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Impact of Different Prophylactic Antibiotic Regimen on Clinical Outcome of Coronary Artery Bypass Graft Surgery

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Abstract

Background: Prevention of surgical site infection is the first concern in cardiac surgery. Deep sternal infection causes death in patients and increases the length of hospitalization and the cost of treatment. Several therapeutic protocols have long been used by cardiac surgeons for antimicrobial prophylaxis. The aim of this study is to evaluate the clinical outcomes of prescribing different antibiotic prophylaxis in patients undergoing coronary artery bypass graft surgery.

Methods: In this prospective cross-sectional study, 200 patients with a mean age of 60 ± 9.5 years (145 male, 55 female) undergoing elective isolated coronary artery bypass graft (CABG) were enrolled. Post-operative infections, renal and pulmonary complications, the incidence of mortality, length of stay in ICU and hospital were compared and evaluated based on the type of prophylactic antibiotics.

Results: Among the studied subjects, 145 patients (72.5%) were males and 55 patients (27.5%) were female. There was no significant relationship between the administration of antibiotic prophylaxis and renal complications, pulmonary complications, wound infections, mortality, and the mean hospitalization time (P = 0.04). Only the association between clindamycin antibody and mortality rate was statistically significant (P = 0.049). The average duration of admission to the ICU in patients receiving cefazolin antibiotics was significantly lower than those who did not receive this antibiotic (P value = 0.04).

Conclusions: We can conclude that the use of different prophylactic antibiotics in isolated CABG patients, according to the physician's personal preference or experience, does not essentially result in better clinical outcomes and less wound complications and infections. Approved protocol for prophylactic antibiotics was only addressed in half of CABG patients.

Keywords: Antibiotic Prophylaxis, Prescription Pattern, Coronary Artery Bypass Graft, Clinical Outcome of Antibiotic Use

1. Background

Surgery site infection (SSI) is the second most common cause of nosocomial infections and is the most common cause of death after surgery (1, 2). Although surgeons follow a certain protocol for antibiotic therapy after open heart surgeries, due to the potentially hazardous post cardiac surgery infections, the duration and type of prophylactic antibiotic remains a controversial challenge (3, 4). Surgical site infection has always been an expensive and uncomfortable problem, and in particular, cardiovascular surgery may have devastating consequences and can occur as an infectious problem in 3-10% of cases (5). Wound infection is associated with side effects in heart surgery and increases the cost of health care (6). In a 2003 study, Bhatia et al reported that between 2% - 20% of patients are susceptible to surgical site infections after heart surgery (7, 8). The mortality rate associated with mediastinitis is estimated to be between 7% - 20% and mortality in patients with superficial sternum infection is estimated in more than 5% of cases (9). Although the rate of post-operative infection in open heart surgery patients is relatively low but may be life-threatening, and doctors have to use antiprophylaxis microbial complementary to surgical methods (10). However, the widespread abuse of prophylactic antibiotics, which mainly involves 50% of the use of antimicrobials in hospitals, has led to changes in the microbial flora in hospitals and the pattern of microbial resistance in the world. Therefore there is a general movement towards the use of shorter periods of antibiotics for sur-

gical prevention in order to reduce toxicity, cope with antibiotic resistance and reduce costs (3, 11). There is no theoretical agreement on the choice of prophylactic antibiotic type, whether single dose or multiple dose or the accurate time of administration (9).

2. Methods

From June to December 2015, 200 patients undergoing coronary artery bypass graft surgery (CABG) in Rajaei cardiovascular medical and research center who were over 18 years of age and had signed a written consent, were selected. Patients with underlying infectious diseases, those who had concomitant heart valve surgery, needed a re-exploration after CABG, were already taking antibiotics for any reason and patients with renal failure or immune suppressive state were excluded from the study. In our center we already do have a certain protocol for prophylactic antibiotic including Cefazolin 2 g just after anesthetic induction and then 4 - 6 g per day based on patient's body surface area and creatinine level for 48 hours or chest drain removal (Either one that happens sooner). However in special situations some surgeons may have certain concerns about the patient's condition and may not follow the protocol exactly and alter the type of medications in this study we left it open so that surgeons could have the ability to decide about the alternative treatment methods and studied the results. All required data containing demographic data (age, gender, BMI, Pre-op LVEF, creatinine level and past medical history), intra-operative details (including CBP time, aortic cross-clamp time, intra-operative blood product transfusion and need for re-explorations), early post-operative data (including ICU stay, hospitalization, mechanical ventilation time, blood product transfusions, prophylactic antibiotic types and doses and drug reactions) and early mortality and morbidity (including acute kidney injuries, pulmonary complications, liver dysfunctions, wound infections and cerebrovascular events) were recorded.

