Role Of Timings Of Administration Of Prophylactic Administration Of Antibiotics And The Risk Of Surgical Site Infection

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PURPOSE:
Surgical site infection is a significant problem for patient and the hospital. The proper choice & timely administered prophylactic antibiotics reduces the infection. We studied the relationship between the timings of administration of prophylactic antibiotics and risk of surgical site infection.

METHODS:
Between 1st September 2013 to 31st December 2014, a total of 800 patients between 12 to 70 years of age, with closed fractures who underwent both open and closed elective Orthopedics Surgery procedure were included. We excluded all patients who had Surgery in the Orthopedics Emergency Department and hip, knee atrhroplasty. We recorded patient's bio-data, the exact timing of administration of antibiotics with respect to the time of incision, status of wound and co-morbidities like Diabetes Mellitus, history of steroids intake and outcomes. We recorded outcome of interest in terms of occurrence of surgical site infection (SSI) within 30 days of the Surgical procedure.

RESULT:
Out of the total 800 participants, only 62 (12.9%) surgical site infection (SSI) were detected. Amongst the total, majority 740 (92.5%) were given antibiotics within 01 hours before the surgery out of which 42 (5.7%) ($p<0.001$) patients developed SSI while 698 (94.3%) did not develop SSI while few patients 14 (1.8%) out of the total participants were given antibiotics prophylaxis within two hours after the surgery and only 4 (28.6%) ($p<0.667$) developed SSI, similarly only 46 (5.8%) patients were given antibiotics within three hours before surgery. (Table 1).

CONCLUSION:
We concluded that there is relationship between timimg of prophylactic antibiotics (PA) and surgical site infection. There is lower risk of infection when PA with short infusion times were given within one hour prior to incision.

KEY WORDS:
Surgical Site Infection (SSI), Time of administration of antibiotics (TAA).

INTRODUCTION

A surgical site infection can occur at or near surgical incision within 30 days of procedure or within one year if an implant is left in place [1,2]. In past 50 years' antibiotics had powerful and effective role in fight against bacterial infection and thus saved millions of lives worldwide. World Health Organization (WHO), recommended rational use of drugs for patients who received medications necessary for one's clinical need in appropriate dose and low cost for patient and community. [3]. In USA, SSI are accounted approximately 50,000 infections annually while in UK it ranged from 2 to 15% for various operations [4-7].

Infection can be primary source of morbidity and mortality in patients who opted for surgery. Antibiotic play important role in preventing post-operative infection [10]. Rate of infections reported after the advent of the antibiotics were noticeably high and there on role of timings of administration of prophylactics antibiotics was established. In Pakistan, most hospital and clinics, we gave conventional antibiotic for 7 to 10 days' post operatively. It results into antibiotic resistance and high cost to patient.

This prolonged and non-recommended use of antibiotics is associated with resistance in Pakistan and high surgical wound infection were reported [11]. Surgical site infections (SSIs) are common fear as complication and they are caused by both endo and exogenous microorganisms that can contaminate the surgical wound.

Guidelines regarding prophylactic administration has been published in recent years. Unfortunately, experience has shown that surgeons' compliance with these recommendations can be hard to obtain [11]. We studied the effectiveness of prophylactic administration of antibiotics and establish an association between the timings of administration of prophylactic antibiotics and the risk of surgical site infections.

METHODOLOGY

Between 1st September 2013 to 31st December 2014, a total of 800 patients between 12 to 70 years of age, with closed fractures who underwent both open and closed elective Orthopedics Surgery procedure were included. We excluded all patients who had Surgery in the Orthopedics Emergency Department and hip, knee atrhroplasty. Ethical approval from the Institutional review board of the Hospital was obtained. All participants were briefed about the purpose of this study. Those participants who gave their willing to participate in this study were included. A written informed consent was obtained.

We recorded patient's bio-data, the exact timing of administration of antibiotics with respect to the time of incision, status of wound and co-morbidities like Diabetes Mellitus, history of steroids intake and outcomes. We recorded outcome of interest in terms of occurrence of surgical site infection (SSI) within 30 days of the Surgical procedure. Three classes of SSIs included: Clean, Clean-Contaminated, Contaminated and dirty [8,9] are based on the centers for Disease Control guidelines. The three classes are combined as composite outcomes.

