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Review of the Appropriateness of Surgical Antimicrobial Prophylaxis

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Authors' contributions

This work was carried out in collaboration among all authors. All authors including study design, statistical analysis, writing the protocol, writing the first draft of the manuscript, managing the analyses of the study, managing the literature searches. All authors read and approved the final manuscript

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Review Article

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ABSTRACT

Aim: This review aims to describe the appropriateness of surgical antimicrobial prophylaxis during the last decade.
Methodology: The review included a searching web of science for articles focused on "the appropriateness of surgical antimicrobial prophylaxis". The searching process was conducted on 29 Nov 2020 and included original articles so the review articles were excluded.
Results: The review included 57 articles; 38 articles were published after 2015 and the rest before 2015. Most of the articles that were included in the review showed a high rate of inappropriate surgical prophylaxis and showed inappropriate duration and time of the antibiotics used.
Conclusion: It can be concluded that the rate of surgical prophylaxis inappropriateness was high and the main cause for this result was inappropriate timing and duration. Numerous interventions including educational interventions such as one-time seminars and online e-learning modules are needed to improve the adherence to the guidelines.

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1. INTRODUCTION

Antimicrobial resistance is considered one of the worldwide threats for both economic development and human health [1]. Resistant microorganisms are the main causative agents of healthcare-associated infections (HAIs) in both high-income and low-income countries. The most reported and surveyed type of HAIs are surgical site infections (SSIs) and account for up to 20% of all hospital-acquired infections [2]. Surgical site infections are defined as postoperative infections that occur within 30 days from a surgical procedure or within 1 year from a permanent implant [3].

Once occurred, surgical site infections are associated with an increased risk of mortality. In addition, they are also connected to a prolonged hospital stay [1,4,5]. Moreover, SSIs cause an increase in healthcare costs that are driven by prolonged hospitalization, additional diagnostic tests, treatment, and re-operations [6]. The prevention of these infections is complex and requires the integration of a range of measures that should be implemented before, during, and after surgery [7]. Of note, 2016 guidelines by the World Health Organization (WHO) highlighted the risk of unnecessary prolongation of surgical antibiotic prophylaxis (SAP) in causing adverse events and developing antimicrobial resistance [7]. One way to minimize this risk is by the implementation of antimicrobial stewardship programs. Positive effects of antimicrobial stewardship interventions in low- and middle-income countries have been previously reported [8,9]. Measures for assessing the effectiveness of antimicrobial stewardship programs (ASPs) are either process measures such as change in antibiotic use, compliance with hospital-specific guidelines, or outcome measures. This review aims to describe the appropriateness of surgical antimicrobial prophylaxis during the last decade [10].

2. METHODOLOGY

The review included a searching web of science for articles focused on “the appropriateness of surgical antimicrobial prophylaxis”. The searching process was conducted on 29 Nov 2020 and included original articles so the review articles were excluded.

The searching process resulted in 86 articles about the topic. After that we limit the search to the last 10 years; 25 articles were excluded and 61 articles were included in the study. After that, we further limit the search to include human research only so another 4 articles were excluded. So, 57 articles were included in the present study. Furthermore, we add several articles that were cited by the included studies.

The inclusion criteria include original articles that were conducted in the last 10 years about the appropriateness of surgical antimicrobial prophylaxis and the exclusion criteria include review articles, articles that were conducted on animals and articles that were conducted before more than 10 years.

The flow diagram for a literature search is shown in Fig. 1. Moreover, the authors of these articles, the year of publications, and the name of the published journals are shown in Table 1 and Table 2.

