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Effect of Perioperative Antibiotic Prophylaxis on Surgical Site Infections Complicating Conventional Cardiothoracic Surgery

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ABSTRACT

Background: Surgical site infections (SSIs) are known to be the third most common type of nosocomial (hospital acquired) infections and represent about 17% of their total incidence. The perioperative antibiotic prophylaxis (PAP) is an effective method for the prevention of surgical site infections (SSIs) because the vast majority of SSIs are caused by endogenous translocation of the patient's own microbiota. The use of perioperative antibiotic prophylaxis results in reduction of the total number of postoperative infections. In cardiothoracic surgery, the surgical site infections incidence is about 0.4-4%. Despite the marked advances in modern cardiothoracic surgical techniques and the use of pre-operative antibiotic prophylaxis, and careful wound treatment, surgical-site infections (SSIs) remain a dangerous and sometimes a lethal post-operative complication of cardiothoracic surgery operations.

Aim of the study: This study aimed to compare and evaluate the difference between the outcome of the patients who didn't receive pre-operative antibiotic prophylaxis prior to elective adult conventional cardiothoracic surgery (Group A) with those patients who received pre-operative antibiotic prophylaxis (Group B) regarding the occurrence of post-operative wound infection, wound complications, patient's outcome, length of hospital stay and other post-operative complications.

Patients and methods: This study was a single-center retrospective observational and comparative study, conducted on 500 adult patients scheduled for elective conventional cardiothoracic surgery operations at the Cardiothoracic Surgery Department, Tanta University Hospitals through the period from January 2018 to January 2023. The studied patients were divided into two groups according to their peri-operative management: (Group A): 250 patients who didn't receive pre-operative antibiotic prophylaxis and (Group B): 250 patients who received pre-operative antibiotic prophylaxis.

Results: The mean ICU duration was 3.05 ± 2.18 days and the mean duration of the cardiothoracic operation was 208.03 ± 55.37 minutes. Among the studied patients there were 26 patients (5.2%) who had transient psychotic syndrome and 2 patients (0.4%) who had peri-operative myocardial infarction. There were 15 patients (3%) who died. There was a statistically significant correlation between the occurrence of postoperative infection and the incidence of post-operative patients' mortality.

Conclusions: The use of perioperative antibiotic prophylaxis in cardiothoracic surgical patients was associated with significant reduction of postoperative wound infection. Most common cause in SSI after cardio-thoracic surgery was deep sternal wound infection. There was a significant corelation between SSI and post-operative mortality incidence in the patients undergoing elective cardio-thoracic surgery.

Keywords: Surgical site infections, Preoperative antibiotic prophylaxis, Conventional thoracic surgery, Postoperative infections.

INTRODUCTION

Despite the use of modern surgical techniques, the use of preoperative antibiotic prophylaxis, and careful wound management, surgical-site infections (SSIs) remain a dangerous and sometimes a lethal complication of cardiothoracic surgery, with an incidence of about 0.4% to 4% [(1)]. As the surgical site is a potential port for entry of pathogenic organisms, it comprises a dangerous threat to the body and infections leading to prolonged and delayed surgical wound healing [(2)].

The Centers for Disease Control and Prevention (CDC) define a SSI as an infection that happens within 30–90 days after a surgical operation. Superficial incisional SSIs are defined as occurring within 30 days after surgery [(3)]. SSI prophylaxis in surgical medicine includes a wide range of several preventive pre-, intra- and post-operative measures. Due to the specificity and the high risk of most cardiothoracic operations, the standard peri-operative management protocol involves many elements that are characteristic of these types of operations, such as: pre-operative optimization of the patient's general condition, pre-operative patients screening and staphylococcus aureus de-colonization, surgical site preparation, antibiotic prophylaxis, topical antibiotic therapy and negative pressure wound therapy [(4)].

The pre-operative phase is considered to be the most crucial period of a cardiothoracic surgical procedure in which the major goal is to decrease the bacterial load that is surrounding the planned incision area. The use of antibiotics prior to a surgical incision is considered to be an effective method in preventing SSIs, which are among

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the most common preventable post-operative complications [5].