The independent variable, timely administration of prophylactic antibiotics (PA) was defined as administration of PA within 60 minutes before incision. Covariates, including patient risk factors for SSIs including age, gender, height, weight, education, diabetes and wound status (clean, clean-contaminated, contaminated) smoking and steroid use were obtained. These covariates were specifically chosen because they were previously shown to be tightly linked to patient risk for SSIs. Multivariable analysis was conducted to examine the possible predictors of surgical site infection (SSI). Based on our working hypothesis that risk of surgical site infection increases amongst patients with developed co-

morbidities and it is associated with various types of surgical procedure. The percentage of timely prophylactic administration (PA), percentage of total cases that were included and percentage of patients in whom a SSI developed was calculated. All statistical tests were performed using SPSS software.

Data was analyzed by using by using SPSS 20 .0 and Chi Square and T-tests were applied. Mean ± SD was given for quantitative variables. Frequencies and percentages were given for qualitative variables. A p-value of <0.05 was considered as statistically significant.

RESULTS

Out of the total 800 patients, 62 (7.8%) were positive for surgical site infection while 738 (92.2%) were found negative for SSI. There were 365 (45.6%) male out of which 32 (8.7%) had SSI and 435 (54.3%) were females out of which 30 (6.9%) were positive for SSI. Amongst the total, 693 (86.6%) belonged to lower socioeconomic status while 107 (13.3%) showed that they had middle socio-economic status. Only 103 (12.9%) were illiterate out of which 04 (3.8%) were positive for SSI, most 650 (81.2%) had education level under matric out of which 58 (8.9%) were SSI positive, similarly few 47 (5.8%) were graduate and they didn't develop SSI. During study, 246 (30.7%) were smokers and 26 (10.5%) developed SSI while 220 (89.43%) were free from SSI and most 554 (69.3%) patients were non-smokers and only 36 (6.4%) developed SSI (p=0.47). Of the 800 patients qualifying for the study, 725 (90.63%) were non-diabetic and 60 (8.3%) cases of SSI were found. Incidence of SSI in 75 (9.37%) cases of diabetes Mellitus was only 2 (2.7%). Among 800 patients, 738 (92 %) had clean wound type. SSI was reported in 18 (2.4%) (p<0.001) and 720 (97%) were found free of SSI**.** Only 48 (6%) patients with contaminated wound were analyzed and SSI were found in 32 (66.7%) and only 16 (33.3%) were free from SSI. Very few 5 (0.62%) patients had clean-contaminated wound and 3 (60%) patients developed SSI. Amongst total, 762 (95.3%) had not been administered steroids. Out of which 703 (92.3%) had not developed SSI while 59 (8.3%) had suffered from SSI. Similarly, 38 (4.8%) were given steroids for various treatment in the past and incidence of SSI was reported in 3 (7.8%) cases only (P= 0.973) (Table 1).

Out of the total, majority 740 (92.5%) were given antibiotics within 01 hours before the surgery out of which 42 (5.7%) (p<0.001) patients developed SSI while 698 (94.3%) did not develop SSI. Amongst 800 participants, 14 (1.8%) patients were given antibiotics prophylaxis within two hours after the surgery while only 4 (28.6%) (p<0.667) developed SSI. Forty six (5.7%) amongst total were given antibiotics within three hours before the surgery and many 16 (34.8%) developed SSI (p<0.001) with confidence interval 4.5 to 17.5. Two intravenous antibiotics were used prophylactic doses included Ceftriaxone 688 (86%) and Co-trimoxazole+Clavulanic Acid 112 (14%) of the surgically operated patients.

DISCUSSION

In this modern era of highly tested health care standards, high rate of SSI becoming quality assurance markers in many institutions. They can cause economic burden, staff overwork, noticeably high morbidity and mortality in surgical patients. It contributes to remarkable burden on patient and the hospital. The medical community has poor understandings about conditions and it results broader impact on overall hospital mortality rates. The mortality rates among sepsis patients were 10.4%, compared to 1.1% among non-sepsis patients. Moreover, of all hospital deaths around the U.S, up to 52 % were among sepsis patients. Sepsis also accounted for

nearly 22% of all hospital charges, according to the statement. [12].

