

Evaluation of prophylactic antibiotic administration in general surgery division of a teaching hospital in north of Iran

Paniz Yousefi¹, Mahila Monajati², Ebrahim Salehifar^{3*}

¹Student Research Committee, Faculty of Pharmacy, Mazandaran University of Medical Sciences, Sari, Iran

²Resident of Clinical Pharmacy, Pharmaceutical Research Center, Mazandaran University of Medical Sciences, Sari, Iran

³Board certified Clinical Pharmacist, Gastrointestinal Cancer Research Center, Mazandaran University of Medical Sciences, Sari, Iran

Received: Oct 29, 2016, Revised: Dec 28, 2016, Accepted: Jan 10, 2017

Abstract

Surgical site infections are one of the most important post-surgery complications. Antimicrobial prophylaxis has been used routinely in surgeries to reduce infection incidence. However, inappropriate selection of antimicrobial agents or dosing can develop antimicrobial resistance, serious adverse reactions and prolong hospitalization. Current study aimed to examine prophylactic antibiotic prescription in surgeries in a teaching hospital in Sari, Mazandaran and evaluate level of adherence to the international guidelines. Between January 2015 to May 2015, 104 patients in general surgery ward were selected and enrolled in the study. The prophylactic antibiotics, dosage, timing and duration of administration were collected by reviewing patients' records and compared to the existing guidelines. Prophylactic antibiotic was given to 85.5% of patients. Prescribed antibiotics were cefazolin (46.1%), metronidazole (24%), ceftriaxone (12.5%), ciprofloxacin (1.9%) and vancomycin (0.96%). Most of the patients (62.9%) received an inappropriate and delayed timing. Proper antibiotic dosage was seen in 45.2% of patients. All patients received post-operative prophylactic antibiotic. Main antibiotics include cefazolin (41.3%), metronidazole (33.7%), ceftriaxone (31.7%) and clindamycin (20.2%). Only 10 (21.9%) patients received cefazolin or vancomycin for a total duration of 48 hours or less. Surgical wound infection occurred in 17 (16.3%) patients during hospital stay. Adherence to antimicrobial prophylaxis guidelines was completely achieved in 14.4% of cases. Results of this study signified that adherence to existing guidelines was poor and the most common mistakes were over usage, inappropriate dosage and choosing of antibiotics.

Keywords: Antimicrobial prophylaxis, general surgery, guideline

Pharm Biomed Res 2016; 2(4): 30-37

Introduction

Surgical site infection (SSI) is one of the most important complications after surgeries. Depending on the type of surgery, rate of SSIs occurrence is different between 1 to 5%. This can cause prolong hospitalization and increase in morbidity and cost. To reduce the incidence of wound infection complication, prophylactic antibiotics are administered before, during and after surgical operations (1). Some studies have shown that inappropriate selection or dosing of the antimicrobial agents and excessive duration of antibiotic usage can develop antimicrobial resistance or serious adverse reactions and prolong hospitalization (2-4). Antibiotic resistance has been described as an

increasing threat to global public health by the World Health Organization (WHO) because there are now few and, in some cases, no antibiotics available to treat certain life threatening infections (5). To choose a proper prophylactic antibiotic regimen, different guidelines have been developed (6). These guidelines help clinicians to make right decision in selecting, timing, dosing and duration of antimicrobial prophylaxis.

There is some patient and operation associated risk factors which may affect the incidence of SSIs. Patient related factors include: age, nutritional status, diabetes, smoking, obesity, coexisting infections at distal body

*E-mail: Esalehifar@mazums.ac.ir; Salehifare@yahoo.com

sites, colonization with resistant microorganisms, altered immune response and length of preoperative stay. Operation related factors are duration of surgical scrub, preoperative skin preparation, preoperative shaving, duration of operation, antimicrobial prophylaxis, operating room ventilation, sterilization of instruments, and implantation of prosthetic materials, surgical drains, surgical technique and cardio-pulmonary bypass use (7). Many studies demonstrated poor adherence to antimicrobial prophylaxis guidelines, and concluded that the most common mistakes of surgical antibiotic prophylaxis prescribing were overuse and misuse of antibiotics. The aim of this cross-sectional study was to examine prophylactic antibiotic prescription in surgeries in a teaching hospital and evaluate the rate of accordant with suggested prophylactic antimicrobial regimens for surgical procedure.