The parenteral use of prophylaxis via a broad-spectrum antibiotic has been recently recommended to reduce the SSI rates significantly [6]. In contrast, some pre-operative procedures, such as local hair removal and mechanical bowel preparation are considered today to be not enough and inefficient at reducing the rate of SSIs [7]. However, the appropriate surgical prophylaxis is a multi-factorial method that depend on the proper case selection, the antibiotic selection, the dosing and the way of administration, the duration of therapy, and, for long duration procedures, intra-operative dosing also [8].

The aim of this study was to compare and evaluate the difference between the outcome of the patients who received pre-operative antibiotic prophylaxis prior to elective adult conventional cardiothoracic surgery with those patients who didn't receive pre-operative antibiotic prophylaxis regarding the occurrence of post-operative surgical wound infection, wound complications, patient's outcome, length of hospital stay and the other post-operative complications.

PATIENTS AND METHODS

This retrospective observational study was conducted on 500 adult patients scheduled for adult conventional cardiothoracic surgery operations at the Cardiothoracic Surgery Department, Tanta University Hospitals between January 2018 and January 2023. The studied patients were divided into two groups: Group A included 250 patients who received preoperative antibiotic prophylaxis and group B that contained 250 patients who didn't receive preoperative antibiotic prophylaxis. The standard surgical procedure was performed for each patient included in the study.

Inclusion criteria: Adult patients scheduled for elective conventional thoracic surgery operations as decortication operation, lobectomy, pneumonectomy, thymectomy, bullectomy and diaphragmatic hernia repair via thoracotomy. Also, cardiac surgery operations as cardiac valve surgery including mitral, aortic and tricuspid valve surgeries and coronary artery bypass grafting surgery.

Exclusion criteria: Patients under the age of 18 years, patients undergoing Mini thoracotomy, and/or those operated on via minimally invasive video assisted thoracoscopic surgery (VATS), patients in septic shock, immuno-compromised patients as patients in severe cachexia, HIV patients and the patients receiving chemotherapy.

METHODS OF THE STUDY

The following data about each patient were collected: Baseline patients' demographic data, personal history, physical examination, routine pre-operative laboratory tests, echocardiography, computed tomography (CT) scan and coronary angiography in each group of patients.

The 250 patients in group A didn't receive preoperative antibiotic prophylaxis prior to the scheduled operation, whereas the 250 patients in group B received the preoperative antibiotic prophylaxis within 2 hours prior to the start of the scheduled surgical procedure in the form of intravenous injection of 3rd generation cephalosporins antibiotics as cefepime, ceftriaxone, ceftazidime at a dose of 1 gm and repeated every 8 hours at regular time intervals.

During hospitalizations, the patients were daily evaluated by the cardiothoracic doctors and 2-3 times per week by the infection control nurse. No mass screening using cultures was done but cultures were obtained as clinically indicated and were processed in the hospital's clinical pathology laboratory. All the patients were also followed up for the appearance of post-discharge SSIs with a minimum of 2 visits, with the first scheduled 1 week after discharge from the hospital and the second 4 weeks later. A follow-up was performed in the hospital's cardiothoracic surgery outpatient clinics. The patients who had pneumonectomy and thymectomy were followed up for about 12 months. Twenty-four patients who did not return to the outpatient clinic were contacted by phone by the infection control nurse. The definitions of the Centers for Disease Control and Prevention were used throughout [9]. Because distinguishing between deep chest wound infection and mediastinitis is not always easy, we analyzed deep infections and organ space infections together (deep/organ space infections). Infecrive endocarditis was defined according to the Duke criteria [10]. SSIs were stratified according to the National Health Safety Network (NHSN) [11].

Selection of perioperative antibiotics:

The choice of perioperative prophylactic antibiotics depends on the most common pathogens likely to cause SSI, which depends on the surgical procedure. In cardiothoracic surgery bacteria from normal skin and respiratory flora are the common cause of SSIs. This includes Staphylococcus Aureus, coagulase negative staphylococci, Streptococcus Pneumoniae, and gram-negative bacilli, with S. Aureus are the most frequently identified bacterial pathogens. Cephalosporins provide adequate coverage for these organisms and are an effective class of broad spectrum antibiotics for infection prophylaxis in cardiothoracic surgery [12].

