Antibiotic Stewardship and Conservation: Considerations for the Pharmacist: Part 1

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INTRODUCTION

The pandemic escalation in antibiotic resistance (ABR) is a global public health challenge with extensive health, economic and societal implications. Resistance emerges because of selection pressure from indiscriminate antibiotic use in human health and the veterinary and agricultural sectors. Infections caused by resistant bacteria constrain the effective treatment of infections, increase the risk of spread, result in longer duration of illness, higher mortality rates, increased costs of alternative treatment[1-2] and AMR is a threat to the world economy.[3]

The high HIV/AIDS burden and the substantive risk factors for communicable diseases in South Africa engenders extensive antibiotic use and subsequent resistance. South Africa is indeed amongst the 5 countries responsible for 76% of the 36% overall increase in antibiotic use in 71 countries over the period 2000-10.[4] Although the nature, extent and burden of ABR is not systematically and/or representatively quantified, available evidence indicates that ABR is an escalating challenge, particularly in the human (http://www.nicd.ac.za/ ?page=germs-sa&id=97) and agricultural sectors.

The South African National Department of Health, published the "Antimicrobial Resistance (AMR) National Strategy Framework 2014-2024" in response to the Global Action Plan (GAP) of the World Health Organization (WHO) in order to provide "a structure for managing AMR to limit further increases in resistant microbial infections and improve patient outcomes" by 4 strategic objectives viz., (1) establish national and health establishment governance structures to strengthen, coordinate and institutionalize interdisciplinary AMR efforts, (2) optimise surveillance and early detection of AMR and enable reporting of resistance trends at local, regional and national levels to optimise empiric and targeted antibiotic choice, (3) enhance infection prevention and control to contain the spread of resistant microbes to patients in healthcare settings, focusing on hand hygiene and patient isolation (community measures include preventing infection through vaccination programmes and improvements in water and sanitation), and, (4) implement antimicrobial stewardship to promote appropriate use of antimicrobials in human and animal health.[5] Pharmacists in hospital or community pharmacy practice are able to make the greatest impact on the containment of AMR and ABR by antibiotic stewardship.

1. RATIONAL ANTIMICROBIAL USE AND ANTIMICROBIAL STEWARDSHIP

The WHO Global Strategy for Containment of Antimicrobial Resistance defines rational use of antimicrobials as "the cost-effective use of antimicrobials which maximizes clinical therapeutic effect while minimizing both drug-related toxicity and the development of antimicrobial resistance".[6]
Antimicrobial stewardship which relates to the rational/prudent use of antimicrobials involves the "appropriate selection, dosing, route of administration and duration of antimicrobial therapy" to "optimize clinical outcomes while minimizing the unintended consequences of antimicrobial use" such as toxicity and the emergence of resistance.[7]

1. THE ROLE OF THE PHARMACIST

As the primary custodians of medicines, pharmacists have extensive knowledge on the patho-physiology of infections, indications for the use of prescription and non-prescription medicines, and, the rational use of antibiotics in terms of choice, dose, duration, dosage forms that best suit patients, dosage adjustments, adverse effects, drug interactions and contraindications. Pharmacists validate/confirm prescribing practice and compliance with treatment guidelines in collaboration and consultation with prescribers (usually medical practitioners) and thus have an oversight role. Pharmacists are further strategically placed to counsel and educate medical practitioners and patients to ensure optimal antibiotic therapy by compliance with treatment guidelines and adherence to antibiotic regimens respectively.

Pharmacists are one of a number of health care professionals who may drive or influence the implementation of an AMR strategy at health establishment level through a multidisciplinary approach. Based on their individual clinical skills or expertise, pharmacists may play a leadership or more supportive role in multidisciplinary work groups and committees on AMR at the health establishment level.

Part 1 of this article has a focus on the Hospital and Community Pharmacist. Other sectors of Pharmacy are covered in Part 2.

1.1 The Community Pharmacist

The community pharmacist is frequently the first point of contact with the health system, partially because pharmacies generally out-number medical practices in most countries and have longer trading hours facilitating access to healthcare. The community pharmacist is able to advise patients on minor ailments with the option of referral to the medical practitioner as appropriate.[8]

The community pharmacist has a pivotal role in the non-antibiotic management of self-limiting infections such as viral upper respiratory tract infections (URTIs) manifesting as colds, sore throat and "flu" for example. URTIs are the most common acute problem encountered in primary care and amongst the infections most prone to antibiotic misuse which ranges from 78% in Thailand to 57% in Europe.[9] The community pharmacy has a comprehensive knowledge non-prescription medicines as alternative symptomatic treatment for infections of viral origin and is strategically placed to educate and work with patients to mitigate against patient demand for antibiotics.