Patients and methods

This retrospective study was conducted on medical records of patients who had a surgery in Imam Khomeini general hospital, an educational hospital affiliated to Mazandaran University of Medical sciences, Sari, Iran. Patients aged over 16 years who were undergone general surgeries including neurosurgery, thoracic, vascular, orthopedic, gasteroduodenal, appendectomy, colorectal and etc were eligible for study. Every effort was done to protect the confidentiality of patients' data. Patient demographics, clinical characteristics and specific data regarding surgery were recorded in a data gathering form. The information extracted from patients' records. The prophylactic antibiotics, dosage, timing of administration, post-operative antibiotics regimen (dose, dosing interval and duration) were collected by reviewing patients' records and evaluated by comparing to the American Society of Health-System Pharmacist (ASHP) guidelines for antimicrobial prophylaxis in surgery which presented in Table 1 (8). The rate of adherence to prophylactic antibiotic administration before surgeries at Imam Khomeini hospital to the guideline was assessed using a descriptive study.

The following parameters were evaluated in this study: 1) indication, 2) choice (with considering type of surgery), 3) dosing adjustment according to the

patient's body weight or renal function, 4) timing: doses given within 60 minutes of skin incision, and 5) total duration: not more than 48 hours postoperatively for most procedures. Any violation of guidelines for each parameter considered as a discordant of guidelines.

Statistical analysis

Data were entered and analyzed using Excel 2007 and SPSS for windows version 22.0 (Chicago, USA). Frequency and percentages were calculated and presented. If a data of parameter was not existed in patient's record, it defined as missing data in the SPSS statistic document and the final assessment of proper prophylactic antibiotic administration was reported based on the valid percent's.

Results

Between January 2015 to May 2015, 104 patients in general surgery ward were selected and enrolled in the study. Patients' characteristics and types of surgeries were presented in table 2.

Per-surgery prophylactic antibiotic

Indication

For 89 (85.5%) patients antimicrobial prophylaxis was administered. Table 3 shows antibiotic selected for different types of surgeries.

Choice

In 48 (46.1%) of patients cefazolin was administered, 25 (24%) patients received metronidazole, 13(12.5%) of them received ceftriaxone, 2 (1.9%) received ciprofloxacin and one (0.96%) received vancomycin as the prophylactic antibiotic at induction of anesthesia. The antibiotic choice was correct according to the ASHP guidelines in 48 (46.2%) patients who received cefazolin.

Timing

In 37.1% of patients, prophylactic antibiotics were administered within 60 minutes of skin incision, which is according to ASHP guidelines. Most of the patients (62.9%) received an inappropriate and delayed timing.

Dose

Proper antibiotic dosage based on ASHP guidelines was administrated in 45.2% of patients. Those who

Table 1 Suggested prophylactic antimicrobial regimens for surgical procedures (1)

