RATIONAL USE OF ANTIBIOTICS AND THE IMPORTANCE OF PHARMACISTS' SUPPORT

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ABSTRACT

There has been a growing concern related to increased antimicrobial resistance (AMR) caused by inappropriate and extensive use of antibiotics around the world. There are many factors contributing to this negative trend such as poor awareness and inadequate resources, inappropriate prescribing, uncontrolled dissemination, etc. The COVID-19 pandemic only made it worse, introducing overuse of antibiotics to prevent superinfections. And again, the pandemic is where the antimicrobial stewardship programs came to light, leading to increased focus on infection prevention rather than control with antibiotics. Pharmacists are more and more trying to control AMR. They have a significant role in coordinating their efforts with both doctors and patients in order to lower the rate of prescription checks, drugs for minor sickness, over-the-counter (OTC) issuance of drugs, overdosing, repetitive prescription usage as well as discarding antibiotics.

The article concludes that the support from pharmacists for the rational use of antibiotics is essential for the achievement of better treatment.

Keywords: *support, pharmacist, rational drug use, antibiotics*

INTRODUCTION

Currently antibiotics are used widely worldwide for treating different infectious diseases. And as good and effective as they are, at some point, the bacteria against which they are used can develop tolerance and become resistant by changing their enzymes and cell wall components. This change is caused by certain DNA in bacteria called plasmid, which can transfer genes to the progeny during reproduction, leading to resistance in the new bacteria (1).

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With time this resistance to antibiotics renders them ineffective in treatment, which causes great concern. A good example of this is the *Salmonella typhi* strain which is resistant to most antibiotics except for azithromycin. However, after using azithromycin, the bacteria become resistant to it as well (2). This is a problem for patients who have already used this drug at some point in their life, because in case of contracting typhoid, they could not be treated with this antibiotic.

Resistant mechanisms are already well known, but there are still limitations in technology and production techniques for drugs to be developed to combat diseases and, in addition to that, newly developed drugs would become useless after certain time of meeting evolving bacteria, which will once again adapt and become resistant to new antibiotics. It seems that at this point we are not able to control these resistance mechanisms (3). The only way to do

that is by limiting the use of antibiotics around the world.

The past several decades mark an extensive use of antibiotics globally either by self-medication or inadequate healthcare policies, and mostly due to poor awareness and education on its effect on personal health. In order to survive, humanity needs to address and combat this problem. Otherwise, a different analysis predicts more than ten million deaths by 2050 caused by antibiotic resistance (1).

Finding a solution to this problem is not easy but it is necessary and it could start with policymaking, creating awareness, and limiting antibiotic prescribing. Key part of this process is training pharmacists on new guidelines and better working tactics as they are primarily involved in the preparation and dispensing of drugs.

AIM

The aim of this article is to present opportunities for pharmacists to contribute to the rational use of antibiotics.

MATERIALS AND METHODS

For the period January 2022–June 2022, in the available databases (PubMed, BioMedCentral, ScienceDirect, Scopus, Web of Science), a systematic analysis of scientific publications examining the rational use of antibiotics and the importance of the support from pharmacists was performed.

RESULTS

Factors Affecting Resistance

The opportunity to eradicate infections by medicinal products and their antimicrobial properties is among the greatest accomplishments of modern medicine. However, their mass usage is now causing resistance in microorganisms causing hospital- and community-acquired infections (4). If the trend continues, it will result in increased levels of morbidity and mortality as well as higher healthcare expenditures (5). Unfortunately, we are still not competent enough to develop new antibiotics and eradicate this resistance mechanism (6). And this mechanism only thrives because of extensive use of these drugs around the world. Different studies performed in and outside of Europe show that 40% of antibiotic prescriptions are inaccurate and again related to self-medication or unnecessary misuse of antibiotics for the treatment of conditions like common cold or sore throat in which these kinds of medicnes are useless (7,8). Self-medication is mostly related to poor awareness or trying to avoid healthcare expenses. Studies show that many people tend to consume leftover medicinal products and there are also issues with abnormal prescribing and sales of antibiotics in some European countries (7,9,10,11).

We cannot expect to overcome this obstacle by ourselves locally. There is a strong need for a new approach to antibiotics to be adopted on a multinational level.