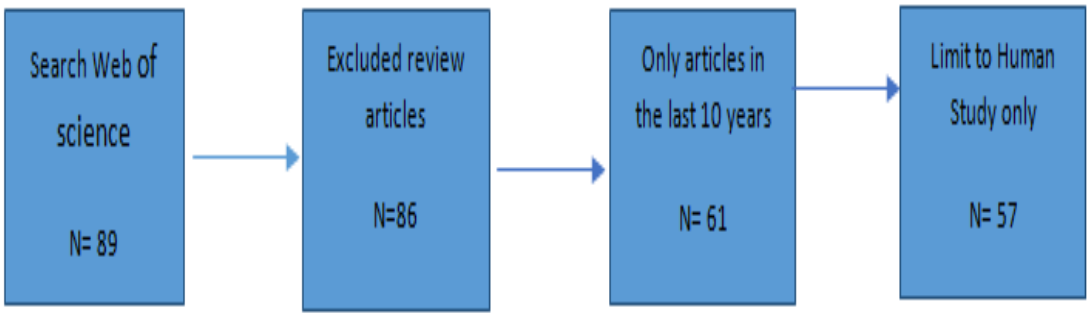

Fig. 1. Literature search flow diagram

3. RESULTS AND DISCUSSION

3.1 Appropriateness of Surgical Prophylaxis

The included studies were 1 discussion paper and 56 original articles. The review included 57 articles; 12 studies were published in 2020, 9 studies in 2019, 6 studies in 2018, 5 studies in 2017, 6 studies in 2016, 4 studies in 2015, 4 studies in 2014, 5 studies in 2013, 3 studies in 2012 and 2 studies were published in 2011.

Most of the articles that were included in the review showed a high rate of inappropriate surgical prophylaxis. Ierano et al. found that the antimicrobials for surgical prophylaxis were poorly prescribed in Australian hospitals with a low rate of the appropriateness of antimicrobials surgical prophylaxis prescription [11,12]. Segala et al. reported that the adherence to perioperative prophylaxis guidelines before the implementation of antimicrobial stewardship was only 36.6% and increased after their intervention [13]. Moreover, Anandalwar et al. reported that regarding the use of surgical antibiotic prophylaxis in general pediatric surgery, 44% of the cases received inappropriate prophylaxis, of which 42% were considered overtreatment and 58% were considered undertreatment [14]. Karaali et al. found that in the pre-intervention phase of their study, the rate at which all stages of surgical prophylaxis were adhered to was found to be low [15].

Osowicki et al. reported that among surgical patients, 65 of 187 antimicrobial prescriptions (35%) were deemed inappropriate and that the common reason for this was excessive prophylaxis duration [16]. Additionally, Cotta et al. found that the rate of the appropriateness of antimicrobials prescribed for surgical prophylaxis was 40.6% and that prolonged duration (>24 hours) was the main reason for inappropriate surgical prophylaxis prescriptions [17]. Gül et al stated that inappropriate antibiotic usage rates in surgical wards were high [18]. They also stated that the inappropriate usage was especially related to prophylaxis and that it is necessary for surgeons to be educated regarding prophylactic antibiotic usage and to stick to the surgical prophylaxis guidelines [18].

Abdel Jalil et al. reported that the overall compliance with the surgical anti microbial prophylaxis guidelines in cesarean deliveries was poor; nevertheless, certain components showed high compliance rates, such as indication and choice of antibiotics [19]. Kara et al. reported that the inappropriate antimicrobial usage rate was 57.1% in surgical wards [20]. Moreover, Degli Atti reported that regarding surgical antibiotic prophylaxis in children the overall appropriateness of antibiotic choice, timing, and duration was 8% [21].

Oshikoya et al. stated that among the 303 surgical pediatric patients, 97.7% received surgical antimicrobial prophylaxis and complete compliance was poor (5.6%) and that timing, re-dosing, and duration of antimicrobial use were the most violated [22]. Gil et al. found that the overall compliance to antibiotic prophylaxis protocol in breast surgery was very high and the low rate of non-compliance was caused mainly due to the inappropriate timing and inappropriate choice of antibiotic [23]. Alonso-García et al. reported that the antibiotic prophylaxis appropriateness was high in patients who underwent renal surgery with an overall compliance rate of 90.6% [24].

