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An Overview Of Preventing Measures Toward Antibiotic Resistance, Pharmacist's Role

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Abstract

Antimicrobial stewardship (AMS) teams around the world include pharmacists, and their impact on this is unclear, therefore we aimed by this review to emphasizes their roles. We have conducted a search through electronic databases; Medline and Embase, for all relevant studies related to our topic which was published till the middle of 2022.

As antibiotic and vaccine regimens become more complex due to the continuously evolving epidemiology of infectious illnesses, the pharmacist's involvement in battling and preventing infectious diseases is vital. The decline in medication development makes the preservation of already existing antibiotics of utmost importance, emphasizing the roles of pharmacists in optimizing the effectiveness of available treatments. While further training in infectious diseases may be required for certain pharmacist roles in preventing antibiotic resistance, there are numerous others that all pharmacists can assume.

Keywords: *Antimicrobial stewardship (AMS), antibiotic resistance, pharmacists.*

Introduction

Abuse of antimicrobials can enhance the proliferation of bacteria strains with resistance. 3 Antibiotic abuse and rising antimicrobial resistance (AMR) have rendered the treatment of common infections ineffective; therefore, a range of solutions are required to combat this developing problem [1]. For instance, 81 percent of antibiotics in England are prescribed in a primary care context and are more likely to proceed during the COVID-19 epidemic due to the remote overprescribing of broad-spectrum antibiotics. The amended antibiotic stewardship policy of the United Kingdom aimed to fundamentally alter the role of primary care dispensing [2]. Slowing the evolution of resistance in individual patients remains a problem, in part because clinicians must balance the most effective treatment for the current

infection with reducing their long-term effects. The development of antibiotic- resistant organisms in a patient may follow any of three distinct routes, each of which necessitates a particular strategy to antibiotic management (Figure 1): I resistance may arise de novo due to mutation, recombination, or horizontal gene transfer, (ii) antibiotic-resistant organisms can be transmitted from one patient to another, and (iii) an antibiotic-resistant organism may be present in the patient's microbial community without contributing to the current clinical infection [3].

Antibiotic stewardship programs (ASPs) supervised by pharmacists have proliferated significantly during the past decade. The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America developed a guideline for the formation of ASPs stating that an infectious diseases-trained clinical pharmacist is an important core member [4]. As resistance has developed and antibiotic research has slowed, antimicrobial peptides (ASPs) have become crucial for improving therapeutic outcomes, preventing resistance, and reducing side effects such as Clostridium difficile infections [5]. ASPs come in a variety of forms, but they all use a team-based approach to optimize antibiotic consumption through interventions on individual patients, guideline creation, and system-wide improvement. ASPs may be administered through a variety of modalities, and pharmacists are typically the essential personnel members following patients and intervening as needed. Some of these therapies necessitate an in- depth understanding of infectious diseases, while others fall within the realm of routine pharmacy practice. For instance, it has been found that vancomycin dose in obese patients may be inadequate [6]. Since it has been shown that inadequate vancomycin administration is connected with the propagation of resistance in Staphylococcus aureus, nonspecialist pharmacists have an opportunity to act [7]. Those pharmacists who have a thorough understanding of diagnostic tests or antibiotic pharmacokinetics and pharmacodynamics [8,9] may apply more advanced antibiotic selection or dose optimization approaches. Each intervention provides an opportunity to offer the prescriber with feedback and education, which is essential to the continuation of a stewardship program and further encourages the improvement of antibiotic usage. In addition, pharmacists typically gather and submit data regarding treatments and antibiotic-use patterns to hospital committees in order to evaluate the program's efficacy, identify areas for improvement, and obtain continued support for stewardship [10].

DISCUSSION:

Initial clinical deterioration of the patient demanded broad-spectrum therapy with vancomycin, aztreonam, and metronidazole, which eradicated drug-susceptible microorganisms, including several in non-target regions, such as the gastrointestinal system. When sub-clinical quantities of an antibiotic-resistant bacterium are present in a patient's microbial population, the administration of antibiotics to which the organism is resistant will accelerate its spread by eliminating rivals [11].

In fact, L.casei, C. albicans, and E. gallinaceum exhibited intrinsic resistance to first broad-spectrum therapy while being classified as gut commensal bacteria with minimal pathogenicity [12]. In this instance, resistance cannot be prevented; instead, the focus should be on preventing the organisms from proliferating to clinically important numbers within the patient and minimizing the risk of transmission to others. Thus, the treatment must either be broad enough to cover these resistant organisms (and risk giving 'too much'; a challenging proposition given the existence of extensively resistant organisms) or be as narrow as possible to preserve the antibiotic-sensitive competitors (and risk giving 'too little'; antibiotic- sensitive bacteria may still cause harm to the patient and contribute to resistance via de novo evolution) [11].

