Timing and Choice of Antibiotic Prophylaxis for Prevention of Surgical Site Infections: A Systemic Review

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Abstract: **BACKGROUND:** Surgical site infection (SSI) doubles the mortality, cost, hospital stay and the rate of ICU admission in post operative patients. Parenteral antibiotic administration in the perioperative period is one of the effective strategies for prevention of SSI. However, the practice around administration of antibiotics in this setting is often not standardized, depending mainly on surgeon's preference. **OBJECTIVE:** We set out to clarify the timing of antibiotic for prophylaxis in surgery and the most appropriate antibiotic choice. **METHODS:** The study was a systematic review of literature on the subject within the last 5 years. Literature was retrieved from "Google Scholar", "Pubmed" and "Medline". Those that met the eligibility criteria were included and analyzed. **RESULTS:** The reviewed literature indicated that antibiotic prophylaxis should be administered within 60 minutes before surgical incision and should not be continued beyond 24 to 48 hours. The choice should be guided by local susceptibility patterns, but cefazolin or cefuroxime or ampicillin-sulbactam are used in most settings. Metronidazole should be added when anaerobic organisms are expected. **CONCLUSIONS AND RECOMMENDATION:** We recommend a review of guidelines or institution of guidelines where none exists, to reinforce the timing and choice of antibiotic for pre-operative prophylaxis.

Key words: Surgical site infection, Peri-operative antibiotic prophylaxis.

1. Background

Surgical site infection (SSI) refers to infection at the site of surgical operation occurring within 30 days of surgery if no implant is in place or 1 year if an implant is in place and the infection appears to be related to the surgical procedure [1]. SSI poses a major burden to patients and the health care system by doubling mortality, ICU admission, length of hospital stay and hospitalization cost as well as increasing hospital readmission by close to five times [2].

Overall, the incidence of SSI has been reported to be relatively high in developing countries with some centers reporting up to 26% considering all wound classes [2].

Surgical Site infection (SSI) is commonly caused by bacterial agents, either a single or multiple agents [3].

Bacterial agents commonly implicated in SSI include *Staphylococcus aureus*, including Methicillin Resistant *Staphylococcus aureus* (MRSA) and Methicillin Sensitive *Staphylococcus aureus* (MSSA) [4]. Others organisms are mainly gram negatives such as *Pseudomonas aeruginosa*, *Klebsiella pneumonia*, *Escherichia coli* and *Proteus mirabilis* [5].

2. Justification

One of the strategies in prevention of Surgical Site Infections is the use of antibiotic prophylaxis. However, the practice around antibiotic prophylaxis in surgery is often not standardized and is left to surgeon's discretion. Many hospitals, especially in developing countries, lack guidelines and protocols on antibiotic use for prophylaxis in the context of surgery and there are often significant variation within the same institution [6]. This leads to inappropriate use of antibiotics in the perioperative setting [7]. We therefore

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set out to find out the recommended time for administration of antibiotic prophylaxis and the choice of antibiotic for prophylaxis in surgery.

3. Methods

A review of the current literature was conducted covering the last 5 years from 2013 to 2017. Articles were retrieved from “Google Scholar”, “Medline” and “PubMed” using the key words “Duration of Antibiotic Prophylaxis”, “Surgical Site Infection”, “Timing of Antibiotic prophylaxis” and “Choice of antibiotic for prophylaxis”. A total of 207 articles were retrieved and considered. Out of these, 43 were found to adequately address the questions of interest and were thus included in the analysis.

4. Results

4.1 Is Antibiotic Prophylaxis Necessary in Surgery?

There were 13 studies that evaluated whether antibiotic prophylaxis was better than placebo in the context of clean surgical wounds. Most showed that antibiotic prophylaxis had significant benefit in prevention of SSI even in the context of clean wounds. In a double-blind randomized controlled trial involving patients undergoing mesh-plug hernia repair, incidence of SSI among patients in the antibiotic group (receiving 1.0g cefazolin 30 minutes before incision) was 2% compared with 13% in the placebo group [8]. A meta-analysis looking into studies involving elective caesarian section, use of prophylactic antibiotic was found to reduce the incidence of SSI by between 60% and 70% [9]. Antibiotic prophylaxis was also shown to be beneficial in elective hysterectomy, plastic surgery, facial fractures among other surgical procedures [10-12]. A randomized control trial that evaluated patients with low SSI risk scores undergoing open reduction and internal fixation (ORIF) however found no significant difference in SSI incidence between patients assigned to control group that received cefuroxime for prophylaxis and those in evaluation group that received placebo [13]. They therefore

concluded that an SSI risk score could be used to select patients who do not need antibiotic prophylaxis when undergoing surgery. Another study also showed that antibiotic prophylaxis confers no benefit in acute cholecystectomy [14].