COVID-19 and Antibiotics

Autopsy studies of most COVID-19 deaths report superinfection. In an effort to avoid superinfections in patients, the COVID-19 pandemic triggered the vast usage of antibiotics. Doctors usually put the patients on broad-spectrum drugs for empirical therapy with synergistic antibiotics which leads to increased levels of antimicrobial resistance (AMR). Some countries with poor economic conditions lack the opportunity of cheap and fast tests to differentiate bacterial from viral infections. This increasing issue created awareness around the antimicrobial stewardship programs leading to more concern and efforts in prevention and control of infectious diseases rather than combating them with drugs. This approach has the potential to bring the necessary change and first results are already showing but it needs to also be adopted in underdeveloped and developing countries. These countries are usually resource-limited and AMR eradication can only be achieved by controlling the spread rather than curing the disease. The COVID-19 pandemic showed us that there are no borders for pathogens. That is why we need to conduct studies to understand the global development of AMR. This is especially important for developing countries where the conditions for infectious spread are prime while the health resources are suboptimal and data resistance is scarce (12).

Optimizing the antibiotic use is among the main means to reduce AMR. The standard guidelines of antimicrobial stewardship programs state that the way to do this is by administering the standard recommended antimicrobial with the appropriate dosage for the correct time and in the form that

allows its maximum efficacy and least side effects and resistance (13). However, ever since the pandemic started, the concern among scientists and physicians about the potential rise in AMR sequelae due to increased antibiotics intake from patients with COVID-19 has been growing (14).

An estimation shows that by 2050 the increase in AMR would cause the death of more than 10 million people, costing a hundred trillion dollars to healthcare systems (15).

The utilization of antibiotics in drugstores and pharmacies is usually done by both expert and inadequate staff from different areas. As long as administrative and economic conditions are different in separate countries, the same goes for the monetary motivators of this staff. Presented with certain monetary motivators, these experts can initiate demand for antibiotics by recommending their further use (16). According to the legislation in the Republic of Bulgaria, drugstores cannot fill and/or dispense medicinal products which are with doctor's prescription.

Communities are usually looking up to their pharmacists for advice, **which turns these pharmacists into key players in the process of reducing the risk of AMR** (17). The pharmacist usually has the initial and final contact with the patient during the patient's treatment process (18).

There are countries and companies with advanced techniques for and guidance on AMR (19,20). But the majority of the associated policy documents no longer consist of steerage at the role of pharmacists and pharmacies or accomplish that to a very restrained extent.

The report additionally maps the role of the pharmacist defined inside the Good Pharmaceutical Practice (GPP) guidelines at both international and US levels and describes potential AMR-associated motion or policy alternatives that countries can also bear in mind when promoting the prudent use of antibiotics.

A recent report describes the need to create a top-level view of the roles and activities of pharmacists, community pharmacies, and pharmaceutical system and the way they could contribute to the right use of antibiotics (21).

In order to control AMR, a pharmacist should follow certain guidelines:

- give legitimate guiding and suitable composing data while apportioning antimicrobials (22,25);
- motivate patients to stick to the recommended treatment routine and discard any unnecessary use of antibiotics;
- work closely with prescribers in order to make sure that measurements are adequate for the duration or continuation of a course of treatment;
- suggest treatments other than antibiotics for minor sicknesses;
- give actual data on antibiotics to prescribers;
- deal with issues related to cleanliness and contamination control;
- screening the stock and utilization of antibiotics by patients.

Table 1. Problems pharmacists can prevent and eliminate.

It is in the pharmacist's hands to assist in preventing and eradicating common problems by:
1. *not giving antibiotics without a prescription;*
2. *stopping the use of repeat prescriptions for antibiotics;*
3. *implementing regulations applicable to unauthorized drug allotting;*
4. *developing appropriate guidelines;*
5. *adjusting quantity disbursed vs. amount prescribed;*
6. *coping with used antibiotics;*
7. *participating in campaigns on behavior attention on the use of antibiotics;*
8. *offering records (pharmacist to affected person) on antibiotics; AMR and AMR-associated problems;*
9. *taking classes in AMR and AMR-associated problems;*
10. *cooperating with prescribing physicians;*
11. *providing antibiotic stewardship in point-of-care settings.*