Alternatively, if resistance is not already present in a patient, it may evolve de novo due to mutation, recombination, or horizontal gene transfer. In diseases, such as HIV and tuberculosis, in which de novo mutations pose

the greatest threat to successful therapy, it is better to adhere to Ehrlich's advice:

"strike hard and early." This necessitates vigorous dosage, maybe with numerous medications, until the bacterial population is greatly reduced, hence decreasing the possibility of a resistance mutation occurring [13]. C.glabrata's resistance to micafungin within the first 20 days of a patient's hospitalization is the clearest evidence of de novo resistance development. Later, it was determined that the isolate had a point mutation in FKS2. This mutation has been detected nearly exclusively in patients with a history of exposure to echinocandin antifungals [14,15], and its emergence has been previously attributed to selective pressure.

Finally, a hospitalized patient may acquire resistant pathogens through hospital-to-patient or patient-to- patient transfer. VRE is included on the CDC's list of dangerous organisms [16]. The vancomycin resistance was conferred by the vanA gene cluster, was typically acquired through patient-to-patient transmission, and was detected in this hospital [17,18]. In this instance, VRE was not found by an early surveillance test performed upon the patient's admission to the ICU, but a second swab performed many weeks later was positive. Correctly done, the perirectal VRE monitoring swab has a sensitivity of >90% [19]. Although this does not rule out the potential that the patient's VRE levels were already low when she was admitted, it is more likely that her second positive swab indicates transmission from her environment. Antibiotic treatment against this pathogen can modify the likelihood of transmission by decreasing the recipient's colonization resistance through as-yet- unidentified mechanisms [20]. It is commonly believed that using antibiotics with a narrow spectrum best preserves the ability of the existing microbial community to resist competitors. However, even the use of antibiotics with a narrow spectrum can facilitate the acquisition of an organism with extensive drug resistance [18,20].

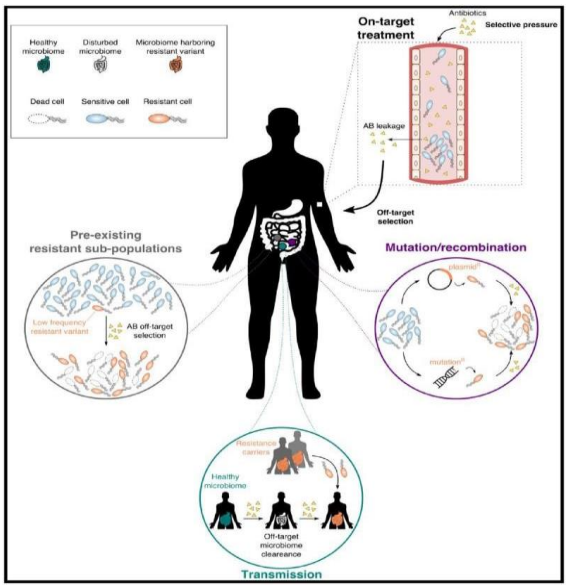

Fig. 1: Evolutionary processes driving antibiotic resistance.

The National Health and Family Planning Commission (NHFPC, formerly the Ministry of Health) of the People's Republic of China issued the first Guidelines for the Clinical Use of Antibiotics (Guidelines) in 2004, describing the characteristics of all types of antibiotics and their appropriate use in the treatment and prevention of infectious diseases; the Guidelines were updated in 2015. Unfortunately, not all medical personnel were aware of the Guidelines or their significance. AMR is currently one of the biggest risks to world health. There are four primary causes that contribute to the spread of AMR: improper use of antibiotics in the community and hospitals, overuse of antibiotics in animal production and agriculture, and the presence of resistant bacteria in the environment. The previous three criteria could exacerbate the last one [21]. Chinese Ministry of Health National Antibacterial Resistance Surveillance Net data revealed that AMR has been continuously increasing year [22].

In 2001, the World Health Organization (WHO) began implementing steps to address the development of AMR and urged nations to undertake antimicrobial stewardship (AMS) [23]. In 2011, AMR was also selected as the theme for World Health Day. In 2011, in response to AMR, the NHFPC of China proposed "National Special Stewardship in the Clinical Use of Antibiotics," the toughest

management of antibiotics in history. To encourage rational antibiotic use and reduce AMR, the NHFPC established numerous goals for the clinical use of antibiotics, including the restriction of antibiotic usage in outpatients and inpatients and the restriction of antibiotic prophylactic use in clean operations. These objectives are explained in full below. This special stewardship policy went into effect on 1 July 2011 and primarily impacted secondary and tertiary public hospitals. After that date, these hospitals were required to submit monthly reports to the government regarding their antibiotic use [24].

In recent years, several research revealed that AMS had positive benefits on decreasing antibiotic-resistant bacteria, rational antibiotic usage, and cost savings, underscoring the significance of AMS. There were additional studies that examined the link between antibiotic use and AMR, despite the fact that these all proved the efficacy of AMS; however, the studied population, drug, and pathogen are distinct, and the correlation results were not identical [25,26,27].

