

Teicoplanin and Meropenem Prophylaxis in Open Heart Surgery- Efficacy and Safety

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Abstracts:

Keywords:

Open heart surgery, Surgical site infection, Teicoplanin, Meropenem, Flucloxacillin, Ceftriaxone.

Background: Prophylactic efficiencies of teicoplanin and meropenem against infections in open heart surgery were investigated in a retrospective observational study.

Method: In new regime of antibiotics single dose of teicoplanin and 72 hours coverage with meropenem were used in open heart surgery. One dose of teicoplanin was administered during induction of general anesthesia. First dose of meropenem was administered during induction of general anesthesia, and then 8 to 12 hourly continued up to 72 hours. This regime of antibiotics was compared retrospectively with previous regime of antibiotics containing flucloxacillin, ceftriaxone and gentamycin continuing from induction of general anesthesia up to 5th post operative day.

Results: In 203 patients receiving new regime containing teicoplanin and meropenem, there was no infection and there was no nephrotoxicity. But in 101 patients receiving conventional regime containing flucloxacillin ceftriaxone and gentamycin, there were 21 patients (21%) with surgical site infections; among them 3 patients expired, and nephrotoxicity developed in 15(14.85%) patients.

Conclusion: As prophylactic agent combination of teicoplanin and meropenem may be more effective and safer against infection in open heart surgery.

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Introduction:

Surgical site infections (SSIs) are one of the most challenging complications of cardiac surgery.¹ Although cardiac surgery in clean surgery, potential infections complications have led to widespread use of prophylaxis with perioperative antibiotics.² SSIs and particularly sternal and mediastinal infections have implications for significantly increasing both morbidity and mortality, as well as their associated costs in both man-hours and dollars spent.^{3,4} Staphylococcus aureus and Staphylococcus epidermidis are the most common culprit in post cardio-thoracic SSI.⁵⁻⁹ Other micro-organisms, including diptheroides, aerobic and anaerobic streptococci and enteric gram-negative bacilli are also involved.¹⁰⁻¹² In an attempt to prevent both wound infections and prosthetic valve endocarditis cardiac surgery presently administer antibiotics to virtually all patients undergoing cardiac surgery.¹⁴ While cephalosporins are widely prescribed, the increasing prevalence of methicillin-resistant staphylococcus aureus (MRSA) and methicillin

resistant coagulase-negative Staphylococci as potential pathogens has prompted a search for alternative prophylactic regimens.¹³ Teicoplanin, a glycopeptide antibiotics that is chemically related to the vancomycin-restocetin group, has activities against methicillin sensitive staphylococcus aureus (MSSA) and MRSA and seems to be less toxic.¹⁵ Meropenem is a carbapenem which has broad spectrum antibiotics especially against gram-negative β -lactamase producing Escherichia coli (E coli), Klebsiella pneumonia (Klebsiella pneumoniae), or efflux pump-overexpressing strains of Pseudomonas aeruginosa (Pseudomonas aeruginosa).¹⁸

We were worried when rate of SSIs, in our institute were significantly increasing at the end of 2013; cephalosporin, gentamycin, amikacin and flucloxacillin developed resistant. We have started a new regime of antibiotic-combination of teicoplanin and meropenem, with the consultation with department of microbiology, to cover virtually all strains of microorganism. Still now we are using both this regime; side by side. This retrospective

study was to observe the effectiveness of our new antibiotic regime by searching our post operative patients who underwent open heart surgery in the department of cardiac surgery.

Methods :

This retrospective observational study was carried out in the Department of Cardiac Surgery in National Institute of Cardiovascular Diseases (NICVD) and Hospital, Dhaka, Bangladesh with the permission of institutional academic council during the period of January 2014 to December 2015, among total 304 patients who underwent open heart surgery in our cardiac surgery unit. In 203 patients with the regime containing teicoplanin and meropenem (Group I), another 101 patients were randomly selected from those who used old regime of antibiotics containing flucloxacillin, ceftriaxone and gentamycin (Group II).

