

Review Article**Timing of Preoperative Antibiotics in Relation with Surgical Site Infections**

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Abstract: Surgical site infections are primarily responsible for the postoperative morbidity and also it increases the cost of illness. To avoid these complications the surgeons usually prefer antibiotic prophylaxis. However there are many controversial opinions for the timing of administering the antibiotics. Most of the guidelines support that the beneficial time for prophylaxis is in between 30 – 60 min prior to the procedure. The duration of the surgical procedure and half-life of the administered antibiotic should be considered when determining the need for an additional intraoperative dose. Expert's opinion from the American Society of Health-System Pharmacists (ASHP) and other guidelines, recommends continuing prophylaxis for up to 72 h after the operation. But many evidence based studies also suggest that prophylactic antibiotics do not add any benefit rather than they increase the emergence of resistant pathogens. Hence the practitioners should take into account the patient and pathogen factors, technical aspects, and duration of the procedure while administering the prophylactic antibiotics. In addition to this they must also consider the need of prophylaxis out of their experience.

Keywords: Surgical Site Infections (SSI'S), Antibiotic Prophylaxis, Timing of Dosing

INTRODUCTION

Surgical site infections remain a major source of postoperative illness and less frequent cause of death in the surgical patient. Therefore in most of the surgical procedures prophylactic antibiotics are given to reduce the incidence of SSI. The selection of prophylactic antibiotics is influenced by the organism most commonly causing wound infection in the specific procedure. The basic principles for the use of antimicrobial surgical prophylaxis include the agents should be delivered to the surgical site prior to the initial incision and bactericidal antibiotic concentrations should be maintained at the surgical site throughout the surgical procedure. Despite of this, timing of administration is critical. Current US guidelines recommends administration of prophylaxis within 120 or 60 minutes of incision and European guidelines recommends administration of prophylaxis within 30 minutes of incision can achieve good tissue penetration and excellent levels of antibiotics in serum throughout the procedure, hence lower the infection rates. For longer procedures readministration at 1 or 2 half-lives of the antibiotic is indicated. Delaying the administration of antibiotic by as little as 3 hrs resulted in surgical site infections identical to those who not receiving preoperative antibiotics [1]. However there are many controversial opinions for the timing of administering the antibiotics. Many evidence based studies also suggest that prophylactic antibiotics do not

add any benefit rather than they increase the emergence of resistant pathogens. Even though antibiotic prophylaxis for appropriate surgical procedures is important and efforts should be made to improve patients receiving antibiotics address an important safety and quality of life in every way. Since timely administration of Antibiotic Prophylaxis before surgery continues to be a difficult challenge, this review mainly focus on guidelines for proper timing of preoperative antibiotics in surgery [2].

ASSOCIATION OF SURGICAL SITE INFECTIONS WITH PROPHYLACTIC ANTIBIOTIC TIMING

In patients who undergo surgery surgical site infections are the most common nosocomial infections. Optimal timing of intravenous antimicrobial prophylaxis helps to achieve adequate concentrations in the tissue during incision and for 2 hrs thereafter and thus provide protection against the serious SSIs. But the suboptimal timing of administration results in an increase in the wound infection rate and become a major concern of morbidity, mortality and costs. These surgical site infections typically occur within 30 days after surgery and may extend upto 1 year in case of prosthetic implantation³. The common signs and symptoms of SSIs are redness, pain, fever, tenderness, irritation, delayed healing, warmth and swelling. Additional signs and symptoms can be seen for specific

types of surgical site infections. Based on National Research Council (NRC) criteria wounds have been classified into 4 categories with increasing risk of surgical site infections. They are (a) clean, (b) clean – contaminated, (c) contaminated and (d) dirty. Dirty wounds have higher chances of developing surgical site infections which include abscess formation, purulent discharge, reopening of wound etc. Also risk of SSIs increases in those patients with obese, diabetes, cancer, and other medical problems [4].

GUIDELINES FOR USE OF PREOPERATIVE ANTIBIOTICS IN SURGERY

Guidelines are mainly intended to make the practitioners to develop standardized approach for the effective use of antibiotics at proper time for the prevention of SSIs. For the antibiotic prophylaxis to be successful, most of the guidelines suggest that agents should be administered to the operative site before contamination occurs [5]. This is said because bacteria are more likely to enter the tissue at the time of incision and continuing until the wound was closed. Classic animal studies conducted by Burke and others clearly demonstrated the need for therapeutic antibiotic concentrations in the bloodstream and in vulnerable tissue at the time of wound contamination. He revealed the term effective period or decisive period i.e, a period of about 2 hrs prior to the creation of the wound in which the administration of antibiotic result the maximal efficacy by achieving adequate therapeutic concentrations of drug as early as possible [6]. Also it is very well understood that postoperative administration does not prevent postoperative wound infections and the infection rates are similar to those in patients who receive no antibiotics. Prophylactic antibiotics are most

effective when given within 1 hour window before surgical incision; rates of infection increase significantly if antibiotics are administered more than 1 hour before incision or postoperatively. Current US guidelines recommend administration of prophylaxis within 120 or 60 minutes of incision and European guidelines recommend administration of prophylaxis within 30 minutes of incision can achieve good tissue penetration and excellent levels of antibiotics in serum throughout the procedure, hence lower the infection rates. For longer procedures readministration at 1 or 2 half-lives of the antibiotic is indicated. Delaying the administration of antibiotic by 3 hrs resulted in surgical site infections identical to those who not receiving preoperative antibiotics. The American Society of Health System Pharmacists also suggested that the antimicrobial agent should be administered at such a time to provide serum and tissue concentrations exceeding the minimum inhibitory concentration (MIC) for the probable organisms associated with the procedure, at the time of incision, and for the duration of the procedure [7]. In 1985, DiPiro *et al.* demonstrated that higher serum and tissue cephalosporin concentrations at the time of surgical incision and at the end of the procedure were achieved when the drugs were given intravenously at the time of anesthesia induction compared with administration in the operating room. The average interval between antimicrobial administration and incision was 17–22 minutes [8].

