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Antimicrobial Stewardship Interventions: Narrative Review

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This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Antimicrobial resistance is a serious health concern with significant economic and clinical sequelae. Antimicrobial stewardship programs are increasingly being promoted and mandated in order to rationalize and reduce the use of antimicrobials in healthcare institutions and as a result decrease antimicrobial resistance. Several interventions could be used to improve antibiotic use that includes broad, pharmacy driven and infection and syndrome specific interventions. Each hospital should prioritize interventions based on its needs as well as based on the availability of resources and content expertise.

Keywords: Antibiotics use; antimicrobial use; antimicrobial resistance; antimicrobial stewardship programs; interventions.

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1. INTRODUCTION

Antimicrobial resistance (AMR) is a serious health concern with significant economic and clinical sequelae. The incidence of it is rapidly increasing around the world, and infections caused by organisms that are resistant to several antibiotics are associated with higher incidences of mortality, morbidity, and prolonged hospital admission [1]. The main driver of the emergence of antimicrobial resistance is the selective pressure of antimicrobial usage on microorganisms; therefore, considerable focus has been placed on ensuring the wise use of antimicrobials [2]. Not only does this have implications for the patient who is infected with multidrug resistant organisms, but also for the spread of these organisms in the community and in healthcare facilities at large [2]. Consequently, antimicrobial stewardship programs are increasingly being promoted and mandated in order to rationalize and reduce the use of antimicrobials in healthcare institutions [3].

Antimicrobial stewardship (AMS) is a systematic approach to ensure that the antimicrobial use is appropriate, it aims to optimize the treatment of infections, minimize the adverse effects associated with antibiotic use and reduce antimicrobial resistance, toxicity and costs [4,5]. Antimicrobial stewardship can have a positive impact the different facilities largely [6]. There are several elements of antimicrobial stewardship programs, including post prescription review, pre-prescription authorization, education of prescribers, regular ward rounds for review of antimicrobial use, and regular audits with feedback [3]. Antimicrobial pharmacists remain leaders for implementing the interventions of antimicrobial stewardship programs across both primary and secondary healthcare institutions [7].

Interventions to decrease the unsuitable antimicrobial prescribing can reduce antimicrobial resistance or healthcare-acquired infections, and interventions to increase effective prescribing are essential in improving patient safety clinical outcomes [8]. This review aims to describe the interventions of antimicrobial stewardship programs.

2. METHODS

This narrative review was included searching Pubmed databases for the key terms (antimicrobial stewardship interventions). The searching process was conducted on 02-Dec-2020 and included the published articles in the last 10 years. So, the studies that were published before 10 years and review articles were excluded from the study.

The searching results were limited to the articles that were published in the 10 years and also the searching was limited by choosing the articles that contain the key terms “antimicrobial stewardship interventions” in the title of the articles that were written in English. We also add other studies from the references of the included articles.

3. RESULTS AND DISCUSSION

The searching process resulted in a total of 34 articles and review articles. After excluding review articles; 26 studies were identified and included in our review. Other studies were added from the references of the included articles after ensuring that they were related to the study topic and that they were published in the last 10 years. Table 1 showed the included publications that were published before 2017 and Table 2 showed the included publications that were published after 2016.

3.1 Antimicrobial Stewardship Interventions

The Infectious Diseases Society of America recommends 2 core strategies for antimicrobial stewardship antimicrobial restriction/preauthorization and postprescription audit and review (PPR) with intervention and feedback [9,10]. Barlam et al. [10] and Davey et al. [8] stated that the primary goal of hospital antimicrobial stewardship programs is to improve patient care. Evidence-based strategies include individualized active interventions to positively impact decisions about antimicrobials and review of patient-specific clinical data and prescriber-targeted. Chavada et al. [11] stated that in addition to optimizing the duration of treatment, other practical interventions may also help to improve prescribing in this particular area such as prospective audit and feedback specifically for discharge antimicrobials, prescriber education, and the introduction of electronic prescribing and flagging. Pettit et al. [12].conducted a study about the use of Epic antimicrobial stewardship module which is Clinical Decision Support Tool and found that this module allowed us to significantly increase the number of antimicrobial reviews and interventions while maintaining a sustained impact on antimicrobial utilization.