Deelen et al. reported that for most prescriptions there was a protocol about antimicrobial prophylaxis outside the operating theatre and that the adherence to the protocols was high [25]. Quattrocchi et al. found overall low compliance to perioperative antibiotic prophylaxis in 2 hospitals in Italy; mainly regarding antibiotic choice and the total duration of prophylaxis [26]. Conaty et al. stated that regarding surgical antimicrobial prophylaxis (SAP) prescribing in orthopedic surgery, the prescribing appropriateness was low (20%) but it was improved 78% after the implementation of their interventions [27]. Dimopoulou et al. found that the percentage of patients receiving appropriate perioperative antibiotic prophylaxis improved from 6.2% to 77.1% after the educational intervention [28]. Bozkurt et al. stated that both in 2011 and 2012, inappropriate antibiotic use was found to be significantly higher in surgical clinics in comparison to the internal diseases clinics and the ICU [29]. This was caused by the high rates of inappropriate perioperative antimicrobial prophylaxis observed in surgical clinics [29].

Abu-Gharbieh and Fahmy reported that the adherence to international antimicrobial prophylaxis guidelines for cardiac surgery was found to be suboptimal in the study hospital in Dubai [30]. Snyder et al. stated that a high

Table 1. The included studies that were published after 2016

Author	Year	Name of journal
Ierano et al.	2020	Infection disease & health
Segala et al.	2020	Antimicrobial resistance and infection control
Eisner et al.	2020	Surgical infections
Khan et al.	2020	Eastern mediterranean health journal
Karaali et al.	2020	Journal of infection in developing countries
Dona et al.	2020	Pathogens
Chautrakarn et al.	2020	Pediatrics international
Tiri et al.	2020	Antibiotics-basel
McMullan et al.	2020	Journal of antimicrobial chemotherapy
Kefale et al.	2020	Infection and drug resistance
Muhammed and Nasir	2020	Drug healthcare and patient safety
Anandalwar et al.	2020	Journal of pediatric surgery
Ierano et al.	2019	Jama network open
Karaali et al.	2019	Journal of infection in developing countries
Nicolas et al.	2019	Swiss medical weekly
Komagamine et al.	2019	Bmj open
Oshikoya et al.	2019	Journal of chemotherapy
Conesa et al.	2019	Anales del sistema sanitario de navarra
Arnoldo et al.	2019	Journal of hospital infection
Dona et al.	2019	Antimicrobial resistance and infection control
degli Atti et al.	2019	Annali di igiene medicina preventiva e di comunita
Alonso-Garcia et al.	2018	Actas urologicas espanolas
Abubakar et al.	2018	International journal of clinical pharmacy
Quattrocchi et al.	2018	Annali di igiene medicina preventiva e di comunita
Toba et al.	2018	Journal of obstetrics and gynaecology research
Broom et al.	2018	American journal of infection control
Conaty et al.	2018	International journal of health care quality assurance
Jalil et al.	2018	American journal of infection control
Pollmann et al.	2017	Canadian journal of surgery
degli Atti et al.	2017	European journal of clinical pharmacology
Giordano et al.	2017	Infection control and hospital epidemiology
Zivanovic et al.	2017	Plos one
Deelen et al.	2017	Bmc infectious diseases

percentage of inappropriateness in antibiotic use in outpatient hemodialysis units including antimicrobial surgical prophylaxis [31]. Simon et al. reported that the overall compliance rate to guidelines for surgical antimicrobial prophylaxis was 37% [32]. Khan et al. found poor treatment adherence to antibiotic prophylaxis guidelines due to poor awareness, underestimation of infection, lack of consensus, and disagreement with guideline recommendations [33]. Karaali et al. stated that the total rate of surgeons' compliance with ASHP guidelines was only 26.8% [34]. They found also that inappropriate use of antimicrobial for surgical prophylaxis is widespread and that antibiotics continue to be prescribed at discharge [34].