Procedure	Predominant organism(s)	Antibiotic regimen Primary (alternative)	Adult preoperative IV Dose (Alternative)
Neurosurgery	<i>Staphylococcus aureus</i> , <i>Staphylococcus epidermidis</i>	Cefazolin (vancomycin) ^b	1–2 ^a g (1 g)
Thoracic	<i>S. aureus</i> , <i>S. epidermidis</i> , gram-negative enterics	Cefazolin (vancomycin)	1–2 ^a g (1 g)
Vascular (aortic resection, groin incision, prosthesis)	<i>S. aureus</i> , <i>S. epidermidis</i> , gram-negative enterics	Cefazolin (vancomycin)	1–2 ^a g (1 g)
Orthopedic (total joint replacement, internal fixation of fractures)	<i>S. aureus</i> , <i>S. epidermidis</i>	Cefazolin (vancomycin)	1–2 ^a g (1 g)
Head and neck (involving incisions through mucosa)	<i>S. aureus</i> , oral anaerobes, streptococci	Cefazolin (clindamycin-gentamicin)	2 g (600 mg clindamycin-1.5 mg/kg gentamicin)
Gastroduodenal (only for procedures entering the stomach)	Gram-negative enterics, <i>S. aureus</i> , mouth flora	Cefazolin	1–2 ^a g
Appendectomy (uncomplicated)	Gram-negative enterics, anaerobes (<i>B. fragilis</i>), enterococci	Cefazolin	1–2 ^a g
Biliary tract (only for high-risk procedures)	Gram-negative enterics, <i>Enterococcus faecalis</i> , <i>Clostridia</i>	Cefazolin	1–2 ^a g
Colorectal	Gram-negative enterics, anaerobes (<i>Bacteroides fragilis</i>), enterococci	Oral neomycin-erythromycin base (IV cefoxitin)	1 g each at 1 pm, 2 pm, and 11 pm day before surgery (1 g)
Cesarean section	Group B streptococci, enterococci, anaerobes, gram-negative enterics	Cefazolin	2 g before umbilical cord clamped
Hysterectomy	Group B streptococci, enterococci, anaerobes, gram-negative enterics	Cefazolin or cefoxitin	1–2 ^a g
Abortion (only for high-risk in first trimester)	Group B streptococci, enterococci, anaerobes, gram-negative enterics	Aqueous penicillin G (doxycycline) (first trimester) Cefazolin (second trimester)	1–2 ^a g
Genitourinary (only for high-risk procedures)	Gram-negative enterics, enterococci	Ciprofloxacin ^b	400 mg

^aCefazolin should be dosed at 2 g in patients weighing more than 80 kg.

^bVancomycin and ciprofloxacin require longer infusion times and should be administered within 2 hours before surgery.

Table 2 Characteristics and types of surgeries for patient enrolled in the study (n = 104)

Age Mean (Range); years	49.5 (16-86)
Sex	
Male, n (%)	61(58.7%)
Female, n (%)	43(41.3%)
Diabetes Mellitus, n (%)	13(12.5%)
Type of surgeries, n (%)	
Neurosurgery	3, (2.9%)
Thoracic	7, (6.7%)
Vascular	23, (22.1%)
Orthopedic	7, (6.7%)
Gastroduodenal	19, (18.3%)
Appendectomy	6, (5.9%)
Colorectal	9, (8.7%)
Biliary tract	6, (5.8%)
Amputation	11, (10.6%)
Angiography	13, (12.5%)

Table 3 Types of surgeries and prophylactic antibiotics administration

Type of surgeries	Cefazolin n (%)	Vancomycin n (%)	Ceftiraxone n (%)	Metronidazole n (%)	Ciprofloxacin n (%)
Antibiotics					
Neurosurgery	-	-	-	-	-
Thoracic	2 (1.92)	-	-	-	-
Vascular	17 (16.3)	-	3 (2.88)	2 (1.92)	1 (0.96)
Orthopedic	1 (0.96)	-	-	-	-
Gastrodoudenal	9 (8.64)	1 (0.96)	4 (3.84)	10 (9.6)	-
Appendectomy	2 (1.92)	-	-	2 (1.92)	1 (0.96)
Colorectal	2 (1.92)	-	3 (2.88)	7	-
Biliary tract	3 (2.88)	-	2 (1.92)	4 (3.84)	-
Amputation	5 (4.8)	-	-	-	-
Angiography	7 (6.72)	-	1 (0.96)	-	-
Total	48 (46.1)	1 (0.96)	13 (12.5)	25 (24)	2 (1.92)

Table 4 A summary of result and adherence to the guidelines.

Prophylactic antibiotic	Concordant if	Number/Total (% of concordance)	Comments
Intra-operative			
Indication	Decision was made to use prophylactic antibiotic	89/104 (85.5%)	
Choice	Appropriate agent based on various indications	48/104 (46.2%)	cefazolin or vancomycin indicated in most surgeries
Dose	As recommended based on body weight	487/104(46.2%)	This rule was used; cefazolin 1g if < 80kg, 2 g if > 80kg
Timing	Within 60 minutes prior to skin incision	38/104 (37.1)	
Post-operative			
Choice	Cefazolin and/or vancomycin with/without gentamycin	43/104 (41.3)	
Duration	48 h or less	10/104 (21.9)	
Adherence to all parameter		15/104 (14.4)	

received cefazolin, the major dosage were one gram of antibiotic.