It is becoming our National mandate for prevention and control of surgical site infection. Reported data had failed to define the association of decrease in SSI with improvement in surgical care project of administration of prophylactic antibiotics. In a retrospective cohort study, the prophylactic antibiotics were administered at a median of 28 minutes (interquartile range, 17-39 minutes) prior to surgical incision, and 1497 cases (4.6%) developed SSI [13] which is low 42 (5.7%) ($p<0.001$) when compared to surgical site infection in our study. The higher SSI were observed when prophylactic antibiotics were administered one hour after the surgery (unadjusted odds ratio [OR]=1.34; 95% CI, 1.08-1.66) but not after incision (unadjusted OR=1.26; 95% CI, 0.92-1.72) [13] while it was found in 04 (40%) out of 14 (1.7%) population who were administered antibiotics within two hours of the surgery.

The risk of SSI can vary by patient to procedure. It may not be associated significantly with prophylactic antibiotic administration. Instead, following guideline for timely antibiotic administration is not included in bad care. Evidence suggest that it is better care. In SSI, difference in gender can exist and they are procedure specific. We need better understanding of underlying reasons and mechanisms to be further elucidated so that focused preventive measures for SSI can be adopted.

Among older patients, (SSIs) are reported as high as 11% of hospital acquired infections. Patients more than 65 years of age, the chances of SSI is not very high. Amongst elderly and younger patients may risk factors for SSI are similar, but economic status and factors related to health services may differ between the groups. Clinicaly, appearance of infection and micro-organisms responsible for these infection are indistinguishable between old age and young patients. However, when we compared the cost with SSI in elderly versus younger patients, the cost to patients, economic burden to Country, the rate of mortality, the length of hospital stays, and the economic burden accepted by hospital in providing care was high in old age patients [14,15] while in another study it varies with older adolescent 12 to17 years, adult between 18 to 49 years of age and older patient above 70 years [16].

In a retrospective cohort study, SSI are significantly lower for females than in males [odds ratios (95 % confidence intervals) were 0.85 (0.77-0.93), 0.82 (0.74-0.91), and 0.78 (0.68-0.91), respectively] [16] when compared to our study it was found that 32 (8.7%) were male amongst the total and 30 (6.9%) were female's participants. In this cohort, the reason of men with high SSI was associated with higher risk for bloodstream, possibly due to differences in tendency of colonization of skin micro-organism or other anatomical variations.

In abdominal surgery females had a low rate of SSI (SSI/100 procedures than men (2.92 vs. 4.37; $p < 0.001$). No gender-related dissimilarities were accounted in Orthopedics Surgery, while women had a greater risk for SSI in cardiac surgery (5.50 vs. 3.02; $p < 0.001$). When they isolated the pathogens, the differences were noticed. They isolated the difference in sensitive Staph aureus and Pseudomonas aeruginosa. Pseudomonas aeruginosa was more common in females (both $p = 0.007$), while coagulase-negative staphylococci occurred more often in male (18.8 vs. 14.0%; $p < 0.001$).

The studies done at American College of Surgeons and University of Athens Medical School the incidences of SSI were higher in diabetic than non-diabetic [17,18]. The patients with insulin dependent diabetes mellitus were found increased risk. It was found similar in our study that 60 (96.8%) patients who developed SSI were diabetic. The

relationship between steroid intake and SSI was sought in a study done at American College of Surgeon which was (3.2%) [19] Which are quite low as compared to the patient in our study which was (8.3%).

CONCLUSION

We concluded from this study that time of administration of prophylactic antibiotics has association with surgical site infection. Increased time has high rate of SSI while patients with diabetes mellitus, smoking and steroid intake at greater risk of developing SSI.

CONFLICT OF INTEREST

The authors have no conflict of interest.

