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Challenges of Antibiotic Resistance in the Treatment of Postoperative Infections

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Abstract

Introduction: Despite improvements in prophylaxis and infection control measures, surgical site infections (SSIs) remain an important cause of nosocomial morbidity and mortality. Methicillin resistant Staphylococcus aureus (MRSA) has become the leading cause of SSI in community hospitals and leads to 15% of SSIs. This review examined the challenges associated with antibiotic resistance in surgical wound infections.

Methods: A literature search of the MEDLINE database was performed, and studies of post-surgical wound infections were included in this review. Keywords used for searches of medical subject headings included: "antibiotic prophylaxis" OR "vancomycin" OR "teicoplainin" AND "surgical procedures" OR "surgical site infections" AND "surgical wound infections." Bibliographies of selected studies and review articles were reviewed to identify additional references. Two independents reviewer screened the included articles and extracted the relevant data about post-surgical infections and antibiotic resistance.

Results: Wound site infections are a major source of postoperative illness, accounting for approximately a quarter of all nosocomial infections. Postoperative surgical site infections remain a major source of illness and a less frequent cause of death in the surgical patient. Infections result in longer hospitalization and higher costs. Most infections are diagnosed and treated in the outpatient clinic or the patient's home. The pathogens isolated from infections differ, primarily depending on the type of surgical procedure. In clean surgical procedures, in which the gastrointestinal, gynecologic, and respiratory tracts have not been entered Staphylococcus aureus from the exogenous environment or the patient's skin flora is the usual cause of infection. In other categories of surgical procedures, including clean-contaminated, contaminated, and dirty, the polymicrobial aerobic and

anaerobic flora closely resembling the normal endogenous microflora of the surgically resected organ are the most frequently isolated pathogens.

Conclusions: Wound site infections are a major source of postoperative illness, accounting for approximately a quarter of all nosocomial infections. Many studies have defined the patients at highest risk for infection in general and in many specific operative procedures.

Keywords: Surgery, Infections, Nosocomial, Post-operative, Antibiotic resistance.

Introduction

Actual antibiotic practices are largely based on training and personal experience instead of evidence-based medicine. The lack of evidence-based guidelines specific to this patient population has led to indiscriminate use of prophylactic antibiotics without clear understanding of either the bacteriology of these infections or the susceptibility of the causative bacteria to commonly used antibiotics [1]. Inappropriate antibiotic selection and prolonged use have negative consequences including increased costs, systemic adverse effects, and growing drug resistance [2]. One of the major problems faced by the surgeons these days is to deal with the post-surgical infections, as most of these are being caused by multiple resistant bacteria. Surgical site infection can be defined as the presence of pus along with signs of inflammation in the surgical wound margin [3].

Despite improvements in prophylaxis and infection control measures, surgical site infections (SSIs) remain an important cause of nosocomial morbidity and mortality. With approximately 15% of elective surgery patients and 30% of patients undergoing contaminated or dirty surgery estimated to develop post-operative wound infections SSIs are the most commonly encountered form of nosocomial infection in surgical patients [4]. Such improvements in healthcare have had to contend with increasing numbers of elderly, debilitated, chronically ill, or immunocompromised patients in the surgical population, who are typically at increased risk of SSI [5]. The introduction of routine prophylactic antibiotic use has reduced postoperative infection rates dramatically. Guidelines addressing these issues have been published. Failure of antimicrobial therapy to prevent or treat infection in the surgical patient may result from poor antimicrobial selection, inappropriate dosage or frequency, poor timing of administration or inappropriate duration of therapy [6]. About a half of hospital-acquired infections in the United States and Europe, and these infections very difficult to treat due to their resistance to multiple antibiotics [7]. The Centre for Disease Control and Prevention (CDC) classify SSIs into three major categories. Superficial infections, which are localized to the skin and subcutaneous tissue, and are characterized locally by redness, pain, warmth and swelling, and are resolved by local incision and the discharge of the pus. Deep incisional infections, affecting muscles and fascia with the presence of abscess, which require the surgical excision of deep wound edges. The infection of abdominal organs or anatomical spaces, which require surgical procedures in locations other than the initial incision site [8].