McMullan et al. stated that surgical prophylaxis was inappropriate in 59% of prescriptions [35]. Dona et al. found that the appropriateness of antimicrobial prophylaxis was low 48.9 % but it was increased in the post-intervention period from 48.9% to 60.0% [36]. Napolitano et al. stated that perioperative antibiotic prophylaxis was appropriate in 18.1% of cases only and that educational interventions are needed to improve perioperative appropriate antibiotic prophylaxis [37]. Rangel et al. reported that a significant variation exists in the use of AP in the pediatric surgical population [38]. They found that children may receive antibiotics when there is no indication and that numerous children do not receive antimicrobial prophylaxis when indicated [38]. Artoisenet et al. stated that 40 % of intravenous amoxicillin/clavulanate prescriptions that were used for surgical prophylaxis were inappropriate [39].

Table 2. The included studies that were published between 2011 and 2016

Author	Year	Name of journal
Turnidge et al.	2016	Medical journal of australia
Huh et al.	2016	American journal of infection control
Dimopoulou et al.	2016	Journal of pediatric surgery
Kara et al.	2016	Journal of pediatric infection
Sandora et al.	2016	Jama pediatrics
Sviestina et al.	2016	International journal of clinical pharmacy
Lim et al.	2015	Journal of infection in developing countries
James et al.	2015	Journal of antimicrobial chemotherapy
Testa et al.	2015	Bmc surgery
degli Atti et al.	2015	European journal of clinical pharmacology
Osowicki et al.	2014	Medical journal of australia
Ramcharan et al.	2014	Future microbiology
Cotta et al.	2014	Internal medicine journal
Bozkurt et al.	2014	Journal of infection and public health
Napolitano et al.	2013	Plos one
Gul et al.	2013	Nobel medicus
Pittalis et al.	2013	Surgical infections
Snyder et al.	2013	Infection control and hospital epidemiology
Artoisenet et al.	2013	Acta clinica belgica
Abu-Gharbieh and Fahmy	2012	Tropical journal of pharmaceutical research
Simon et al.	2012	Annales francaises d anesthesie et de reanimation
Akalin et al.	2012	International journal of clinical pharmacy
Imai-Kamata and Fushimi	2011	International journal for quality in health care
Rangel et al.	2011	Journal of pediatric surgery

Tiri et al. reported that the overall compliance rate to surgical antibiotic prophylaxis guidelines was low (40.2%) [40]. Alamrew et al. and Afzal khan et al. found that 30–50% of surgical patients received prophylactic antibiotics, and of which, 30–90% was inappropriate [41,42]. Pollmann et al. found that among the 251 abdominal operations that were performed on older adult patients, the perioperative antibiotic prophylaxis was appropriate in 49.5% of cases and that the most common prophylaxis errors were incorrect timing (15.5%) and incorrect dose (12.4%) [43]. Previous reports also have shown similarly low rates of full compliance to surgical antibiotic prophylaxis [21, 44,45].

Zivanovic et al. found that the very high consumption and incorrect prescription of antimicrobials need special attention in the surgical wards [46]. Furthermore, Sandora et al. stated that among 603 734 children younger than 18 years, surgical antibiotic prophylaxis use was considered appropriate for 64.6% of the cases [47]. Sviestina et al. showed that the overall adherence rate to the international and hospital guidelines in hospitalized children suffering upper and lower extremity injuries was low; indicating that in order to improve this situation, there is a need for multiple interventions [48]. Lim et al. stated that the prevalence of inappropriate antibiotic use was 66.3% for prophylactic purposes and that the most common causes of inappropriate prophylactic antibiotics were inappropriate timing (36.4%) and inappropriate duration of prophylaxis (34.5%) [49]. Moreover, Testa et al. found inappropriate surgical prophylaxis practices including the continuation of antimicrobial prophylaxis in 17.1% of the cases, an unjustified re-start of antimicrobial therapy in 9.7%, and a re-dosing omission in 7.8 % [50].

It is important to identify the main causes of surgical prophylaxis inappropriateness in order to tailor the antimicrobial stewardship interventions for each health section. Inappropriate surgical prophylaxis includes inappropriate indication, inappropriate selection and dosing, inappropriate timing, and inappropriate duration. Previous studies found that inappropriate choice, timing, and surgical prophylaxis duration were the commonly reported irrational use of prophylactic antibiotics [51-53].