REFERENCES

1. Horan TC, Gaynes RP, Martone WJ, et al. CDC definitions of nosocomial surgical site infections, 1992: a modification of CDC definitions of surgical wound infections. *Infect Control Hosp Epidemiol.* 1992;13(10):606-608.
2. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol.* 1999;20(4):250-278.
3. Antimicrobial prophylaxis for surgery. Med Lett drugs their 2010;27:105-8.
4. Weinstein RA. Nosocomial infection update. Emerg Infect Dis1998;4:416–20.
5. Burke JP. Patient safety: infection control – a problem for patient safety. N Engl J Med 2003;348:651–6.
6. Health Protection Agency. Surgical site surveillance service, 2005.Available at: www.hpa.org.
7. Perencevich EN, Sands KE, Cosgrove SE, et al. Health and economic impact of surgical site infections diagnosed after hospital discharge. *Emerg Infect Dis.* 2003;9(2):196-203.
8. Altemeir WA, Culbertson WR. Surgical infection. In: Moyer CA, Rhoads JE, Allen JG, Harkins HN, eds. Surgery, principles and practice. Philadelphia: JB Lippincott, 1965:51–77. 3.
9. National Academy of Sciences/National Research Council. Postoperative wound infections: the influence of ultraviolet irradiation of the operating room and of various other factors. Ann Surg 1964; 160(Suppl 2):1–132.
10. Scheel O, Stormark M. National prevalence survey on hospital infections in Norway. J Hosp Infect 1999;41:331–5.
11. Moleski RJ, Andriolee VT. Role of the infectious disease specialist containing cost of antibiotics in the hospital. Rev infect dis 2010;27:105-8.
12. Liu, V.; Lei, X.; Prescott, H. C.; Kipnis, P.; Iwashyna, T. J.; Escobar, G. J.; Hospital readmission and healthcare utilization following sepsis in community settings. J Hosp Med. 2014; 9(8):502-7
13. Mary T. Hawn, MD, MPH; Joshua S. Richman, MD, PhD; Catherine C. Vick, MS; Rhiannon J. Deierhoi, MPH; Laura A. Graham, MPH; William G. Henderson, MPH, PhD; Kamal M. F. Itani, MD. Timing of Surgical Antibiotic Prophylaxis and the Risk of Surgical Site Infection. JAMA Surg. 2013;148(7):649-657.
14. Keith S. Kaye, Kenneth E, Schmader, Robert Sawyer. Surgical Site Infection in the Elderly Population. Clinical Infectious Diseases 2004; 39:1835–41.

15. Keith S. Kaye, Deverick J. Anderson, Richard Sloane, Luke F. Chen, Yong Choi RN, Katherine Link RN, Daniel J. Sexton MD and Kenneth E. Schmader MD. The Effect of Surgical Site Infection on Older Operative Patients. Jour of the American Geriat Soci. Jan 2009; 57 :46–54,
16. Bevin Cohen, Yoon Jeong Choi RN , Sandra Hyman RN, Yoko Furuya , Matthew Neidell, Elaine Larson RN. Gender differences in risk of bloodstream and surgical site infections. jour of general internal medicine,October 2013; 28(10):1318-1325
17. Athanasios Dervisoglou, Helen Giamarellou, Kyriaki Kanellakopoulou, Sotirios Tsiodras, Stamatios Pinis, Stavroula Liveranou, and A. Dervisoglou. Diabetes Mellitus is Associated with Intraoperative Bactibilia and Postoperative Surgical Site Infections in Elective Cholecystectomy: A Case-Control Study; 43 annual meeting; 2005.
18. Ata, Ashar; Valerian, Brian T.; Lee, Edward C.; Bestle, Sharon L.; Elmendorf, Sarah L.; Stain, Steven C. The Effect of Diabetes Mellitus on Surgical Site Infections after Colorectal and Noncolorectal General Surgical Operations. The American Surgeon; 2010;76(7): 697-702(6)
19. Mira Shiloach, Stanley K. Frencher, Janet E. Steeger, Katherine S. Rowell, Kristine Bartzokis, Majed G. Tomeh, Karen E. Richards, Clifford Y. Ko, Bruce L. Hall, Mira Shiloach, Stanley K. Frencher, Janet E. Steeger, Katherine S. Rowell, Kristine Bartzokis, Majed G. Tomeh, Karen E. Richards, Clifford Y. Ko, Bruce L. Hall. Toward Robust Information: Data Quality and Inter-Rater Reliability in the American College of Surgeons National Surgical Quality Improvement Program; American Jour of Surg; 2009:10:6-16.