The knowledge of the antibiotic resistance of bacteria recovered from SSIs is critical in for the optimization of the prophylactic antibiotic therapy of surgical maneuvers, in an effort to avoid the selection of multi-resistant microorganisms (Călina et al., 2017). Surgical site infections (SSIs) are well known to lead to adverse clinical and financial outcomes for patients. In total SSIs cost the US healthcare system approximately $10 billion annually [9]. Methicillin resistant Staphylococcus aureus (MRSA) has become the leading cause of SSI in community hospitals and leads to 15% of SSIs. To date, only a few studies have specifically examined outcomes related to SSI due to MRSA. These studies have been limited to single institutions, small numbers, and/or a single surgical procedure. The authors of these studies reached conflicting conclusions regarding the impact of

methicillin resistance on outcomes among patients with S. aureus SSI [10]. This review examined the challenges associated with antibiotic resistance in surgical wound infections.

Methods

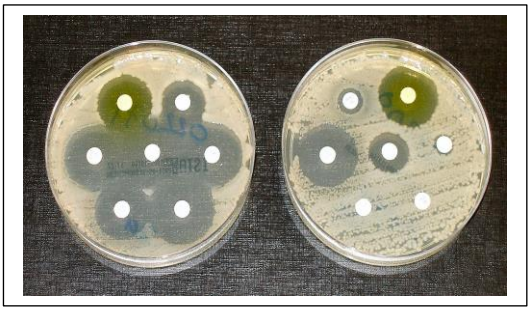
A literature search of the MEDLINE database was performed, and studies of post-surgical wound infections were included in this review. Keywords used for searches of medical subject headings included: "antibiotic prophylaxis" OR "vancomycin" OR "teicoplainin" AND "surgical procedures" OR "surgical site infections" AND "surgical wound infections." Bibliographies of selected studies and review articles were reviewed to identify additional references. Two independents reviewer screened the included articles and extracted the relevant data about post-surgical infections and antibiotic resistance.

Results and discussion

Despite evidence from randomized clinical trials and other data supporting antibiotic prophylaxis (ABP) for no longer than 48 hours, controversy persists about the optimal duration of prophylaxis [11]. Some authors have advocated routine prophylaxis for clean procedures, such as breast surgery, which do not involve implantation of foreign bodies, but this is more difficult to justify unless patients are at high risk of infection because of host factors. With gastrointestinal surgery or surgery of the head and neck, in which pharyngoesophageal tissues are incised, there is an increased likelihood of infection due to enteric aerobic. For instance, reflecting the microbiology of SSI, a first-or second-generation cephalosporin with high antistaphylococcal activity, such as cefazolin, is the most often used drug for antibiotic prophylaxis for clean surgery and high-risk clean-contaminated elective surgery. Vancomycin or teichoplanin are appropriate first choice agents for prophylaxis where the risk of meticillin-resistant S. aureus (MRSA) infection is high, although what threshold should be used to define a high incidence has not been set. Despite the existence of published guidelines, timely antibiotic administration relative to surgery is poor, occurring in just over half of cases [12]. In contrast, recommendations for the duration of antibiotic prophylaxis are less clear. In the hospital environment, particularly in ICUs, antibiotic use is extensive, resulting in selective pressure for antibiotic-resistant pathogens. Mobile genetic elements have facilitated the rapid spread of antibiotic resistance within and among species [13].