The community pharmacist is also the last point of contact with the health system, when the patient presents at the pharmacy with a prescription. As the intermediary between medical practitioners and patients, pharmacists are well placed to validate and confirm the need for antibiotics in consultation with the prescriber. Once the indication for antibiotics is verified, the community pharmacist is able to counsel and educate the patient on the appropriate use of antibiotics, including but not limited to:

- The importance of completing the course even when the symptoms are alleviated,
- Ensuring that the antibiotic is taken as prescribed at the recommended intervals,
- An awareness of side-effects and potential interactions and how these may be avoided,
- How best to take antibiotics to ensure optimal bioavailability, e.g. before, with or after food.[8]

Where community pharmacists are licensed to prescribe and dispense antibiotics as primary care drug therapy (PCDT) permit holders[1] as enacted in section 22A (15) of the Medicines and Related Substances Act, it is imperative that the community pharmacists does so on the comprehensive knowledge of antibiotic susceptibility patterns of common causative bacteria implicated in different infections. Such susceptibility patterns should be ideally determined by local, regional or national surveillance of antibiotic use and resistance and form the evidence base for empirical treatment guidelines. Noting that antibiotic stewardship is not covered as comprehensively as it should be in the vast majority of medical and pharmacy curricula globally, it is imperative that community pharmacists actively pursue continuous professional development in this area, a pre-requisite for the PCDT permit.

From a public health perspective, the community pharmacist has a role in:

- Health promotion by encouraging vaccination for influenza , particularly during winter months when URTIs are common,
- Health education campaigns focused on the importance of conserving antibiotics in the face of escalating resistance amongst both prescribers and patients,
- Infection prevention and control by education on hygiene and sanitation,[10]
- Upholding regulations related to dispensing antibiotics only on prescription and ensuring that antibiotics are not sold over-the-counter,
- Actively discouraging self-medication and storage of antibiotics by patients,[10] and,
- The correct disposal of unused antibiotics.[8]

1.2 The Hospital and Community Pharmacist

Antibiotic stewardship is clearly within the purview of the hospital pharmacist ideally as a core member of an antibiotic stewardship team. Similarly, the community pharmacist has a crucial role in the multidisciplinary healthcare team in influencing strategies for AMR. Although the discussion that follows has been proposed by the American Society of Health-System Pharmacists[7] for hospital pharmacists, similar responsibilities apply to the community pharmacist. The roles and responsibilities of the hospital pharmacist as mooted by the American Society of Health-System Pharmacists[7] may take the form of *inter alia*:

- Prospective monitoring and evaluation of antibiotic prescriptions together with direct intervention and feedback to reduce inappropriate use and modify prescribing practice.
- Participating and encouraging multidisciplinary collaboration within the health establishment to ensure that the prophylactic, empirical, and therapeutic uses of antimicrobial agents result in optimal patient outcomes. These activities may include aiding in appropriate selection, optimal dosing, rapid initiation, appropriate administration and duration, proper monitoring, and de-escalation of antimicrobial therapies as well as the development of restricted antimicrobial-use procedures, therapeutic interchange (e.g., intravenous-to-oral dosage form switch), treatment guidelines, and pharmaceutical care plans
- Limiting the use of certain antibiotics to specific indications, durations of therapy, specialties, prescribers, infections or patient populations based on hospital susceptibility patterns and/or patient safety issues by formulary restriction and/or pre-authorization. Prescription of antibiotics on the pre-authorization list engenders consultation and collaboration between the hospital pharmacist and other specialists in the interests of optimal antibiotic therapy.

[1] http://www.mm3admin.co.za/documents/docmanager/0C43CA52-121E-4F58-B8F6-81F656F2FD17/00088611.pdf