The duration of perioperative antibiotic prophylaxis:

There is general consensus that perioperative prophylactic antibiotics should be stopped within 24 hours of most major surgical operations. There are important reasons why open heart surgery operations have a higher predisposition to infective complications. These have been summarized in a report from the Society of Thoracic Surgeons Work-force on Evidence-Based Surgery on the duration of antibiotic perioperative prophylaxis in cardiac surgery. Potential risk factors for the occurrence of infection include cardiopulmonary bypass, that impairs humoral immunologic defences and causes degradation of clotting factors, systemic hypothermia, the use of chest tubes and central lines that give an external routes for bacterial entry, the use of deep hypothermic circulatory arrest, which lowers the immune function, the longer duration of operation, practice of delayed sternal closure, the need for extra-corporeal life support, the longer duration of chest tube drainage, and sometimes the prolonged central venous access for parenteral nutrition. Several cardiothoracic surgeons consider their patients to be at a high risk of infection and employ prolonged antibiotic prophylaxis until all chest tubes and central intravenous lines are removed [(13)]. In our study the duration of perioperative prophylactic antibiotics ranged from 3-7 days, according to the postoperative patients outcome.

Study outcomes: Occurrence of fever, presence of post-operative wound infection, the occurrence of leukocytosis, the need for secondary surgical sutures and the need for surgical wound debridement were compared between the two groups.

Ethics of the study: In accordance with The Declaration of Helsinki developed by the World Medical Association as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data. The approval from The Ethical Committee was obtained {Tanta Ethical Committee approval code (36251/12/22)}. Informed written consents were taken from patients after explanation of benefits and risks. Any unexpected risk appeared during the course of the study was cleared to the patients and the ethical committee on time. The proper measures were taken to overcome these risks. There was adequate provision to maintain privacy of participants' confidentiality of data through putting a code number for each participant from the beginning to the end of the study. The results of this research were used only for scientific purposes.

Statistical analysis

Using SPSS 26.0 for Windows (SPSS Inc., Chicago, IL, USA), all study data have been gathered, tabulated, & statistically analyzed. Numbers & percentages had been used to express qualitative data. The range (minimum & maximum), mean, standard deviation, & median had been used to characterize quantitative data. Every statistical comparison used a 2-tailed significance test. P-value ≤ 0.05 indicated substantial differences, while $p > 0.05$ denotes insignificant ones. The Chi-square (X^2) test of significance was used for comparing proportions among qualitative parameters and the independent T-test was used to compare two independent groups with parametric quantitative data.

RESULTS

Table (1) showed that the mean age of the studied patients was 68.87 ± 9.47 years with a range between 52 and 85 years. There were 128 female patients (25.6%) and 372 male patients (74.4%). There were 140 patients (28%) with DM, 287 patients (57.4%) with HTN, 58 patients (11.6%) with COPD, 45 patients (9%) with obesity and 8 patients (1.6%) with drug abuse. There were 5 patients (1%) who were put on pre-operative mechanical ventilation and 11 patients (2.2%) who had intra-aortic balloon pulsation.

Table (1): Distribution of the studied cases according to Baseline patients' demographic data

	Cases (n = 500)	
Age		
Range.	52 – 85	
Mean ± SD.	68.87 ± 9.47	
Sex		
Female	128	25.6
Male	372	74.4
Co-morbidities		
Diabetes	140	28.0
Hypertension	287	57.4
COPD	58	11.6
Obesity	45	9.0
Drug abuse	8	1.6
Pre-operative mechanical ventilation	5	1.0
IABP	11	2.2

Table (2) showed that among the studied patients there were 397 patients (79.4%) with elective operation, 69 patients (13.8%) with urgent operation and 34 patients (6.8%) with emergency operation. 100 patients (20%) had isolated CABG operation, 20 patients (4%) had

combined surgery (CABG + valve surgery), 130 patients (26%) had valve surgery, 100 patients (20%) with lung resection surgery, 100 patients (20%) had decortication operations and 50 patients (10%) had surgical fixation of rib fractures. The mean duration of the cardiothoracic operations was 208.03 ± 55.37 minutes with a range of 117-307 minutes. The mean duration of cardiopulmonary bypass time was 95.27 ± 29.83 minutes with a range of 43-147 minutes and the mean duration of the aortic cross-clamp time was 69.49 ± 29.87 minutes with a range of (13-124 minutes).