Postoperative infection has been estimated to occur following 1% to 2% of all total hip arthroplasties and 2% to 4% of all total knee arthro-plasties in the United States [14, 15]. Staphylococcus species are the most important group of bacteria responsible for postoperative infection, with Staphylococcus aureus and Staphylococcus epidermidis accounting for 50% to 60% of all infections contracted during total hip arthroplasties since 1980 [15]. Various antibiotic delivery methods, such as implantable pumps, antibiotic-containing plaster of Paris, antibioticcontaining bone cement, topical agents, and local administration, have been developed for the treatment of established infection . A laboratory study showed an injection of gentamicin into the surgical wound cavity after closure of the incision to be two orders of magnitude more effective than preoperative systemic administration of antibiotics for reducing in-wound bacterial counts two days postoperatively [16] . One benefit of local administration is that the antibiotic is delivered directly to the wound cavity rather than diffusing into the cavity from the bloodstream as occurs with systemic administration. Another advantage is the ability to obtain a high antibiotic concentration within the wound cavity while maintaining safe systemic levels. In many cases, at this high concentration, bacteria that are normally considered resistant to an antibiotic fall within its spectrum of effective activity [17].

Bacteriological studies have shown that SSIs are universal and the etiological agents involved may vary with geographical location, between various procedures, between surgeons, from hospital to hospital or even in different wards of the same hospital. In the recent years there has been a growing prevalence of gram negative organisms as a cause of serious infections in many hospitals. In addition irrational use of broad spectrum antibiotics and resulting anti-microbial resistance (AMR) has further



deteriorated the condition in this regard. The problem gets more complicated in developing countries due to poor infection control practices, overcrowded hospitals and inappropriate use of antimicrobials [18]. In clean surgical procedures, in which the gastrointestinal, gynecologic, and respiratory tracts have not been entered Staphylococcus aureus from the exogenous environment or the patient's skin flora is the usual cause of infection [19]. However, more of these pathogens show antimicrobial-drug resistance, especially methicillin-resistant S. aureus. Wound site infections are a major source of postoperative illness, accounting for approximately a quarter of all nosocomial infections. Many studies have defined the patients at highest risk for infection in general and in many specific operative procedures. Other factors influence the development of postoperative wound infection, especially in clean surgical procedures, for which the infection rate (<3%) is generally low [20].

The use of antibiotic prophylaxis before surgery has evolved greatly in the last 20 years. Further advances in understanding of antibiotic prophylaxis in abdominal surgery occurred in the 1970s. The choice of parenteral prophylactic antibiotic agents and the timing and route of administration have become standardized on the basis of well-planned prospective clinical studies. Wound infection after appendectomy for perforative or gangrenous appendicitis is four to five times higher than for early disease. A prospective study of nonperforated appendicitis, using a logistic regression analysis of risk factors, showed that the risk for postoperative infection is related to lack of perioperative antibiotic prophylaxis and to the determination that the appendix was gangrenous. Recently published studies have shown the value of parenteral antibiotic prophylaxis in the prevention of pneumonia or empyema after the placement of a chest tube to correct the hemopneumothorax associated with chest trauma. Recent improvements in antibiotic prophylaxis, including the timing of initial administration, appropriate choice of antibiotic agents, and shortening the duration of administration, have established the value of this technique in many clinical surgical settings [21]. MRSA infections is higher than that of those with methicillin-sensitive S. aureus, as reported in multiple studies. Several studies have attempted to assess risk factors of MRSA SSI in noncancer patients. Multiple studies have been conducted to identify risk factors for surgical-site infections in patients undergoing surgery for a variety of cancers. However, these studies did not attempt to identify the organisms associated with the SSI [22]. One recent Japanese study reported prolonged duration of surgery and advanced American Society of Anesthesiologists (ASA) physical status score as independent predictors of MRSA SSI in elective colon cancer surgery patients. We experienced an increase in the rate of nosocomial MRSA infections and colonizations at our institution since the year 2002 [23]. Based on the type of surgery, surgical site infection is a devastating complication in spine surgeries that prolongs the duration of the hospital stay, increases medical expenditures, and worsens the quality of life [24]. In cardiology, because of their activity against resistant gram-positive organisms, glycopeptide antibiotics, such as vancomycin and teicoplanin, have been recommended as alternative prophylactic agents.