4. INAPPROPRIATE INDICATION

The first basic parameter of antimicrobial prophylaxis in surgery is the indication. Segala et

al. stated that the adherence to guidelines regarding indication was 58.5% and was improved to 93.2% after the implementation of antimicrobial stewardship interventions [13]. Tiri et al. reported Out of 2059 elective surgical procedures the percentage of appropriate indication was 73.6% [40]. Degli Atti et al. reported that the adherence to surgical antibiotic prophylaxis regarding indications was 82.0% before the intervention and improved after their intervention [54]. Akalin et al. stated that perioperative antibiotic prophylaxis was indicated in 12.5% of the group where it was not used, and not indicated in 7.1% of the group where it was used [55]. Rangel et al. found that many children don't receive antimicrobial prophylaxis when indicated, and an even greater proportion may receive antibiotics when there is no indication [38].

5. INAPPROPRIATE SELECTION AND DOSING

In addition to indication, parameters of antimicrobial prophylaxis in surgery include antimicrobial selection and dosing. Khan et al. stated that only 9.5% of the surgeons adhered to guidelines concerning correct choice [33]. Ramcharan et al. stated that cefuroxime or cefazolin is used commonly as a prophylactic agent and the rate of appropriateness is high [56]. Eisner et al. reported that the most commonly used antibiotics for surgical prophylaxis were cephalosporins and in their study the most frequently used antibiotics were cefuroxime [57]. They stated that the use of cefuroxime was inappropriate due to high percentage of bacterial resistance [57].

Segala et al stated that the adherence to guidelines regarding the selection and dosing of antimicrobial was 58.5 and was improved to 80.6% after the implementation of their interventions [13]. Dimopoulou et al. reported that regarding perioperative antimicrobial prophylaxis, the correct antimicrobial agent was used in 28.7% of the surgeries only [28]. Moreover, Giordano stated that the guidelines of Surgical Antibiotic Prophylaxis for appropriate drug choice were followed in 5.7% of cases and that the guidelines of Surgical Antibiotic Prophylaxis for appropriate drug choice were followed for dose in 91.5% of cases [45].

Chautrakarn et al. and Kefale et al. reported inappropriate use of antibiotics in the surgical ward; mainly due to the inappropriate selection of antibiotics [58,59]. Tiri et al. reported that out of 2059 elective surgical procedures, the dose was appropriate with a rate of 69.7% and that the choice of antibiotic was appropriate with a rate of 78.4% [40]. In addition, Oshikoya et al. stated that most antimicrobials used by pediatric patients were underdosed (44.5%) or overdosed (31.5%) [22]. Toba et al. also stated that due to the inappropriate antibiotic dose it is important to follow the dosing regimens according to the guidelines because this would be useful to reduce the complications associated with antibiotics, reduce antibiotic medicine costs and prevent resistant bacteria [60].

6. INAPPROPRIATE TIMING

Khan et al. stated that about 40% of the surgeons adhered to guidelines concerning timing [33]. Ierano et al. stated that when procedural Surgical Antibiotic Prophylaxis was clinically indicated but considered inappropriate, the most common reason for inappropriateness was timing (49.5%) [12]. Giordano stated that the adherence rate to guidelines of Surgical Antibiotic Prophylaxis for timing was 48.6% [45]. Napolitano et al. stated that the appropriateness of the timing of prophylactic antibiotic administration was observed in 53.4% of the procedures [37].

Ierano et al. found that the most common reason for inappropriate procedural use was incorrect timing [11]. Segala et al. stated that the adherence to guidelines regarding timing was improved from 92.4 before the implementation of antimicrobial stewardship interventions to 97.6% after the implementation [13]. Abubakar et al. stated that excessive and inappropriate use of antibiotic prophylaxis was observed in women who had obstetrics and gynecology surgeries and that timing of antibiotic prophylaxis was optimal in only 16.5% of surgeries [61]. Pittalis et al. stated that there was a high percentage of inappropriateness in the timing and duration of antibiotic prophylaxis in the Latium region of Italy [62].