Data were analyzed by IBM SPSS Statistics for Windows software, version 21. (IBM Corp. Released 2012. IBM SPSS Statistics for Windows, version 21.0. Armonk, NY: IBM Corp.). Mean ± standard deviation were used to summarize the descriptive variables. P values less than 0.05 was considered significant. Categorical variables were presented as frequencies and percentages. Continuous variables were presented as means and standard deviations.

3. Results

The mean age of patients who entered this study was 60 ± 9.5 years, ranged 25 - 83. Among these 200 patients, 145 patients (72.5%) were male and 55 patients (27.5%) were female. The mean body mass index was 27 ± 4.0 (ranged from 16 to 51). Elective CABGs were done on 183 patients (91.5%) and 17 patients (8.5%) underwent emergent operations (Table 1). Diabetes mellitus was the most common comorbidity (46%) followed by COPD (12%) (Table 2).

Table 1. Descriptive Statistics of Research Samples Based on Demographic Data

Variables	Mean ± SD	Range
Age, y	60 ± 9.5	25 - 83
BMI, %	27 ± 4.0	16 - 51
Pre-op Hemoglobin, mg/dL	13 ± 1.4	9 - 19
Pre-op Creatinine, mg/dL	0.8 ± 0.27	0.5 - 2.7
Pre-op BUN, mg/dL	16 ± 6.7	10 - 70
Pre- op LVEF, %	41 ± 9.9	15 - 60

Table 2. Relative Frequency of Underlying Diseases

Underlying Diseases	No. (%)
None	175 (87.5)
DM	92 (46)
Controlled	62 (31)
Poor controlled	30(15)
Esrd	1 (0.5)
Copd	24 (12)
Old age (> 70)	
Morbid obesity	

About half of patients (102 patients) received one type of antibiotic and the others received more than 1 type of antibiotic. Cefazolin was the most common prophylactic antibiotic (46.5%). Based on some surgeons' preferences 24% of patients received an additional single dose of Vancomycin (1g) besides Cefazolin as the first dose in ICU. Ceftriaxone and Vancomycin was the most common combined antibiotic therapy (23%). Patients received their prophylactic antibiotic for an average of 4 days. Table 3 demonstrates the relative frequency distribution based on different prophylactic antibiotic regimen.

The mean length of stay in the ICU was 3.6 ± 1.3 (2 - 13 days) in the ICU. The mean hospital stay was 11 ± 3.9 (7 - 29 days). More than half of patients received at least one unit of blood transfusion products (69.5%). Details of the post-operative findings are shown in Table 4.

Of the 200 cases that were included in this study, 23 patients (11.5%) had wound infections, of which 18 (9%) had superficial wound infections and 5 (2.5%) had deep wounds.

Table 3. Relative Frequency of Different Prophylactic Antibiotic Regimen

Type of Antibiotic	No. (%)
Cefazolin	93 (46.5)
Cefazolin + Single dose Vancomycin	48 (24)
Ceftriaxone + Vancomycin	46 (23)
Ceftriaxone	9 (4.5)
Ceftriaxone + Clindamycin	2 (1)
Cefazolin + Ciprofloxacin	1 (0.5)
Clindamycin + Ciprofloxacin	1 (0.5)

Table 4. Post-Operative Findings[a]

Variables	Values
Post-op Creatinine	1 ± 0.4
Post-op BUN	19 ± 8.6
CPB time	83 ± 27
AOX	45 ± 41
Post-op transfusion, units (mean)	
PC	1.3 ± 1.2
FFP	1 ± 1
Plt	0.5 ± 0.9
Post-op Mediastinal bleeding, cc (mean)	376 ± 260
Intubation time, h (mean)	11.9 ± 12.7
ICU stay, d (mean)	3.5 ± 1.3
Hospitalization, d (mean)	11.2 ± 3.9

Abbreviations: AOX, Aortic cross-clamp; BUN, blood urea nitrogen; CPB, cardiopulmonary bypass; FFP, fresh frozen plasma; ICU, intensive care unit; PC, packed cell; Plt, platelets.
[a]Values are expressed as mean ± SD.