Post-surgery prophylactic antibiotics

All patients received post-operative prophylactic antibiotic.

Choice

Main antibiotics include cefazolin (41.3%), metronidazole (33.7%), ceftriaxone (31.7%) and clindamycin (20.2%).

Duration of prophylactic antibiotic use

Only 10 (21.9%) patients received cefazolin or vancomycin for a total duration of 48 hours or less, in accordance to the recommendations. For cefazolin and vancomycin, mean duration of administration were 5.6 ± 3.6 and 9.6 ± 8.1 days; respectively.

Infection rate

Surgical wound infection occurred in 17 (16.3%) patients during hospital stay, 10 of these patients had a co-infection with diabetic foot prior hospital admission.

Adherence to ASHP antimicrobial prophylaxis guidelines was completely achieved in 14.4% of cases. The most common errors were administration of different antibiotics and over usage of prophylactic antibiotics.

Results and adherence to the guidelines were presented in table 4.

Discussion

Based on developing of antimicrobial resistance related to inappropriate usage of antibiotics and vast usage of antimicrobial prophylaxis in surgeries, comparing the employed methods with international guidelines is necessary for recognizing prescription errors. Lack of a local hospital antimicrobial prophylaxis guideline, this study was performed to compare the appropriateness of antimicrobial prophylaxis use according to American Society of Health-System Pharmacists guidelines (8). In the current study, patients' records were examined and all related factors were analyzed. This study is an introduction to reveal problems with prescribing prophylactic antibiotics.

Unfortunately results of present study showed little adherence to the guidelines. These results are similar to

the studies performed earlier in this teaching hospital (9) and in other part of the country (10), Nicaragua (11) and Jordan (12). The adherence to antimicrobial prophylaxis was unfavorable in most of studies, though the percentage of adherence in previous studies was higher than our study. For example Gorecki *et al.* (3), van Kasteren *et al.*(13), Lallemand *et al.*(14) and Voit *et al.*(15) found out that overall adherence was achieved in 26%, 28%, 41.1%, and 50% of surgical patients, respectively.

In the current study anesthesiologists administrated the intra-operative antibiotics and recorded them only on the anesthesia chart. After surgery, senior surgeons or surgery residents prescribed post-operative antimicrobial regimens and recorded data on the order sheet of patients' record. The absence of a standardized antimicrobial practice guideline, lack of communication between anesthesiologists and surgeons, and even among the members of surgical team, resulted in poor monitoring of prophylactic antibiotic administration, excess doses administrated to the patients and choosing irrational antibiotics.

Most previous studies reported a wound infection rate between 0.4 to 2.5%, (14,16). Surgical site infections occurred in 16.5 % of cases of current study which was higher than the other reports.

Administering prophylactic antibiotic is indicated in all patients undergoing clean-contaminated and contaminated surgeries. In current study, major surgery included vascular, gasteroduodenal and orthopedic surgeries and 85.5% of patients received prophylactic antibiotic. Ozgun *et al.* (17) found a lower level of prophylactic antibiotics prescription in the indicated patients, which included orthopedic surgery, vascular surgery, skin and deep tissue surgery, endocrine and abdominal surgery.

The most common antimicrobial prophylaxis agent used in the operating room and at the induction of anesthesia of this study was cefazolin (a first-generation cephalosporin), with the best activity against *Staphylococci* and recommended by all guidelines (8,18).

Appropriate timing of first dose of pre-operative prophylactic antibiotic was observed in 37.1% of surgeries. Almomany *et al.*(12), Paradiso-Hardy *et al.* (19), Lallemand *etal.* (14), van Kasteren *et al.* (13) and van Disseldorp *et al.* (11) reported that timing of the

first dose was in concordant with guidelines in 99.1%, 72%, 61.4%, 50%, and 22% of cases, respectively.