Procedures of wound management: Full thickness of the dermis of skin was sharply incised with knife, no diathermy used for the skin incision. Skin was covered with antiseptic (povidon iodine) soaked gauge during sternum retraction and operation procedure. Skin closure was done meticulously avoiding any residual space to prevent collection and infection. Skin wound covered with dry sterile gauge and surgical -pad, and re-check and dressing done on 2nd POD again.

Antibiotic regime:

In our new regime for the poor economical condition of patients single dose of teicoplanin, and meropenem was given to cover 72 hours. The dose of teicoplanin

(400mg for body weight above 40 Kgs, 200mg for body weight below 40 kgs) was administered during induction of general anesthesia. First dose of meropenem (1gm for body weight above 40 kgs, 500mg for body weight below 40 kgs) was administered during induction of anesthesia and subsequently continued in ICU 8 hourly up to 72 hours. In previous regime of antibiotics, first dose of ceftriaxone (1gm in patients above 40 kgs and 500mg in patients below 40 kgs) and first dose of flucloxacillin 500mg were administered during induction of general anesthesia, and first dose of gentamycin was given at the entry into ICU from operation theatre (OT). All three antibiotics were continued for five post operative days. Ceftriaxone (1gm in adult, 500 mg for weight below 30 kgs) was given 12 Hourly, flucloxacillin (500mg for adult ad 250mg to below 30 kgs) 6 hourly, and gentamycin (3-5 mg/ kg body weight) was given 8 hourly. If there was any renal impairment, gentamycin was stopped.

Data collection: Data were collected retrospectively from records from register in OT, ICU, wards and concerned units. Infection was considered when there was serous discharge from stitches, wound dehiscence, high temperature at temperature chart at ICU and wards, evidence of secondary suturing, sternal restabilization, antiseptic dressing, report of culture sensitivity of pus with positive infective micro-organisms and list of antibiotics sensitive or resistant to it, or any mortality due to infection in ICU and wards; or any evidence of renal impairment and other adverse effect such as 'red man syndrome'.

Results:

Table-I
Demographic characteristics of the study population.

	Age(mean)years	p value	Sex	p value
Group-I	33.82	.125	F 85(41.9%) M 118 (58.1%)	.256
Group-II	34.99		F 39(38.6%) M 62 (61.4%)	

Table-IIA
Outcome of the groups.

	Total pt.	Infection	Percent (%)	Free of Infection	Percent (%)	P value
Group-I	203	0	0	203	100	0.001
Group-II	101	21	20.79	80	79.20	

Table-IIB
Outcome of the groups.

	Total pt.	Nephrotoxicity	Percent (%)	P value
Group-I	203	0	0	0.001
Group-II	101	15	14.855	

Table-III
Organisms isolated by culture from discharge.

Organisms	Infected pts.	Percent %
E.Coli	11	52.38%
Pseudomonas	6	28.57%
Coagulase negative Staphylococcus	3	14.28%
Staph. Epidermidis	1	4.76%

Table-IV
Comparison of cost of prophylactic drug between two groups per patient.

	Duration and dose	Calculation of price	Total price in BD taka
Group-I	3 days TDS meropeneme + 1dose of Tecoplanin	(3X3X700)+ 1X1500	=7,800/-
Group-II	5 days of Ceftriaxone, Flucloxacilin and Gentamycines	(5X2X500)+ (5X4X50)+ (5X3X20)	=6300/-

Discussion:

We used teicoplanin against MSSA, MRSA, Staph. epidermidis, and meropenem against β -lactamase producing strains of E. coli, Kleb. pneumoniae and efflux pump expressing strains of Pseudo. Aeruginosa. There was no infection in 203 patients who received our new regime. In other group of 101 patients who were treated with flucloxacillin, ceftriaxone and gentamycin, 21 patients developed SSIs; culture and sensitivity showed in 3 patients coagulase-negative Staph. aureus, in 1 patient Staph. epidermidis, in 11 patients E. coli and in 6 patients Pseud. aeruginosa. Most of the micro organisms in culture were sensitive to teicoplanin and/or meropenem. The infected patients were treated with meropenem and teicoplanin after diagnosis. In two studies by Shahidullah and associates in the Dept. of Microbiology at NICVD found Escherichia coli, Pseudomonas species, coagulase negative Staphylococcus and coagulase positive Staphylococcus, Streptococcus pyogenes, and

Proteus species most of these are resistant to commonly used antibiotics.²⁵ Antibiotics included Amoxicillin, Amikacin (30 mcg), Ciprofloxacin (5 mcg), Cotrimoxazole (1.25/23.75 mcg), Ceftriaxone (30 mcg), Cephalexin (30 mcg), Ceftazidime (10 mcg), Gentamycin (10 mcg), Tobramycin (10 mcg), Imipenem, Netilmicin, Vamcomycin (5 mcg).²⁶ These findings were similar to this study. Teicoplanin was used to prevent sternal infection as Tecoplanin penetrates in to the bony tissue very well.¹⁵

Atahan and associates performed a study in a rat model to see efficacy of cefazolin, teicoplanin and vancomycin prophylaxis, they found that as a prophylactic agent, teicoplanin is more effective than vancomycin and cefazolin against infections caused by MSSA and MRSA.¹⁹

Martin et al.²⁰ performed a study on teicoplanin in cardiac surgery. They found that there is a significant teicoplanin concentration in heart and

mediastinal tissues, and teicoplanin makes it possible to achieve and maintain, in most patients and throughout the operative procedure, antibiotic concentrations in tissues that equal or exceed the MIC_{90s} for pathogens that cause infection after open heart surgery. Frank et al.¹⁴ performed a study on penetration of teicoplanin into heart valves, subcutaneous and muscle tissues of patients undergoing open heart surgery. They concluded that teicoplanin concentrations in heart valve were high enough to inhibit MRSA and coagulase- negative staphylococci which are known to cause post operative wound infections and endocarditis, they used high first dose of teicoplanin (12 mg/kg) and second dose after 4-to 5 hours after the first dose. We administered second dose after 24 hours at ICU. Saginur et al.²¹ performed a multi-centre double-blind randomized controlled trial of 3027 adult patients undergoing elective coronary artery and Valve operations. They reported teicoplanin is not better than cefazolin; this difference with our study may be due to their large number of patients and our study is single centered smaller study. Meropenem has action against gram- negative and also gram-positive organism and due to its low toxicity, meropenem remains a suitable choice for treatment of infection in critically ill patient. It is currently established that meropenem, Like other β -Lactam antibiotics displays time dependant bactericidal activity and the percentage of the dosing interval that free drug concentrations remain above the minimum inhibitory concentration of pathogen (% FT>MIC) is the most important parameter of predicting their antibacterial efficacy.^{22,23} Meropenem has action against E. coli, Kleb. pneumoniae and Psud. aeruginosa.⁷⁻⁹ So our regime of antibiotics containing teicoplanin and meropenem was justified to use as prophylaxis of all types of open Heart surgery. Glycopeptides have some adverse events particularly 'red man' syndrome and nephrotoxicity. Wood et al.²⁴ showed in their study that teicoplanin is associated with lower incidence of these adverse events than vancomycin. Lack of toxicities and lack of routine assay costs make teicoplanin an attractive and cost effective option for treating infections. Our patients were free from nephrotoxicity and 'red man syndrome'. Though safety and efficacy was the main objectives of the study but still cost was another point to discuss,

the new regime was slightly costly (TK 7800/- vs TK 6300/-) but when infection occurs with the old regime more cost it will require to control with costly antibiotics.

Conclusion: As prophylactic agent, combination of teicoplanin and meropenem is safe and effective against infections of open heart surgery caused by both gram-positive and gram-negative organism.

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Conflict of Interest - None.

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