Among other duties of the pharmacist should be to urge local authorities to act on the different procedures related to antibiotic supply and dissemination. For example:

- create and execute measures for the proper utilization of antibiotics and deny their distribution, sale or supply without a prescription or request from certified medical professionals;
- reinforce control of approvals to advertising, import, trade, recommendation, distribution and supply of antibiotics and make the necessary updates to current rules and guidelines;
- guarantee the utilization of the main approved channels of circulation to limit fake and unacceptable drugs and thus guarantee that the available antibiotics meet the guidelines;
- pay attention to the danger of the disruption of the medication compliance caused by irrational drug use;
- lead wellbeing instruction activities for suitable antibiotic use;
- create instructions that will help prescribers stick to the recommendations.

In order to optimize the use of antibiotics, it is critically important for countries around the world to reevaluate and, if needed, to improve the current role of pharmacists, incl. the ones who work at clinics and hospitals, as the primary supplier and regulator of these drugs.

Survey responses from 44 countries show that the provision of antibiotics is regulated to a maximum extent in countrywide contexts in Europe (23). In several countries, access to antibiotics without a prescription is feasible in emergency conditions. The guidelines in others allow for a higher amount of over-the-counter (OTC) sales. The majority of nations have implemented pharmacy-stage activities or initiatives to foster the prudent use of antibiotics, which include educational campaigns and the improvement of suggestions for customers. Moreover, even as the role and effect of the pharmacist vary, the majority of respondents are of the opinion that pharmacists are in the position to help fight AMR given their role as a mediator between the healthcare system and the affected person. At the same time, it is reported that the doctor's role vis-à-vis antibiotic guidance, in partnership with pharmacists, can be reinforced (22). When discussing the specific function of the pharmacist, the document looks at the survey results in detail and relates those related to the four pharmacist roles defined within the joint FIP/WHO suggestions on GPP (the GPP guidelines) (23). More antibiotic stewardship and a strengthening of the clinical and pharmacy curricula have been recognized as critical considerations for the future. The record affords some issues, which policy-makers may additionally desire to keep in mind with the intention of strengthening their efforts to tackle AMR, such as enhancing the prudent use of antibiotics. In this regard, the role of the pharmacist is seen as a key one, and collaboration between pharmacists and prescribers is essential (22).

The pharmacy plays a role in the development of antimicrobial stewardship (AMS), evaluation, and introduction of AMS guidelines and rules; clinical monitoring to optimize antimicrobial prescribing and use; tracking, audit, and comments; training and schooling of healthcare specialists, patients, and the general population; development and establishment of virtual AMS platforms, which include digital prescribing, e-learning, and mobile applications; there is a possibility to increase pharmacy roles, with appropriate incorporation, and infrastructural assistance being provided (24).

Seven key regions for action are mentioned, such as:

- contamination prevention and control;
- antimicrobial prescribing;
- training of medical professionals and the general population;
- discovery and improvement of recent drugs, remedies, and diagnostics;
- better access to and use of surveillance information;
- research;
- increased collaboration.

Pharmacy experts can also take part in developing, reviewing, and enforcing AMS rules and guidelines, have advisory roles, and be part of the training of other healthcare experts, as well as provide information to patients, and most of the people (25). It is possible that these roles have not been developed to their full potential yet; in addition, integration of pharmacy teams and infrastructural guide

(e.g., investment) are recommended as vital measures to enhance effective results (26,27). The levels of antimicrobial prescribing and use vary substantially throughout the globe, at national and international level, and within exclusive healthcare sectors or organizations; degrees might also depend on the individual practitioner's prescribing experience (28,29). A predicted 6% growth in general antibiotic prescribing in England became pronounced between 2010 and 2013, with a 12% growth in inpatient clinics (30). However, proof shows that different prescribing and monitoring systems are being adopted, making it challenging to compare and evaluate ranges of AMR, antibiotic prescribing and use.

Key Strategies in Secondary and Tertiary Care

Execution of AMS is fundamental, which can assist with advanced antimicrobial treatment and work on understanding results while diminishing the weight of nosocomial infections, the spread of AMR, and ensuing medical care costs (30).