Using chi-square test, there was no significant relationship between prescriptive antibiotics and administration of an antibiotic or more than one antibiotic and the incidence of wound infection in patients (P = 0.207).

Using statistical t-test showed that the average duration of hospitalization in the intensive care unit in patients receiving cefazolin antibiotics was significantly lower than those who did not receive this antibiotic (P value = 0.047). However, ICU stay was not affected by other prophylactic antibiotics. It has also been shown than the mean hospital stay was significantly higher in patients receiving ciprofloxacin (P value = 0.049) than those who received other antibiotics. However, there was no significant relationship between the mean hospital stay and other prescriptive antibiotics (Table 5).

In-hospital mortality rate was 2.5%. Despite the fact that all dead patients received a wide spectrum of combined prophylactic antibiotics, interestingly all of them had pulmonary infection in their hospitalization. Diabetic mellitus and COPD were the most common underlying diseases. Table 6 shows the clinical characteristics of these patients.

We could not also find any significant relationship between the type and length of prophylactic antibiotics administration and deep sternal wound infection (Table 7).

Table 5. Post-Operative Mortality and Morbidity

Variables	Single Antibiotic	Combination Therapy	P Value
Mortality (30 days), %	1 (1.0)	4 (4.1)	0.20
AKI	9 (8.7)	13 (13.4)	0.29
Need for Hemodialysis	1 (1.0)	0	0.33
Pulmonary complications	10 (9.7)	13 (13.4)	0.41
Drug reactions	None	None	-
Need for surgical re-explorations	2 (1.9)	5 (5.2)	0.26
Wound infection	9 (8.7)	14 (14.4)	0.20
Superficial	7 (6.8)	11 (11.3)	
Deep	2 (1.9)	3 (3.1)	
CVA	0	1 (1.0)	0.48
Hepatic insufficiencies	None	None	-

Abbreviations: CVA, cerebrovascular accident; KI, acute kidney injury.

4. Discussion

Although the rate of post-operative infection in open heart surgery patients is relatively low but may be life-threatening, and the cardiac surgeons routinely use prophylactic antibiotic complementary to surgical methods (10). However, the widespread abuse of prophylactic antibiotics, which mainly involves 50% of the use of antimicrobials in hospitals, has led to changes in the microbial flora in hospitals and the pattern of microbial resistance in the world (12, 13). Therefore there is a general movement towards the use of shorter periods of antibiotics for surgical prevention in order to reduce toxicity, cope with antibiotic resistance and reduce costs (3, 11).

In the current study, the pattern of administration and use of prophylactic antibiotics and its clinical implications on patients undergoing CABG in Rajaie Cardiovascular, Medical and Research Center were studied. Surprisingly only half of the patients received their prophylactic

Table 6. Clinical Characteristics of Mortality Patients

Characteristics	Patients				
	1	2	3	4	5
Age	63	56	69	60	49
Gender	M	M	M	M	M
BMI	27	24	28	31	22
Type of Surgery	Elective	Emergent	Elective	Elective	Elective
Underlying Diseases	ESRD	No	DM + COPD	COPD	DM
Pre-op Cr	2.7	1.3	0.8	1	0.8
Pre-op LVEF, %	55	40	25	35	25
CPB Time, min	96	106	98	125	85
AOX, min	48	55	48	74	52
Prophylactic Antibiotics	Ceft + Clinda	Cefa + Vanco	Cefa + Vanco	Cefa + Vanco	Cefa + Cipro
AKI	-	Yes	Yes	Yes	No
Pulmonary Infection	No	Yes	Yes	Yes	Yes
Packed Cell (Unit No)	5	4	2	3	0
FFP (Unit No)	3	4	3	2	0
Volume of Bleeding, cc	1800	950	300	600	250
Re-Exploration	Yes	Yes	No	Yes	No
Intubation Time, h	9	168	2	17	12
Sternal Infection	No	No	No	Superficial	Deep
ICU Stay, d	4	9	6	13	7
Hospital Stay, d	7	24	7	29	27