Table (2): Distribution of the studied patients according to the surgical data

	Cases (n = 500)	
State of operation		
Elective	397	79.4
Urgent	69	13.8
Emergency	34	6.8
Type of procedure		
isolated CABG	100	20.0
CABG + valve surgery	20	4.0
Valve surgery	130	26.0
Lung resection (Wedge resection, lobectomy, pneumonectomy)	100	20.0
Decortication	100	20.0
Surgical fixation of rib fractures	50	10.0
Operating time (min)		
Range.	117 – 307	
Mean ± SD.	208.03 ± 55.37	
Cardiopulmonary bypass time (min)		
Range.	43 – 147	
Mean ± SD.	95.27 ± 29.83	
Aortic cross-clamp time (min)		
Range.	13 – 124	
Mean ± SD.	69.49 ± 29.87	

Table (3) showed that the mean ICU duration was 3.05 ± 2.18 days with a range of 0-7 days. There were 26 patients (5.2%) who had transient psychotic syndrome and 2 patients (0.4%) who had peri-operative myocardial infarction.

Table (3): Distribution of the studied patients according to the surgical outcome

	Cases (n = 500)	
ICU duration (days)		
Range.	0 – 7	
Mean ± SD.	3.05 ± 2.18	
Complications		
TPS	26	5.2
Periop. MI	2	0.4

Table (4) showed that there were 7 patients (1.4%) had deep sternal wound infection, 13 patients (2.6%) had superficial sternal wound infection, 3 patients (0.6%) had vein harvesting site infection, 20 patients (4%) had respiratory tract infection and 32 (6.4%) had urinary tract infection with a total number of 75 patients (14%) who had post-operative infection. There were 15 patients (3%) who died.

Table (4): Distribution of the studied patients according to post-operative infection

	Cases (n = 500)	
Infection	75	14.0
Primary endpoints		
DSWI (deep sternal infection)	7	1.4
SSWI (superficial sternal infection)	13	2.6
VHSI (vein harvesting site infection)	3	0.6
Secondary endpoints		
Respiratory tract infection	20	4.0
Urinary tract infection	32	6.4
Mortality	15	3.0

Table (5) showed that there was a statistically significant correlation between the occurrence of post-operative infection and mortality.

Table (5): Relation between post-operative infection and mortality

	Infection				χ^2	**p**
	Yes		**No**			
	No.	%	No.	%		
Mortality	6	8.6	9	2.1	8.682	0.003*

χ^2: **Chi square test**, p: p value for comparing between studied groups, *: Statistically significant at $p \leq 0.05$

DISCUSSION

The results of our study revealed that the mean age of the studied patients was 68.87 ± 9.47 years. There were 128 female patients (25.6%) and 372 male patients (74.4%). There were 140 patients (28%) had diabetes mellitus (DM), 287 patients (57.4%) had hypertension (HTN), 58 patients (11.6%) had chronic obstructive pulmonary disease (COPD), 45 patients (9%) had obesity and 8 patients (1.6%) had a history of drug abuse. There were 5 patients (1%) had pre-operative mechanical ventilation and 11 patients (2.2%) had intra-aortic balloon pump. Also, our results revealed that there were 100 patients (20%) had isolated coronary artery bypass grafting (CABG) surgery, 20 patients (4%) had combined cardiac surgery (CABG + valve surgery), 130 patients (26%) had isolated valve surgery, 100 patients (20%) had lung resection surgery, 100 patients (20%) had decortication operations and 50 patients (10%) had surgical fixation of rib fractures. The mean duration of the operation was 208.03 ± 55.37 minutes. In open heart surgery cases, the mean duration of cardiopulmonary bypass was 95.27 ± 29.83 minutes and the mean duration of aortic cross-clamp time was 69.49 ± 29.87 minutes. In addition, our results demonstrated that the mean ICU stay duration was 3.05 ± 2.18 days. There were 26 patients (5.2%) had transient psychotic syndrome and 2 patients (0.4%) had peri-operative myocardial infarction. Also, among the studied cases there were 7 patients (1.4%) who had deep sternal wound infection, 13 patients (2.6%) had superficial sternal wound infection, 3 patients (0.6%) had vein harvesting site infection, 20 patients (4) had respiratory tract infection, 32 patients (6.4%) had urinary tract infection with total number of 75 patients (14%) who had post-operative infection. There were 15 patients (3%) died. Also, there was a statistically significant correlation between the occurrence of surgical site infection and the incidence of post-operative mortality.