Programmed and administrative intervention:

The AMS committee established the stewardship activity program and published the following antibiotic use regulations: (1) categorization management system for antibiotics All antibiotics were categorized as either non-restricted, restricted, or special grade. Physicians with various professional titles were paired with the proper level of antibiotic prescribing privileges; (2) a system for managing antibiotic prescribing privileges. The NHFPC approved the Regulations on Clinical Applications of Antibiotics in May 2012, and they went into effect on August 1, 2012. These were China's first valid antibiotic restrictions [28,29]. The regulations stipulated that physicians were not permitted to prescribe antibiotics until they passed a test and received instruction on the prudent use of antibiotics. This prescribing privilege restriction was incorporated into the HIS; (3) regulation of perioperative prophylactic antibiotic usage in clean procedures, which detailed the choice of antibiotics, dose, timing of the starting dose, and length of antibiotic prophylaxis.

In accordance with the objectives of the national antibiotic stewardship program, the AMS group defined (Table 1) the hospital's antibiotic application goals [29].

Table 1: Goals of clinical antibiotic use established by the NHFPC in 2011

Antibiotic outcome measures	Goals
1. Proportion of inpatients receiving antibiotics	≤60%
2. Proportion of outpatients receiving antibiotics	≤20%
3. Intensity of inpatients' antibiotic consumption	≤40 DDD/100 bed-days
4. Proportion of antibiotic prophylaxis in patients receiving type Iincision operations/clean operations	≤30%
5. Timing of initial dose of preoperative antibiotic prophylaxis	Within 0.5–2 hours before surgical incision
6. Duration of antibiotic prophylaxis in patients receiving type Iincision operations/clean operations	Within 24 hours after the end of operation

DDD, defined daily dose; NHFPC, National Health and Family Planning Commission.

Antibiotic intake intensity was lowered to 37.38 DDD/100 bed-days. These results are comparable to those of Bao et al. [30] In type I incision procedures, the proportion of antibiotic prophylaxis reduced to 18.93%, whereas the proportion of rational timing of the initial dose climbed to 96. percent; For the following reasons, only the fraction of rational length of antibiotic prophylaxis (42,63%) did not meet the national standard: First, coronary artery bypass graft (CABG) surgery is classified as a type I incision procedure. According to the Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery, the length of prophylaxis for cardiothoracic surgeries is up to 48 hours, notwithstanding the lack of evidence to support this recommendation. The Chinese Guidelines recommend a maximum preventative duration of 48 hours. However, CABG involves vital viscera, where infection would have grave effects [31]. Therefore, physicians are hesitant to discontinue antibiotics within 48 hours of surgery. In orthopedic

procedures, such as open reduction and plate or screw internal fixation of fractures, clinicians hesitate to cease antibiotics within 24 hours following surgery due to the presence of implants. Thirdly, the challenging doctor-patient relationships in China discourage clinicians from discontinuing antibiotics prematurely [31].

The purpose of AMS is to reduce the incidence of AMR. The results indicated that the resistance rates of E. coli and P. aeruginosa to FQs and the incidence rate of MRSA showed declining trends and were positively connected with the intensity of FQ consumption. This suggested that limiting the use of FQs could reduce the prevalence of AMR as well as the emergence of MRSA, which is consistent with prior research [32,33]. According to other research, a reduction in the use of second-generation/third-generation cephalosporins and clindamycin contributed to a decrease in the incidence rate and prevalence density of MRSA bacteremia. The incidence rate of MRSA was adversely linked with the usage of imipenem/cilastatin, which was difficult to explain. To our knowledge, few research have produced comparable findings. Lai et al. [34] found a strong link between an increase in the use of linezolid and teicoplanin and a decline in the prevalence of MRSA. Consequently, we hypothesize that the decreased use of non-special grade antibiotics (such as FQs and others) results in a compensatory increase in the use of carbapenems; however, this negative correlation requires more investigation. In addition, we discovered that the resistance rate of E. coli and K. pneumoniae to carbapenems was on the rise, indicating that carbapenem-resistant Enterobacteriaceae (CRE) could pose a significant concern. The NHFPC issued a notice on 2 March 2017 requiring medical institutions to collect, archive, and analyze patient information pertaining to the use of carbapenems in an effort to control the prevalence of CRE [35]. The notice emphasized the need for further reinforcement in the management of clinical application of antibacterial to control bacterial resistance.

CONCLUSION:

Pharmacists have a duty to aid in the fight against antibiotic resistance. They are equipped with the knowledge and resources necessary to raise awareness and take action. Multiple chances exist for pharmacists to participate in this campaign. Infectious-diseases pharmacy practice has reached a milestone with the acknowledgement of pharmacists as crucial members of antibiotic stewardship teams in health systems. As first-line practitioners who can educate and immunize patients, community pharmacists play a crucial role in the fight against antibiotic resistance. The clinical course of the patient reveals all three paths to resistance and the therapeutic difficulty of balancing them. Her case is not exceptional in terms of the severity of the infection, the amount and length of antibiotics used, or its eventual outcome. Before prescribing antibiotics, practitioners would ideally be able to assess the probability of infection with a drug- resistant bacteria for each patient.

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