Prolonged prophylaxis duration was reported in 87.7% of cases of Lallemand *et al.* (14), 82.8% by Ozgun *et al.*(17), 58.9% by Al-Momany and colleagues (12) and 15% by van Kasteren *et al.* (13). In the study of Rafati *et al.*(9), Ozkurt and coworkers (20) and Ozgun *et al.* (17), the most frequent error was prolonged use of prophylactic antibiotics as in our study (79.1%). Another study from Turkey showed that in 80.4% of surgical procedures, prophylactic antibiotics were used for more than 5 days (21). These studies showed that prolonged use of antibiotic prophylaxis leads to emergence of bacterial resistance and high costs of therapy.

One reason for the violation of guidelines reported by van Kasteren *et al.* was that some surgeons felt insecure about the length of prophylaxis recommended by the guidelines (16), and Ozgun *et al.* suggested that surgeons should be reassured that it is sufficient to use prophylactic antibiotics within a limited time period and unnecessary and prolonged antibiotic administration will not reduce infections, and may lead to resistant infections and increased costs (17). The Jordanian study agreed that prolonged antibiotic prophylaxis is, at best, of no benefit and, at worst, potentially harmful to patients because of drug toxicity, the risk of super-infections, and the risk of inducing more bacterial resistance, both in surgical patients and throughout the hospital (12). Use of antibiotics for longer than the recommended period, was observed in 79.1% of patients. This was reported in 58% and 4.3% by Al-Momany *et al.*(12) and Prado *et al.* studies (22). This was done in an attempt to prevent infection while patients were hospitalized.

Considering the inappropriate pattern of antimicrobial prophylaxis observed in this study, several interventions would be helpful to improve the current practice. Educational programs regarding the antimicrobial prophylaxis for surgeons/anesthesiologists (23,24), developing a local guideline based on agreement and consensus of several major specialties derived from the scientific evidences in the literatures (25), contribution of clinical pharmacists in antimicrobial prescribing (26), or in providing a protocol (22) and using a checklist which covers the entire pathway of prophylactic antibiotic administration (27) would be among the

useful interventions through rationalization of antimicrobial prophylaxis.

Conclusion

The current study shows that adherence to international antimicrobial prophylaxis guidelines in general surgery ward of Imam Khomeini medical teaching hospital was poor. All health care staffs who are involved with the administration of prophylactic antibiotic in surgery wards especially surgeons should be aware of the complications of inappropriate using of antibiotics. It is necessary to take measures, such as mentioned above, to improve the adherence of antimicrobial prophylaxis in that setting.

Conflict of interests

Nothing to declare.

References

1. Koda-Kimble MA, Alldredge BK, Corelli RL, Ernst ME. Koda-Kimble and Young's Applied Therapeutics: The Clinical Use of Drugs: Lippincott Williams & Wilkins; 2013.
2. Kurz X, Mertens R, Ronveaux O. Antimicrobial prophylaxis in surgery in Belgian hospitals: room for improvement. *Eur J Surg* 1996;162:15-21.
3. Gorecki P, Schein M, Rucinski J, Wise L. Antibiotic administration in patients undergoing common surgical procedures in a community teaching hospital: the chaos continues. *World J Surg* 1999;23:429-32.
4. Burke JP. Maximizing appropriate antibiotic prophylaxis for surgical patients: an update from LDS Hospital, Salt Lake City. *Clin Infect Dis* 2001;33(Suppl 2):S78-S83.
5. World Health Organization (WHO). Antimicrobial resistance: the facts. *Essential Drugs Monitor* 2000;28 and 29:8-9.
6. Harvey K, Dartnell J, Hemming M. Improving antibiotic use: 25 years of antibiotic guidelines and related initiatives. *Commun Dis Intell Q Rep* 2003;Suppl 27:S9-S12.
7. Mangram AJ, Horan TC, Pearson ML, Silver LC, Jarvis WR. Guideline for Prevention of Surgical Site Infection, 1999. Centers for Disease Control and Prevention (CDC) Hospital Infection Control Practices Advisory Committee. *Am J Infect Control* 1999;27:97-132.
8. Pharmacists ASoH-S. ASHP therapeutic guidelines on antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm* 1999;56:1839-88.
9. Rafati M, Shiva A, Ahmadi A, Habibi O. Adherence to American society of health-system pharmacists surgical antibiotic prophylaxis guidelines in a teaching hospital. *J Res Pharm Pract* 2014;3:62-6.
10. Askarian M, Moravveji AR, Mirkhani H, Namazi S, Weed H. Adherence to American Society of Health-System