The following table demonstrates the most extensive and probably best-studied prophylactic antibiotics in preventing wound infections after various surgical procedures [9].

Type of Procedure	Organisms Isolated	Recommended Agents	Time of Administration
Thoracic, vascular, and orthopedic, neurosurgery	S.aureus, staphylococcus epidermis, coryn bacterium, pseudomonas	Cefazolin(1 g IV) & Vancomycin (1g IV)	At induction of anesthesia
Cardiac device insertion procedures	Fungal organisms, most notably candida species, S.aureus, staphylococcus epidermis	Cefazolin & cefuroxime, vancomycin for known MRSA or high risk for MRSA	Single preoperative dose before incision and discontinue within 48-72 hr of surgical end time
Ophthalmic	S.aureus, gram negative bacilli	Gentamycin or neomycin- gramicidin-polymixin B ophthalmic drops; multiple drugs at intervals for first 24 hours.	At induction of anesthesia.
gastroduodenal	E.coli, proteus species, klebsiella species, staphylococci, streptococci, enterococci	First & second generation cephalosporins. Amoxicillin clavulanate	At induction of anesthesia. Discontinue within 24 hr of surgical end time
Biliary tract	Enteric gram negative bacilli, gram positive cocci, clostridia	Cefazolin (1 g iv). In major reaction clindamycin plus gentamycin	At induction of anesthesia
Appendectomy	S.aureus and oral anaerobes	Cefoxitin or cefotetan (1 g IV)	At induction of anesthesia
Head and neck	S.aureus and oral anaerobes	Cefazolin (1 to 2 g IV) or Clindamycin (600mg IV)	At induction of anesthesia. Discontinue within 24 hr

DURATION OF ANTIMICROBIAL PROPHYLAXIS

Treatment duration generally reflects severity of infection and the accessibility of the infected site to antimicrobial agents. Most of the published evidence demonstrates that antimicrobial prophylaxis after wound closure is unnecessary and not beneficial [10]. The duration of the surgical procedure and half-life of the administered antibiotic should be considered when determining the need for an additional intraoperative dose. The longer the duration of surgical procedure, particularly with short half-life antibacterial the greater the incidence of postoperative infection [11]. The National performance measure that prophylactic antimicrobials should be discontinued within 24 h after the end of surgery and should be given just before the surgery begins. Prolonged use of prophylactic antimicrobials is associated with emergence of resistant bacterial strains. But an exception to this guideline is the preferred regimen of antimicrobial prophylaxis for cardiothoracic surgery recommended by the American Society of Health-System Pharmacists (ASHP), which recommends continuing prophylaxis for up to 72 h after the operation. This ASHP recommendation was based on expert opinion, and its authors suggest that prophylaxis for 24 h may be appropriate, and there is no need to continue coverage beyond 24 hours [12].

OBSTACLES TO THE IDEAL TIMING OF ANTIBIOTICS

Most of the evidence based studies recommend that appropriate use of preoperative antibiotics reduce the incidence of SSI, but guidelines have remained ineffective at implementing this practice due to some obstacles. The major issue of workflow arises when prophylactic antibiotics are given either too early or too late. This improperly timed delivery of antibiotics often occurs due to concept of “on-call” drug administration which is a protocol, in which antibiotics are given by ward nurse when the patient is called to the operating room [13]. If a delay occurs for surgery due to any reason it results in administration of preoperative antibiotics before the recommended interval. Such problems lead to subsequent interventions by infection control organizations resulting in the administration of prophylactic antibiotics closer to the time of surgery. But some studies revealed that this late administration contributes to poor antibiotic coverage. Also shift in the hospital workflow may have negative impact on the timing of prophylactic antibiotics. This is said because the environment and personnel outside and inside the operating room are entirely different. Therefore confusion occurs regarding who had administered or who should administer the antibiotics. To resolve such issues it is essential to bring an effective communication between the healthcare team both inside and outside the operating room [14, 15]. Of course, an

effective change in the organizational workflow pattern and communication between the healthcare professionals will definitely create a ripple effect and improve the practical implementation of guidelines [16].

CONCLUSION

From the various studies it is found that antibiotic prophylaxis initiated within 30-60 minutes before the surgical procedure is beneficial to achieve adequate levels at the time of incision and throughout the operation. In spite of this, evidences are mounting up that postoperative prophylaxis are not necessary for most of the procedures. The critical aspects of prophylactic antibiotic administration are in choosing an appropriate antibiotic, delivering an adequate dose, achieving proper timing before incision, and maintaining therapeutic levels of antibiotic throughout the operation. To achieve the proper timing and redosing when necessary are dependent on the multidisciplinary organization of the hospital, the duration of the procedure and the operating room. However it is clear through various evidence based studies that postoperative doses do not add any benefit and can increase the incidence of resistant pathogens in subsequent nosocomial infections. Antibiotic prophylactic guidelines are no substitute for clinical judgement. Hence practitioners must exercise their own clinical judgement out of their experience in determining if an antibiotic prophylaxis is appropriate or not. However the surgical site infections can be reduced by modifying the timing of prophylactic antibiotic in surgical process as per the guidelines.

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