Table 1. Demographic variables and covariate relationship with surgical site infection.

Covariate	Surgical Site Infection Positive (n=62) (%)	Surgical Site Infection Negative (n=738) (%)	N=800 (Percent)	p-value
Gender				
• Male	32 (51.6%)	333 (45.1%)	365 (45.6%)	0.324
• Female	30 (48.4%)	405 (54.9%)	435 (54.4%)	
Socioeconomic status				
• Lower	53 (85.5%)	640 (86.7%)	693 (86.6%)	0.78
• Middle	09 (14.5%)	98 (13.3%)	107 (13.4%)	
Education				
• Illiterate	04 (6.4%)	99 (13.4%)	103 (12.9%)	0.25
• Under Matric	58 (93.6%)	592 (80.2%)	650 (81.2%)	
• Graduate	00	47 (6.4%)	47 (5.8%)	
Smoking				
• Yes	36 (58.1%)	518 (70.2%)	554 (69.2%)	0.47
• No	26 (41.9%)	220 (29.8%)	246 (30.8%)	
Diabetes Mellitus				
• Yes	60 (96.8%)	665 (90.1%)	725 (90.6%)	0.84
• No	02 (3.2%)	73 (9.9%)	75 (9.4%)	
Wound Type				
• Clean	18 (29.1%)	720 (97.6%)	738 (92.2%)	0.000
• Clean contaminated	32 (51.6%)	16 (2.1%)	48 (06%)	
• Contaminated	03 (4.8%)	02 (0.27%)	05 (0.62%)	
Time of administration of antibiotics	42 (67.7%)	698 (94.5%)	740 (92.5%)	
• Within 01 hours before surgery	04 (6.4%)	10 (1.3%)	14 (1.7%)	0.000
• Within 02 hours before surgery	16 (25.8%)	30 (4.1%)	46 (5.7%)	
• Within 03 hours before surgery				
Steroid Intake				
• Yes	03 (14.5%)	35 (4.7%)	38 (4.8%)	0.973
• No	59 (85.5%)	703 (95.3%)	762 (95.2%)	

Table 2: Cross tabulation of surgical site infection with time of administration of antibiotics

	Surgical Site Infection		Total	pvalue*
	Yes (n=738) (%)	No (n=62) (%)		
Time of administration of antibiotics				
• Within 01 hour before surgery	698 (94.5%)	42 (67.7%)	740 (92.5%)	0.001
• Within 02 hour before surgery	10 (1.3%)	04 (6.4%)	14 (1.7%)	0.667
• Within 03 hour before surgery	30 (4.1%)	16 (25.8%)	46 (5.7%)	0.001

Table 3: Odd ratio and confidence interval of time of administration of antibiotics and surgical site infection

Surgical site infection and Time of administration of antibiotics (TAA)	Odd ratio with 95% confidence interval	pvalue*
Duration		
• TAA 1	8.9 **[**4.5, 17.5]	0.000
• TAA 2	1.3[0.4, 4.9]	0.667
• TAA 3		
Gender		
• TAA 1	9.2 [4.6, 18.4]	0.000
• TAA 2	1.4 [0.38, 5.35]	0.593
• TAA3		
Socioeconomic Status		
• TAA 1	0.92[058, 1.4]	0.727
• TAA 2	9.2[4.6, 18.5]	0.000
• TAA3		
Education		
• TAA 1	9.2[4.6, 18.5]	0.000
• TAA 2	1.3[0.35, 5.1]	0.656
• TAA3		
Smoking		
• TAA 1	8.6[4.2, 17.6]	0.000
• TAA 2	1.4[0.35, 5.2]	0.647
• TAA3		
Diabetes Mellitus		
• TAA 1	9.2[4.6, 18.6]	0.000
• TAA 2	1.5[0.39, 5.5]	0.574
• TAA3		
Wound type		
• TAA 1	8.7[4.3, 17.7]	0.000
• TAA 2	1.5[0.39, 5.7]	0.561
• TAA3		
Steroid use		
• TAA 1	8.7[4.3, 17.7]	0.000
• TAA 2	1.5[0.39, 5.7]	0.564
• TAA3		