- Pharmacists surgical antibiotic prophylaxis guidelines in Iran. *Infect Control Hosp Epidemiol* 2006;27:876-8.
11. van Disseldorp J, Slingenberg EJ, Matute A, Delgado E, Hak E, Hoepelman IM. Application of guidelines on preoperative antibiotic prophylaxis in Leon, Nicaragua. *Neth J Med* 2006;64:411-6.
12. Al-Momany NH, Al-Bakri AG, Makahleh ZM, Wazaify MM. Adherence to international antimicrobial prophylaxis guidelines in cardiac surgery: a Jordanian study demonstrates need for quality improvement. *J Manag Care Pharm* 2009;15:262-71.
13. van Kasteren M, Kullberg BJ, de Boer AS, Mintjes-de Groot J, Gyssens I. Adherence to local hospital guidelines for surgical antimicrobial prophylaxis: a multicentre audit in Dutch hospitals. *J Antimicrob Chemother* 2003;51:1389-96.
14. Lallemand S, Thouverez M, Bailly P, Bertrand X, Talon D. Non-observance of guidelines for surgical antimicrobial prophylaxis and surgical-site infections. *Pharm World Sci* 2002;24:95-9.
15. Voit SB, Todd JK, Nelson B, Nyquist AC. Electronic surveillance system for monitoring surgical antimicrobial prophylaxis. *Pediatrics* 2005;116:1317-22.
16. Kriaras I, Michalopoulos A, Turina M, Geroulanos S. Evolution of antimicrobial prophylaxis in cardiovascular surgery. *Eur J Cardiothorac Surg* 2000;18:440-6.
17. Ozgun H, Ertugrul BM, Soyder A, Ozturk B, Aydemir M. Peri-operative antibiotic prophylaxis: Adherence to guidelines and effects of educational intervention. *Int J Surg* 2010;8:159-63.
18. Engelman R, Shahian D, Shemin R, Guy TS, Bratzler D, Edwards F, et al. The Society of Thoracic Surgeons practice guideline series: antibiotic prophylaxis in cardiac surgery, part II: antibiotic choice. *Ann Thorac Surg* 2007;83:1569-76.
19. Paradiso-Hardy FL, Cornish P, Pharand C, Fremes SE. A national survey of antimicrobial prophylaxis in adult cardiac surgery across Canada. *Can J Infect Dis* 2002;13:21-7.
20. Ozkurt Z, Kadanali A, Ertek M, Erol S, Parlak M. Cerrahi profilakside antibiyotik kullanımı *Ankem Derg. J Ankem* 2005;19:111-4.
21. Hosoglu S, Aslan S, Akalin S, Bosnak V. Audit of quality of perioperative antimicrobial prophylaxis. *Pharm World Sci* 2009;31:14-7.
22. Prado MA, Lima MP, Gomes Ida R, Bergsten-Mendes G. The implementation of a surgical antibiotic prophylaxis program: the pivotal contribution of the hospital pharmacy. *Am J Infect Control* 2002;30:49-56.
23. Khan SA, Rodrigues G, Kumar P, Rao P. Current challenges in adherence to clinical guidelines for antibiotic prophylaxis in surgery. *J Coll Physicians Surg Pak* 2006;16:435-7.
24. Kuper KM, Septimus EJ. Health-care-associated infections: The legislative perspective and the pharmacist's role. *Am J Health Syst Pharm* 2009;66:488-94.
25. Talon D, Mourey F, Touratier S, Marie O, Arlet G, Decazes J, et al. Evaluation of current practices in surgical

- antimicrobial prophylaxis before and after implementation of local guidelines. *J Hosp Infect* 2001;49:193-8.
26. Knox K, Lawson W, Dean B, Holmes A. Multidisciplinary antimicrobial management and the role of the infectious diseases pharmacist—a UK perspective. *J Hosp Infect* 2003;53:85-90.
 27. De Vries EN, Dijkstra L, Smorenburg SM, Meijer RP, Boermeester MA. The SURgical PATient Safety System (SURPASS) checklist optimizes timing of antibiotic prophylaxis. *Patient Saf Surg* 2010;4:6.