

Meropenem VS Cefoperazone Prophylaxis for Prevention of Surgical Site Infection In Colorectal Surgery

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Abstract

Introduction:

Surgical site infection (SSI) is a potentially morbid complication following both elective as well as emergency operations. This increases the overall expenditure to the patient and health care system. Colorectal surgeries in particular are associated with increased incidence of SSI. Antimicrobial prophylaxis reduces the rate of SSI, but the choice of antibiotic is not yet established.

Methods :

This was a prospective study at a high volume centre for colorectal surgery in a tertiary care institute. All patients who underwent colorectal surgery in both elective as well as emergency settings were included in the study & allocated randomly to receive either meropenem or cefoperazone as prophylactic antibiotic and compare the rate of SSI in two groups.

Result:

A total of 538 patients were included, 316 (58.7%) were males while 222 (41.3%) were females. Mean age of the patients was 47.36 ± 15.57 years. Elective procedures contributed for 84.01% (452) while 15.98% (86) cases were performed as emergency procedures. 67 out of 452 (14.8%) patients developed SSI in elective settings, while as 31 out of 86 (36.0%) patients developed SSI in emergency settings. There is a decreased rate of SSI in the cases where meropenem (9%) was administered as compared to cefepazone (19.8%) (P value < 0.001).

Conclusion:

The incidence of SSI in colorectal surgeries is substantial, which leads to significant morbidity to the patients and the healthcare system. Meropenem is superior to cefoperazone in prevention of surgical site infection in patients following elective colorectal surgery.

Introduction

Surgical Site Infections (SSIs) have been recognised as the third most common Healthcare Associated Infections (HAI). Hospital acquired infections are not only an important cause of morbidity and mortality but also cause severe economic impact throughout the world (1,2).

Colon and rectal surgery (CRS) is consistently associated with higher SSI rates relative to other surgery. CR surgery SSI rates range from 4% to 45% (3, 4, 5). Nearly all the same risk factors that correlate with any type of SSI are similarly identified in CRS. Frequently identified predictive factors for CRS SSIs are obesity, diabetes, type of procedure, technique (e.g. open vs. laparoscopic) longer operative time, and emergency operations (4, 6, 7).

To prevent surgical site infection various techniques starting from considering the aspect of health-care provider, environment of the operating room to the preoperative preparation for the patient, can be performed. The lower rates of SSI in developed countries compared to the developing countries indicate better implementation of infection control practices along with availability of proper surveillance system. Use of antimicrobial prophylaxis might lead to variations in incidence of SSI.

Antibiotic Prophylaxis in Surgery

Prophylaxis refers to the prevention of an infection. It can be primary prophylaxis, secondary prophylaxis, or eradication. Primary prophylaxis is the prevention of an initial infection whereas secondary prophylaxis refers to the prevention of recurrence or reactivation of a preexisting infection. Elimination of a colonized organism to prevent the development of an infection is known as eradication.

In administering antibiotic prophylaxis, some general principles should be followed. The selected prophylaxis antibiotics must have been shown to reduce SSI based on valid clinical trials. It should be safe, cost effective and bactericidal with in vitro spectrum that covers the most probable intraoperative contaminants for the operation. The timing of administration should be appropriate so that the antibiotic concentration is established relatively high in serum and tissue by the initial time of incision. The antibiotic concentration should be maintained high throughout the operation and until a few hours later after the incision is closed.

The optimal time for administration of preoperative doses is within 60 minutes before surgical incision. This is a more-specific time frame than the previously recommended time, which was "at induction of anesthesia." Some agents, such as fluoroquinolones and vancomycin, require administration over one to two hours; therefore, the administration of these agents should begin within 120 minutes before surgical incision.

Information is included regarding the approach to weight-based dosing in obese patients and the need for repeat doses during prolonged procedures (8-13). Obesity has been linked to an increased risk for SSI. The pharmacokinetics of drugs may be altered in obese patients, so dosage adjustments based on body weight may be warranted in these patients. For all patients, intraoperative redosing is needed to ensure adequate serum and tissue concentrations of the antimicrobial if the duration of the procedure exceeds two half-lives of the drug or there is excessive blood loss during the procedure.

New recommendations for a shortened postoperative course of antimicrobials involving a single dose or continuation for less than 24 hours are provided.

A single-dose prophylaxis is usually sufficient with adult patients. If antimicrobial prophylaxis is continued postoperatively, the duration should be less than 24 hours, regardless of the presence of intravascular catheters or indwelling drains (14,15).