In 2011, a public electronic survey involving antimicrobial drug specialists and chief drug specialists from 153 intensive care units in England was conducted (n=120; 78% response rate). All who participated in the survey declared having at least one expert antimicrobial drug specialist, with 35% having at least two such professionals; 16% of these specialists were full-time employees. Compared to a previous study, in 2005, the overall number of specialist antimicrobial pharmacists, as well as their level of experience, had increased. Over 95% of hospitals provided empirical usage guidance, antimicrobial formularies and surgical prophylaxis guidelines. Two-thirds of pharmacy departments provided antimicrobial usage reports in terms of defined daily doses at least yearly, and over 80% conducted yearly antimicrobial point prevalence studies. The vast majority of pharmacy departments indicated willingness to supply data and audit results to a national database for benchmarking purposes (27).

In 2007, another antimicrobial care pack—the gathering of key components of care to provide a methodical strategy for improvement and screening the provision of care measures—was proposed as an action to improve the treatment and prophylaxis of antimicrobial resistance (31,32). Similarly, as with other consideration packages effectively executed around that time, various key suggestions were proposed, including proper example assortment and introductory antimicrobial choice, followed by an everyday survey for increasing intravenous-to-oral switch, or halting the antibiotic as required (31). The pharmacy's commitment to the plan, improvement, and execution of antimicrobial consideration packs has been documented beforehand (33,34).

In accordance with these underlying suggestions, the evidence-based toolkit ‚Start Smart—Then Focus' was distributed in 2011 by Public Health England (updated in 2015) (34). Explicitly intended for use in optional consideration, the toolkit incorporates proposals from NICE and other important proof to help prevent and control antimicrobial resistance (35). Proposals incorporate an evidence-based decision on the administering an antimicrobial (narrow-spectrum, sooner rather than later) at the start of the treatment, followed by an intermediate stage survey at 48 hours, and treatment adjustment once the results are reviewed by the relevant specialist. Five choices would then be available, including: ***stopping*** the treatment in case of no proof of infection; ***change*** from intravenous to oral; ***changing*** the antimicrobial (ideally to a narrow-spectrum one, or to one with broader spectrum if needed); ***proceed*** with the treatment with an audit at 72 hours; or ***outpatient parenteral antimicrobial treatment*** (35).

Toolkits can be handy aids to good antimicrobial stewardship. But none of them can take the place of fearless introspection, feedback seeking, and committed efforts to behavioral change for greater effectiveness and increased positive impact on medical professionals.

The participation of pharmacy experts in essential and local area care (for example, nursing homes) can be instrumental, attributable to their drug aptitude along with the provision of help, openness, and active outreach. The role of local area pharmacy administrations as the main place of call for patient guidance has been specially promoted in the last years (21).

The hospital pharmacy is the centerpiece of multidisciplinary AMS groups. As of now, the majority of hospitals that have antimicrobial administration or stewardship groups frequently incorporate at least one antimicrobial pharmacist (19).

DISCUSSION

Governments, healthcare institutions, individual medical care providers, and patients all have a responsibility to promote the rational use of medicines.

It is evident from the aforementioned that rational use of antibiotics is an important current issue, affecting the common professional aspects of the pharmacist profession.

Irrational use of medicines continues to be a serious and widespread public health problem. However, the rational drug use for all medical conditions is fundamental to ensuring universal access to adequate health care, and satisfaction of health-related needs. Therefore, it is crucial that measures be taken to improve the rational use of medicines.

CONCLUSION

The support from pharmacists for the rational use of antibiotics is essential for the achievement of better treatment. Some future steps need to be taken:

1. maintaining better collaboration between pharmacists and medical doctors;
2. inclusion of a pharmacist in the creation and execution of every local and national AMR plan;
3. participation of pharmacists in the establishment of essential medicines (especially antibiotics) lists based on treatments of choice in hospitals;
4. launching guidelines and recommendations for prescribing at the different levels of the healthcare system;
5. dissemination of good practices and activities for their implementation;
6. affirmation of the community pharmacists' role and importance in all the strategies for fighting AMR, thereby making it visible to health authorities, other healthcare workers, and professional medical organizations;
7. raised efforts to fight illegal drugstores (pharmacies) operating online and the illegitimate trade of pharmaceuticals on the black market, in stores, or from other outlets.

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