The results of our study are in agreement with the results of the study done by **Segers *et al.*** [(14)] who found that the mean patients age was 65.1 years, and 90 patients were males and 77 patients were females who were included in the study to assess the risk control of the surgical site infection after conventional cardio-thoracic operations. They also reported that the mean total hospital stays for the patients suffering from SSI was 18.8 days, and the mean intensive care unit (ICU) stay for the patients suffering from SSI was 3.6 days. 21 patients out of 167 patients died (12.5%). In 8 patients, all diagnosed with mediastinitis, the primary cause of death was SSI (4.8%), and 7 of these patients died from multi-organ failure due to sepsis, 1 patient died due to bleeding from the ascending aorta caused by aortitis and the other patients died because of non-surgical causes after discharge. Significant factors that determine the patient's survival after SSI were: EuroSCORE (P=0.007), duration of surgical procedure (P=0.01) and prolonged need for cardiac support (P=0.007). They reported that SSI increased the mortality risk after cardio-thoracic surgery.

The results of our study are in agreement with the results of the study done by **Finkelstein *et al.*** [(8)] who found that there were 1,942 male patients (73.6%), and the mean age was 63.1 ± 11.8 years. They reported a significant positive effect of the use of preoperative antibiotic prophylaxis on the reduction of surgical site infections complicating cardiac surgery. Also, In 2015, a meta-analysis of 14 studies with 22135 patients demonstrated a significant risk reduction for sternal wound infection using implantable local gentamicin-impregnated collagen sponges [(15)]. Otherwise, in a large randomized study of 1502 cardiac surgical patients at 48 United States sites, these findings could not be confirmed [(16)].

The results of our study are in agreement with the results of the study done by **Schimmer *et al.*** [(17)] who found that the mean patients age was 67.7 ± 9.4 years, 18.6% of the studied patients were women, the mean body mass index (BMI) was 28.4 ± 7.4 kg/m^2 and 94.2% had a left ventricular ejection fraction (LVEF) of > 30% pre-operatively. They also found that all the 996 studied patients underwent isolated elective or urgent CABG ,the mean operation duration was 243.9 ± 79.3 minutes, the mean duration of cardiopulmonary bypass time (CPB) was 105.2 ± 63.6 minutes and the mean aortic cross-clamping time was 70.4 ± 35.1 minutes. They also found that the mean duration of mechanical ventilation post-operatively was 21.1 ± 52.4 hours, the mean bleeding volume was 1201 ± 876 ml and there was 10.5 % of the studied patients had transient psychotic syndrome and the overall SSI rate of the sternum was 6.2% and the overall rates of superficial and deep SSI were 5.2% & 2.2% respectively. They also found that there was a significant positive correlation between the mortality rate and the occurrence of post-operative deep sternal wound infection (P value = 0.04).

The results of our study are in agreement with the results of the study done by **Marti *et al.*** [(18)] who found that there was no difference in the incidence of SSI with the use of either 1st generation of Cephalosporin or Glycopeptides such as Vancomycin or Teicoplanin. Also, they found that, the use of 1st generation Cephalosporin reduces the incidence of postoperative iinfections caused by Staphylococcus. Whereas, the use of Glycopeptides is better at avoiding postoperative infection caused by Staphylococcus and Enterococcus than Cephalosporin.

Study limitations: The limitations of our study were the relatively small sample size of the study, being a retrospective single center study, the lack of long term follow up for the patients with SSI for re-operation or surgical interventions and the lack of preoperative

patients screening based diagnosis of the patients' own microbiota.

CONCLUSION

The use of perioperative antibiotic prophylaxis in cardiothoracic surgical patients is associated with significant reduction of the occurrence of post-operative surgical site infections and significant reduction of the incidence of post-operative patients' mortality.

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