Table 1. The included publications that were published before 2017

Publications	Year
Dellit et al.	2007
Scottish Intercollegiate Guidelines Network	2008
De Kraker ME et al.	2011
Holtzman et al.	2011
SNLG	2011
Shrestha et al.	2012
Patel et al.	2012
Vlek et al.	2012
Abdel-Aziz et al.	2013
Huang et al.	2013
Dellinger et al.	2013
Davey et al.	2013
The Centers for Disease Control and Prevention	2014
Hamilton and Fishman	2014
Reed et al.	2014
Gauthier et al.	2014
Cairns et al.	2015
Ashiru-Oredope et al.	2016
Barlam et al.	2016
Caplinger et al.	2016
Morton et al.	2016
Ashiru-Oredope et al.	2016
Cao et al.	2016
Pardo et al.	2016
Hersh et al.	2016
Turnidge et al.	2016

Table 2. The included publications that were published after 2016

Publications	Year
Sartelli et al.	2017
Badia et al.	2017
Schmitt et al.	2017
Goff et al.	2017
Berríos-Torres et al.	2017
Dilworth et al.	2017
Dumkow et al.	2017
Beganovic et al.	2017
Jones et al.	2017
Avdic et al.	2017
Bates et al.	2017
Chavada et al.	2018
Ruscelli et al.	2018
Gillespie et al.	2018
Patton et al.	2018
Flett et al.	2018
Pettit et al.	2018
Borek et al.	2019
Tang et al.	2019
Nguyen et al.	2019
Niwa et al.	2019
Hecker et al.	2019
Anderson et al.	2019
Stevens et al.	2020

Publications	Year
Jones et al.	2020
Staub et al.	2020
Atkins et al.	2020
Shallcross et al.	2020
Tiri et al.	2020
Society of Infectious Diseases Pharmacists	2021

Davey et al. [8] stated that interventions to reduce inappropriate antimicrobial prescribing can reduce healthcare-acquired infections or antimicrobial resistance. Moreover, interventions to increase effective prescribing are important in improving patient safety clinical outcomes. Previous studies suggested several strategies including a pharmacy-based triage algorithm for pneumonia, the implementation of an antimicrobial stewardship model following patients discharged on antimicrobial therapy with pending culture results and subsequent modification of antimicrobial therapy, a checklist framework for pediatric patients, and a mandatory Infectious Disease Consultation of intended community-based parenteral antimicrobial therapy [13–15].

Morton et al. [16] stated that antimicrobial stewardship interventions were organized into 11 categories including drug dose or duration optimization, antimicrobial discontinuation, vancomycin dosing, de-escalation of therapy, intravenous to oral switch, ordering of a pertinent Laboratory test for monitoring purposes, broadening of antimicrobial spectrum, therapeutic drug monitoring, Infectious Disease consultation, addressing a drug–drug interaction between an antimicrobial and another medication, or change in antimicrobial regimen due to reported allergic reaction. They also found that verbal communication is now the primary method of providing antimicrobial stewardship interventions at their facility and that stewardship practices may be improved by limiting the use of potentially less effective communication methods; this will lead to improving patient outcomes, potentially reducing inappropriate antimicrobial use, and decreasing resistance rates [17]. Stevens et al. [17] compared the acceptance rates of interventions communicated with a temporary note left in the electronic medical record versus those communicated telephonically and found that telephonic communication produced superior overall acceptance rates.

Borek et al. reported that the most promising and feasible antimicrobial stewardship interventions included multidisciplinary peer learning, quality improvement, auditing individual-level prescribing, appointing AMS leads, improving inductions for new prescribers, developing tools for prescribing audits, providing online AMS training to all patient-facing staff, increasing staff time available for AMS work with standardizing AMS-related roles, and ensuring consistent local approaches to antibiotic prescribing [18]. They also stated that these interventions could be developed as stand-alone interventions or incorporated into existing national interventions to optimize antibiotic prescribing in primary care in England [18]. Centers for Disease Control and Prevention said that stewardship interventions are listed in three categories below: broad, pharmacy-driven; and infection and syndrome specific [19].