4.2 What Is the Optimal Timing of Antibiotic Prophylaxis in Surgery?

A total of 27 of the reviewed studies evaluated the timing of administration of antibiotic prophylaxis in surgery. Overall, administration of prophylaxis within 60 minutes before incision was preferred [15]. One practical time to do this is at induction of anesthesia which is often adequate for prevention of SSI [16]. Administration of antibiotic prophylaxis after this time is however questionable. Most studies found that post operative antibiotic administration did not reduce the incidence of SSI compared to patients who received placebo on the post operative period [17, 18]. A study involving patients undergoing renal transplant showed that a single dose of appropriate antibiotic agent was as good as multiple doses especially in patients with no additional co-morbidities [19]. In a systematic review of 4 randomized control trials, it was found that post operative prophylactic antibiotic administration in total knee and total hip arthroplasty did not lead to any reduction in surgical site infection [20].

Others however underscored the importance of post operative antibiotic prophylaxis [21]. In cases where post operative antibiotic was given, it was shown that prolonging the course beyond 24 hours did not lead to any additional benefit in preventing SSI [12, 22-25]. A randomized control trial involving patients undergoing thoracolumbar spinal surgery in whom a drain was left showed no statistically significant difference on SSI rates among patients given antibiotics for 24 hours and those on antibiotics for the entire period when drain remained in situ [26]. This suggests that post operative antibiotic prophylaxis can be discontinued at 24 hours even when a drain remains in situ. Other studies however placed the cut off at 48 hours suggesting that

prolonging antibiotic prophylaxis beyond the day of surgery may have additional benefit [27, 28]. The 48 hour course has been shown to be similar to a 5 day course in prevention of SSI hence no need for prolongation beyond 48 hours [29-31].

Prolonged administration of antibiotics postoperatively was associated with complications including diarrhea due to *Clostridium difficile* colitis [32]. Other complications include skin rash, itching, nausea, vomiting and candidiasis [33, 34]. Long course of antibiotics also lead to selection of resistant bacteria hence leading to high rates of infection with multi-drug resistant organisms and the increase of resistant bacteria in the community [30]. Furthermore, despite having no additional benefit in preventing SSI, prolongation of antibiotic prophylaxis beyond 24 hours after surgery is associated with increased cost [35].

4.3 Choice of Antibiotic for Prophylaxis

Where skin commensal is expected, antibiotics with good gram positive cover are preferred. Most studies used cefazolin, ampicillin/sulbactam or clindamycin. A retrospective study that compared SSI incidence among patients receiving vancomycin for prophylaxis versus those receiving cefazolin and quinolones with or without combination with an anaerobic agent cover showed that the vancomycin group had higher SSI rates [15]. Another study however showed that infection rates were similar among patients receiving cefazolin and those receiving vancomycin for prophylaxis [36]. In a context where either clindamycin alone or ampicillin-sulbactam alone was used, use of clindamycin was found to be associated with higher incidence of SSI than ampicillin-sulbactam [22]. In a study involving patients undergoing elective colorectal procedures, use of cefazolin in combination with metronidazole was shown to be associated with lower SSI incidence than use of ampicillin/sulbactam and second generation cephalosporins [37].

However, a systematic review of several randomized control trials comparing different antibacterial agents

used as prophylaxis in surgery found no statistically significant difference between cefazolin, cefotaxime, clindamycin, ampicillin-sulbactam, cefoperazone and clindamycin-gentamycin [38]. Another review however concluded that ampicillin-sulbactam is the most preferred agent for antibiotic prophylaxis especially in major head and neck surgeries with clindamycin being associated with higher SSI incidence [23]. On the other hand, a systemic review of studies on surgeries in obese patients however recommended cefazolin either 1g or 2g as the drug of choice as perioperative antibiotic prophylaxis [39]. There was therefore no conclusive agreement on which antibiotic is preferred.

5. Conclusion

Antibiotic prophylaxis is an important intervention in prevention of surgical site infection. Prolonged use of the antibiotic prophylaxis is however not necessary and is associated with adverse effects and selection of antibiotic resistant strains. The antibiotic should be given within 60 minutes before skin incision and not continued beyond 24 hours unless in rare situations where it is continued up to 48 hours. Several options exist in choice of antibiotic. Cefazolin, cefuroxime or ampicillin-sulbactam seems to be the most commonly used either alone or in combination with metronidazole where anaerobic organisms are anticipated.

6. Recommendation

We recommend development of site specific guidelines to reinforce antibiotic stewardship in the perioperative period. Choice of antibiotic for prophylaxis should be guided by local susceptibility patterns.

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