Abbreviations: AKI, acute kidney injury; AOX, aortic cross clamp; BMI, body mass index; Cefa, Cefazolin; Ceft, Ceftriaxone; Cipro, Ciprofloxacin; Clinda, Clindamycin; CPB, cardio-pulmonary bypass; Cr, Creatinine; FFP, fresh frozen plasma; ICU, intensive care; LVEF, Left ventricle ejection fraction; Vanco, Vancomycin.

antibiotic based on the hospital protocol and about 50% had a combination antibiotic prophylaxis. In this study, there was no statistically significant relationship between the different prophylaxis antibiotics in patients and the incidence of wound infections in these patients. The same result was evident in previous studies, Harbarth showed that the combined or prolonged prophylactic antibiotic strategy, not only cannot reduce the incidence of post-op sternal infections but also may increase the resistance of bacteria (11). The mean duration of antibiotic administration was 4 days in current study that was longer than the approved hospital protocol and most of the previous study recommendations (11-13).

There were no statistic relationship between the prescribed antibiotic and patients' preoperative characteristics including age, gender, BMI, underlying disease, so the surgeons' preference and concern about the potential infectious complication was the most important issue in choice of antibiotics. Meanwhile the type of prophylactic antibiotic was not the independent predictor of deep sternal wound infection or in-hospital death.

Also, there was no significant relationship between the prophylactic antibiotic type and the incidence of pulmonary infections. The incidence of acute kidney injury (AKI) was relatively higher in patients who received combined prophylactic antibiotics (13.4% vs 8.7%) however this difference was not statistically significant in our study. Pulmonary infection and low output syndrome were the leading causes of early mortality.

In this study 9 patients received only ceftriaxone as prophylaxis, that could be a good choice because of poor staphylococcus coverage but these cases had no excessive infections.

The ICU stay was overall one day less in patients who received cefazolin as prophylaxis antibiotic than the others (P = 0.47) that may also reflect surgeons' concerns about a higher risk of infection in other patients' postoperative course. Moreover patients who need mediastinal

Table 7. Clinical Characteristics of Patients with Mediastinitis

Characteristics	Patients				
	1	2	3	4	5
Age	50	51	63	78	49
Gender	F	M	M	F	M
BMI	23	30	22	31	22
Type of Surgery	Elective	Elective	Elective	Elective	Elective
Underlying Diseases	No	No	DM	DM	DM
Pre-op Cr	0.6	0.9	0.9	0.8	0.6
Hemoglobin, g/dL	13	13.4	14.9	13	13.1
CPB Time, min	57	60	100	65	85
AOX, min	30	28	45	32	52
Prophylactic Antibiotics	Ceft + Vanco	Ceft + Vanco	Cefa + Vanco	Cefa	Cefa
AKI	No	No	No	No	No
Pulmonary Infection	No	No	No	No	Yes
Packed cell (Unit No)	0	0	0	1	0
FFP (Unit No)	0	0	0	0	0
Volume of Bleeding, cc	100	550	250	200	250
Re-Exploration	No	No	No	No	No
Intubation Time, h	7	10	13	10	12
ICU Stay, d	5	7	4	6	7
Hospital Stay, d	13	28	10	13	27
Mortality	No	No	No	No	Yes

Abbreviations: AKI, acute kidney injury; AOX, aortic cross clamp; BMI, body mass index; Cefa, Cefazolin; Ceft, Ceftriaxone; Cipro, Ciprofloxacin; Clinda, Clindamycin; CPB, cardio-pulmonary bypass; Cr, Creatinine; FFP, fresh frozen plasma; ICU, intensive care; LVEF, Left ventricle ejection fraction; Vanco, Vancomycin.

re-exploration or have mediastinal wound infection usually receive a widespread antibiotic coverage with combined antibiotics.

In summery we can conclude that the use of different prophylactic antibiotics in isolated CABG patients, according to the physician's personal preference or experience, does not essentially result in better clinical outcomes and less wound complications and infections.

4.1. Limitations of the Study

The present study draws data from a single institution. This observational study was done on limited number of patients with isolated CABG, however cardiac surgeons face more complex patients on their daily practice.

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