7. INAPPROPRIATE DURATION

Ierano et al. found that duration greater than 24 hours was the most common reason for inappropriate postprocedural surgical antimicrobial prophylaxis [11]. Turnidge et al. found that the rate of surgical antimicrobial prophylaxis exceeding the benchmark of 24 hours was high (36%) [63]. Abu-Gharbieh and

Fahmy reported that 93.5% of the patients received the right antibiotic dose while the total duration of all antimicrobial agents used for prophylaxis was concordant with the guidelines in only 67.4% of the patients [30]. Akalin et al. stated that unnecessarily prolonged antimicrobial prophylaxis was observed in 56.9% of the procedures [55]. Giordano et al. stated that the guidelines of surgical antibiotics for the duration were followed in 14.5% of cases [45].

Segala et al. stated that the adherence to guidelines regarding duration was 71% and was improved to 80.1% after their intervention [13]. Arnoldo et al. stated that the appropriateness of duration of surgical prophylaxis was poor but after the implementation of the recommended protocol it is increased significantly [64]. Moreover, Ierano et al. found that prolonged duration was the most common reason for inappropriateness for all surgical procedure groups [12]. Abubakar et al. stated that regarding surgical antibiotic prophylaxis for obstetrics and gynecology surgeries, among the 248 procedures included in their study the duration of prophylaxis was prolonged in all of the procedures [61].

James et al. stated that about 59% of all surgical prophylaxis prescriptions in their study were for more than 24 h [65]. As well, Muhammed et al. stated that about half (49.3%) of noncompliance to the guidelines in their study was found from surgical and gynecologic/obstetrics wards due to either longer duration of therapy or wrong timing ceftriaxone use in surgical prophylaxis [66]. Gürtler et al. stated that 19.9% of all prophylactic prescriptions in a Swiss tertiary care hospital violated one or more appropriateness criteria, of which 40% concerned with extended postoperative surgical prophylaxis [67].

Komagamine et al. stated that more than two-thirds of the antimicrobial drugs used for surgical prophylaxis were administered for durations longer than 1 day, whereas the duration of antimicrobial drugs for surgical prophylaxis of 1 day or less has been found to be sufficient in most cases [68]. An unnecessarily long duration of surgical antimicrobial prophylaxis was also found to be common in past studies investigating the antimicrobial drug use for surgical prophylaxis [69-73]. The continuation of prophylactic antibiotic treatment postoperatively on surgical wards is of major concern, as no benefit has been demonstrated in previous studies [74-78]. Ciofi et al. highlighted several areas of improvement, such as actions for screening patients in case of occurrence of multi-drug resistant bacteria, antimicrobial stewardship programs, and implementation of policies targeting antibiotic prescriptions for therapeutic purposes and medical prophylaxis [79]. Broom et al. stated that the interventions that are implemented to optimize surgical prophylaxis are more likely to be effective in enacting sustained change if they consider the interpersonal and social contexts, including issues of familiarity and cohesiveness, hierarchical patterns, and sense of place within a team [80]. Huh et al. reported that monitoring of surgical prophylactic antibiotics and implementation of the computerized decision support system can be effective measures for antimicrobial stewardship [81]. The implementation of an antimicrobial stewardship program based on clinical pathway and education is an effective and sustainable antimicrobial stewardship tool for improving the correct use of perioperative antibiotic prophylaxis [82].

8. CONCLUSION

It can be concluded that the rate of surgical prophylaxis inappropriateness was high and the main cause for this result was inappropriate timing and duration. Numerous interventions including educational interventions such as one-time seminars and online e-learning modules are needed to improve the adherence to the guidelines. Numerous approaches should be used to encourage adherence to clinical guidelines on surgical antibiotic use, especially on the duration of treatment.

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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