Mustag *et al.* reported that the use of access antibiotics is less (25%) and watch antibiotics is more (72.5%) in a teaching hospital in Faisalabad. Use of AWaRe tool keeps a check over the prescription of the antibiotic and prevents the emergence of multidrug-resistant organisms.[27]

A global point prevalent survey on the consumption of antibiotics among 664 hospitals from 69 countries reported that the use of watch antibiotics was higher in low- and middle-income countries.[28]

A study on the antibiotic prescribing pattern among the outpatient departments in a tertiary hospital assessed the prescriptions using the AWaRe tool. The commonly used antibiotics in the outpatient belonged to the access group, and ciprofloxacin was the drug mostly prescribed in the watch group.[29]

Conclusion

Any failure to tackle antibiotic resistance will result in a tremendous rise of super bugs, riskier surgeries, and increased mortality rates, and hence the measures of antibiotic stewardship should be strengthened further. Though India did not adopt AWaRe tool, yet many countries have been using the tool to assess the usage of the antibiotics. This tool guides policy makers, doctors to treat everyone and preserves the antibiotics for future. The idea is that today's medicines should be helpful for tomorrow's children too.

Keypoints

Periodical auditing of prescriptions at various time intervals by the antibiotic stewardship team can reduce the threat of antibiotic resistance.

In doubt while prescribing and auditing, standard treatment guidelines, tools like WHO prescribing and AWaRe assessment tool can be adopted as checklist.

Prescription of access antibiotics is preferred, and its better if 60% of the prescriptions has access antibiotics.

Watch antibiotics like fluoroquinolones should be strictly monitored for irrational use.

Reserve antibiotics should be utilized as the last resort options for multi-drug-resistant infections.

Take home message

Primary health care facilities in countries like India treat most of the common infections among the public, and every physician in primary care facility should be cautious in treating common infections.

Irrational prescribing of antibiotics should be avoided while treating infections.

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There are no conflicts of interest.

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