3.1.1 Broad interventions

Broad interventions include several interventions such as prior authorization and prospective audit and feedback [19]. Some authors have reported some suggested actions from the European Centre for Disease Prevention and Control to increase compliance to the recommendations that include audit and feedback, shifting the responsibility of surgical antibiotic prophylaxis administration to the anesthesiologist, education and training, implementation of a multidisciplinary management team and implementation of standardized order form [11]. Tang et al. [20]. stated that the implementation of multidisciplinary, frontline provider-driven approaches to antimicrobial stewardship in addition to educational bundle may lead to reduced antibiotic use and length of hospital stay. Dellinger et al. [21] reported that education antibiotic stewardship programs should provide regular updates on antibiotic resistance, antibiotic prescribing, and infectious disease treatment that address both local and national. Patel et al. [22] and Gauthier et al. [23] stated that there are a variety of web-based educational resources such as CDC TRAIN Learning Network available that can help facilities develop education content

Nguyen et al. reported that the implemented interventions include prospective audit with feedback and intervention, provider education using educational sessions and pocket cards, and institutional guideline update [24]. They also support the call for antimicrobial stewardship programs to improve antibiotic use upon discharge and to reduce overall antimicrobial exposure [25]. Ashiru-Oredope et al. recommended numerous interventions which are the provision of an antimicrobial stewardship committee, the implementation of audits, a written education and training strategy, and a written dedicated antimicrobial policy [24].

Anderson et al. reported that post-prescription audit and review was a feasible and effective strategy for antimicrobial stewardship in settings with limited resources and expertise and that it led to more interventions, particularly de-escalation, which likely influenced overall antimicrobial use [26]. They also stated that these interventions led to more interactions between prescribers and pharmacists, providing additional opportunities to optimize antimicrobial therapy [26]. Atkins et al. reported that the majority of interventions in their study focused on education and training, which target knowledge and skills through the provision of instructions on how to perform a behavior and information about health consequences. Atkins et al study highlights the need to review existing interventions to ensure they are optimized to influence AMR-related behaviors [27].

3.1.2 Pharmacy-driven interventions

These interventions include automatic changes from intravenous to oral antibiotic therapy, dose adjustments, dose optimization, automatic alerts in situations where therapy might be unnecessarily duplicative, time-sensitive automatic stop orders for specified antibiotic prescriptions, especially antibiotics administered for surgical prophylaxis and detection and prevention of antibiotic-related drug-drug interactions [19]. Previous studies with pharmacist-led initiatives have shown an improvement in the overall appropriateness of antimicrobial therapy [28,29]. Chavada et al. envisage the introduction of several strategies such as training and upskilling of clinical pharmacists who already perform discharge medication reconciliation for antimicrobial therapy prescribed on hospital discharge [11].

Cao et al. conducted an institutional review of antimicrobial stewardship interventions and reported that the most frequent types of interventions were pharmacy-driven interventions and were related to inappropriate dosing (39.0%), antimicrobial selection (20.5%) and drug allergy (13.0%). They also stated that serious adverse drug events were potentially avoided in about 20.7% of all interventions and that the cumulative potential cost avoidance was more than US$6.5 million [30].

3.1.3 Infection and syndrome specific interventions

These interventions are implemented for specific infection and syndrome, such as interventions for community-acquired pneumonia, urinary tract infections, skin and soft tissue infections, surgical antibiotic prophylaxis, empiric coverage of methicillin-resistant staphylococcus aureus infections, clostridium difficile infections, and treatment of culture proven invasive infections.

One of the most common Infections and syndrome specific interventions are the interventions that are implemented to improve surgical antibiotic prophylaxis. Badia et al. reported that the appropriate usage of surgical antibiotic prophylaxis significantly decreases the risk of surgical site infections [31], while the inappropriate usage increases surgical site infections, multidrug-resistant strains, and hospital costs [32-34]. For this reason, international and national guidelines have been developed to guide clinicians in the optimal use of surgical antibiotic prophylaxis [35–37]. Tiri et al. stated that many guidelines about surgical antibiotic prophylaxis have been published, but the overall compliance remains poor [38]. They used educational audit intervention and found that this intervention improves appropriateness on surgical antibiotic prophylaxis [38].