- Education on rational antibiotic use, which is the most common intervention in antibiotic stewardship but rarely elicits substantive change in use or prescribing practice on its own. Education is thus recommended in combination with other interventions.
- Expert pharmacy-related input into empirical treatment guidelines and algorithms on the basis of continuous surveillance of antibiotic use and resistance at hospital level. Such guidelines should be periodically reviewed and updated and they generally reduce wide variations in prescribing. This may include working within the Pharmaceutical and Therapeutics Committee (or equivalent) structure, to ensure that the number and types of antimicrobial agents available are appropriate for the patient population served. Such decisions should be based on the needs of specific patient populations, microbiological trends and the essential medicine list within the health establishment and province. High priority should be given to developing antimicrobial-use policies that result in optimal therapeutic outcomes while minimising the risk of the emergence of resistant strains of microorganisms.
- Antibiotic cycling where a specific antibiotic class or agent is scheduled for substitution with another to reduce selection pressure and minimize resistance by diversifying use.
- Implementation of antibiotic order forms with automatic stop orders or justification of antibiotic prescription allow a review of indication, choice, dose and duration and ensure compliance with guidelines.
- Combination therapy where two antibiotics with different mechanisms of action are prescribed to ensure the eradication of infection by broadening the spectrum of coverage. This should however be limited to special patient cohorts as there is insufficient, often conflicting data on whether combination therapy improves clinical outcome or reduces resistance.
- De-escalation of therapy where inappropriate or redundant empiric therapy is discontinued on the basis on culture and susceptibility testing thereby reducing antibiotic exposure, selection of resistant pathogens and healthcare costs. This can take the form of stopping therapy or switching to a narrower spectrum agent active against the bacterial pathogen identified.
- Dose optimization involves dose adjustments after due consideration of patient characteristics (age, weight and renal function etc.), the causative organism, the site of infection (bone, soft tissue etc.) and antibiotic pharmacokinetics and pharmacodynamics.
- Parenteral to oral conversion that reduces length of hospital stay when the bioavailability profile of the antibiotic so allows.[7]

The hospital pharmacist's expertise is essential to the initiation and continuation of therapy as well as surgical prophylaxis. The hospital pharmacist advises on and documents the clinical rationale for initiating antibiotic therapy, ensures that specimens are collected for microbiological evaluations and informs the selection of antibiotics according to local antibiotic policies. The hospital pharmacist further monitors antibiotic therapy daily to facilitate decision making related to discontinuation, de-escalation or parenteral to oral conversion on the basis of patient progress and laboratory results.[7] Ideally, pharmacists should be working with the microbiology, laboratory and infection control personnel to ensure that appropriate microbial susceptibility tests are reported on individual patients in a timely manner, and collaborating with the laboratory, infectious diseases specialists, and infection prevention and control practitioners in compiling susceptibility reports (at least annually) for distribution to prescribers within the health establishment to guide empirical therapy.

The role of the hospital pharmacist in surgical prophylaxis encompasses selection of the appropriate regimen based on local guidelines, ensuring administration of the first dose before incision as contained in the guideline and discontinuing therapy within the duration defined by the guideline.[7]

Documentation of the above stewardship interventions together with analyses of antibiotic use, viz., use in daily-defined doses (DDD), expenditure on antibiotics and antibiotic point prevalence surveys

allows the hospital pharmacist to correlate stewardship interventions with improvements in clinical outcome and rational prescribing as well as reduction in resistance and expenditure.[11]

Pharmacists should participate in efforts to prevent or reduce the transmission of infections among patients, health care workers, and others within the health establishment's practice settings by:

1. Participating in the infection prevention and control committee (or its equivalent).

2. Ensuring the availability of cleaning agents and personal protective equipment for effective prevention and control practices to be implemented by staff.

3. Establishing internal pharmacy policies, procedures, and quality-control programmes to prevent contamination of pharmaceutical products prepared in or dispensed by the pharmacy department. This is of paramount importance in the preparation and handling of sterile products. Other considerations include (but are not limited to) provisions for cleaning pharmaceutical equipment (e.g. laminar-airflow hoods and bulk compounding equipment) and establishment of appropriate personnel policies (e.g., limiting the activities of staff members who exhibit symptoms of a viral respiratory illness or other infectious condition).

4. Encouraging the use of single-dose packages of sterile drug products rather than multiple-dose containers, except in sterile environments.

5. Recommending proper labelling, dating, and storage of sterile products and multiple-dose sterile-product containers (if used).

6. Supporting the infection prevention and control practitioners and clinicians to strive for zero tolerance of health care-associated infections, including surgical site infections, catheter-associated bloodstream infections, catheter-associated urinary tract infections, and ventilator-associated pneumonia.

2. CONCLUSION

The pharmacist has immense capacity to contribute to the conservation of dwindling antibiotic resources by virtue of their education and training. Hospital and community pharmacists should actively mobilize and entrench their leadership roles in the prevention and containment of antibiotic resistance both individually and collectively through pharmacy associations, organizations and regulatory bodies in policy and practice domains.

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