Many persons have adopted the use of glycopeptides for cardiac surgery prophylaxis due to concerns about drug-resistant organisms. A recent cost-effectiveness analysis of strategies for cardiac surgery prophylaxis supports this practice ; the authors compared no prophylaxis, routine cefazolin use, and routine vancomycin use and identified vancomycin use as the most cost-effective option. A metanalysis was conducted with aim to compare the risk of SSI after cardiac surgery for subjects receiving glycopeptide prophylaxis, compared with that for those receiving b-lactam agent prophylaxis. Classification of SSI departed from the National Nosocomial Infection Surveillance System (NNIS) definitions of superficial

incisional, deep incisional, and organ-space SSIs, owing to low numbers of organ-space SSIs reported and the failure of some of the trials to adhere to these NNIS classes. They anticipated that the prevalence of methicillin-resistant S. aureus (MRSA) might influence the efficacy of surgical prophylaxis. A single trial reported that teicoplanin was significantly inferior to the beta-lactam comparator for prevention of infections with gram-positive bacteria [25]. Furthermore, nosocomial blood stream infections are usually caused by Gram-positive organisms including Coagulase negative Staphylococcus S. aureus Enterococci and these microorganisms nearly always represent true bacteremia such as E. coli and other members of the Enterobacteriaceae Pseudomonas aeruginosa, and Streptococcus pyogenes. The emergence of poly antimicrobial resistant strains of hospital pathogens has also presented a challenge in the provision of good quality inpatient care. The battle between bacteria and their susceptibility to drugs is yet problematic among public, researchers, clinicians and drug companies who are looking for effective drugs. In USA, more than 8000 patients get admitted in surgical and gynaecology wards per year and on average ten major operations would performed per day. Examples include gross spillage from a hollow viscous during the operation or compound/open injuries operated within four hrs. Dirty Operations: a wound in the presence of pus, where there is a previously perforated hollow viscous or compound/open injury more than four hours old. Nosocomial infections, including surgical site infection, still form a large health problem and contribute substantially to patient morbidity, mortality, prolonged hospital stay, expensive hospitalization and prolonged therapy [26].

Surgical site infections (SSI) remain a common and widespread problem that contributes to significant morbidity and mortality, prolongs hospital stay and consequently increasing health care cost. Globally SSI is reported to be the third most common nosocomial infection preceded only by urinary tract infections and pneumonias . The outcome of SSI is partly attributed to increase in antimicrobial resistant bacterial pathogens, which make the choice of empirical therapy more difficult. I the developing countries, the incidence of SSIs may range from 1.5 -20% depending on the diversity and complexity of procedures performed, age of patients, pre-operative hospitalization, length of surgery as well as geographical locations [8]. A study at Bugando Medical Centre (BMC) reported resistance to ciprofloxacin of 86%, 80% and 54% for E. coli Klebsiella pneumoniae and S. aureus respectively. Rural settings have not been spared of the antibacterial drug resistance problem as shown by a study done at a remote district hospital in Tanzania which reported more than 95% of S. aureus isolates being resistant to penicillin with 1 (0.8%) being resistant to methicillin . However, recent data from the same geographical location has revealed significant increase of methicillin resistant S. aureus (MRSA) (18.8%) causing SSI [27].

Conclusions

Wound site infections are a major source of postoperative illness, accounting for approximately a quarter of all nosocomial infections. Postoperative surgical site infections remain a major source of illness and a less frequent cause of death in the surgical patient. Infections result in longer hospitalization and higher costs. Most infections are diagnosed and treated in the outpatient clinic or the patient's home. The pathogens isolated from infections differ, primarily depending on the type of surgical procedure. In clean surgical procedures, in which the gastrointestinal, gynecologic, and respiratory tracts have not been entered Staphylococcus aureus from the exogenous environment or the patient's skin flora is the usual cause of infection. In other categories of surgical procedures, including clean-contaminated, contaminated, and dirty, the polymicrobial aerobic and anaerobic flora closely resembling the normal endogenous microflora of the surgically resected organ are the most frequently isolated pathogens. However, more of these pathogens show antimicrobial-drug resistance, especially methicillin-resistant S. aureus..

Conflict of interests

The authors declared no conflict of interests.

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