Pardo et al. reported that the Blood Culture Identification, coupled with antimicrobial stewardship intervention, was a cost-effective tool to improve patient care [39]. Niwa et al. reported that Matrix-assisted laser desorption ionization-time of flight mass spectrometry combined with antimicrobial stewardship intervention facilitated early optimization of antimicrobial therapy with a remarkable concomitant reduction in adverse events and clinical failure in patients with bloodstream infections [40]. Bates et al. found that C-reactive protein point-of-care testing was effective in safely decreasing antibiotic use in patients with an acute exacerbation of chronic obstructive

pulmonary disease [41]. ISRCTN 11369832 study is investigating the effect of procalcitonin-guided management on the use of antibiotics in children with severe bacterial infection [42]. Hecker et al study conducted specific interventions on the use of and resistance to fluoroquinolones and found that Antimicrobial stewardship interventions focused on specific syndromes may be effective in decreasing the use of fluoroquinolone use. They also found that the reduction in fluoroquinolone use resulted in a decrease in the resistance of *P. aeruginosa* to fluoroquinolone [43].

Several studies also reported that rapid diagnostic tests such as fluorescence in situ hybridization using peptide nucleic acid probes, procalcitonin and matrix-assisted laser desorption/ionization time of flight mass spectrometric analysis have been effectively incorporated by some stewardship programs and may become essential additions to stewardship programs [44-47]. Reed et al. conducted a study regarding the use of antimicrobial stewardship interventions in the management of candidemia and found that the pharmacist interventions in antimicrobial stewardship programs standardized and improved the quality of care of candidemia patients [48]. Moreover, Jones et al stated that antimicrobial stewardship programs developed management pathways to monitor the use of potential COVID-19 therapies to confirm that the treatment is appropriate and to lessen toxicities and adverse events [49]. They also stated that their interventions served as a model for leveraging the collaborative relationship between antimicrobial stewardship programs and pharmacists during the pandemic of COVID-19 [49].

Avdic et al. found that the use of a real-time antimicrobial stewardship intervention implemented with the introduction of the Verigene Gram-Positive Blood Culture assay for patients with bacteraemia due to gram-positive cocci led to improvements in antibiotic therapy [50]. Patton et al. stated that despite the decreases in high-risk antimicrobials prescribing and decreases in clostridium difficile infection, establishing the real-world impact of antimicrobial stewardship interventions remains challenging [51]. Staub et al conducted a study about the effect of antimicrobial stewardship interventions in improving outpatient antibiotic prescriptions and said that the best strategy to implement effective antimicrobial stewardship interventions is targeting high prescribers [52]. Flett et al. found that antimicrobial stewardship interventions and spaced education decreased the redundant anaerobic therapy [53]. Beganovic et al confirmed that rapid identification with matrix-assisted laser desorption ionization–time of flight mass spectrometry combined with real-time antimicrobial stewardship intervention is more impactful than matrix-assisted laser desorption ionization–time of flight mass spectrometry alone [54]. Shallcross et al. prepared a protocol for preserving antibiotics through a safe stewardship research program and reported that this protocol aimed to develop evidence-based antibiotic stewardship interventions targeted to specific healthcare settings [55]. Dilworth et al. reported that the use of frontline pharmacists to improve compliance and quality of care components for Staphylococcus aureus bacteremia is impressive and meets the workflow needs of advanced antimicrobial stewardship programs [56].

4. CONCLUSION

Several interventions could be used to improve antibiotic use that can be divided into three categories: broad, pharmacy driven and infection and syndrome specific interventions. Each hospital should determine the appropriate interventions that it will implement and should prioritize interventions based on its needs as well as based on the availability of resources and content expertise. Centers for Disease Control and Prevention advised hospitals to avoid implementing too many policies and interventions at the same time [19].

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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