Objectives:

The main objective of the study was to evaluate the colorectal SSI outcomes. The objectives may be summarized as follows:

1. To determine the frequency of surgical site infections.
2. To compare meropenem, a long-acting carbapenem, as an alternative to the recommended prophylactic antibiotic cefoperazone in colorectal surgery patients

Methods:

Type of study: Prospective randomised control trial

Place of study: The study was conducted in the Department of General and Minimal Invasive Surgery, Colorectal Division, Sheri-i-Kashmir Institute of Medical Science (SKIMS), Srinagar.

Period of study: The study includes all the patients presented to General Surgery department with any type of colorectal surgery from 1st July-2014 to 31st June-2016.

Sample size: 538 cases

Inclusion criteria: Study includes all surgical inpatients, undergoing emergency and elective colorectal surgery (following the ACS NSQIPs defined CPT codes)

Exclusion criteria: Patients with trauma and transplant patients and patients under 18 were excluded from the study.

Study Procedure and Data collection

During the study period, data was collected on a predesigned proforma for all the patients who underwent surgery in the General Surgery Ward of SKIMS. The patients were monitored for any signs of infection, daily.

Infected cases were identified using CDC, USA definition for SSI. After discharge patients were followed-up at weekly interval to check for any sign of infection. The patients were followed for a period of 30 days to look for surgical site infection. If there were no signs of infection within 30 days of operation, the patient was regarded as having no SSI. Patient who were not able to visit every week were contacted on phone to inquire about their wound condition.

A total of 538 patients who underwent CRS between the above mentioned time period were randomly allocated in a short term antibiotic regime into two groups (cefoperazone or meropenem group).

One gram of cefoperazone was administered one hour before incision. An additional one gram of cefoperazone was administered intra-operatively in cases where surgery time exceeded four hours. Postoperatively, one gram cefoperazone was administered eight hourly and the drug was discontinued after 24 hours of surgery.

For the other antibiotic i.e. meropenem, one gram was administered one hour before incision and one gram was administered eight hourly postoperatively and the drug was discontinued after 24 hours of surgery.

In post operative period patients were checked for fever/ discharge or wound dehiscence, tenderness, localized swelling, redness, or heat. The surgical wound was dressed and checked for SSI daily.

Data Analysis

Statistical software SPSS (version 20.0) and Microsoft Excel were used to carry out the statistical analysis of data. Data was analyzed by means of descriptive statistics namely, means, standard deviations and percentages and presented by Bar diagrams. For parametric data, Student's independent t-test was employed. Chi-square test or Fisher's exact test, whichever appropriate, was used for non-parametric data. A P value of less than 0.05 was considered statistically significant.

RESULTS AND OBSERVATIONS

This study was conducted in the Department of General and Minimal Invasive Surgery, Colorectal Division, Sher-i-Kashmir Institute of Medical Science (SKIMS), Srinagar. The study includes 538 patients who presented to the said department with any type of colorectal surgery from 1st July 2014 to 31st June 2016 and was a prospective study. Patients from age groups above 18 years were included in the study. The following observations were made.

Of the total 538 patients, 316 (58.7%) were males while 222 (41.3%) were females. Mean age of the patients was 47.36 ± 15.57 years, with a minimum age of 18 years and a maximum of 85 years.

Elective procedures contributed for 84.01% (452) while 15.98% (86) cases were performed as emergency procedures. Of the total 538 patients 452 patients were electively operated, of which 67 (14.8%) developed SSIs. In emergency procedures 86 patient were operated, of which 31 (36.0%) developed SSI.

In our study, total SSI was observed in 67 cases, of which superficial SSI were 46 (68.65%), and deep SSI cases, were 11 (16.4%), and organ space SSI cases were 10 (14.9%). Fig 1

Effect of meropenem and cefeparozone as prophylactic antibiotic on SSI rate

The patients were comparable in terms of age, operating time (Table 1) as well as gender & BMI (Table 2)

The SSI rate in emergency surgeries was (36%) and was considerably more than the SSI rate in elective surgeries (14.8%) & overall percentage of SSI in our series was 18.2.

A large number of patients presented with multiple comorbidities; however they did not differ in terms of either of the antibiotics they received (Table 4)

A significant difference was observed in the rate of SSI between cases receiving meropenem or cefeparozone as prophylactic antibiotic. As shown in Table 5, there is a decreased rate of SSI in the cases where meropenem (9%) was administered as compared to cefeparozone (19.8%).

In our study, total SSI was observed in 67 cases in elective setting, of which superficial SSI were 46 (68.65%), and deep SSI cases, were 11 (16.4%), and organ space SSI cases were 10 (14.9%). Fig 1

Discussion:

Meropenem is an ultra-broad-spectrum injectable antibiotic used to treat a wide variety of infections. It is a β -lactam and belongs to the subgroup of carbapenem, similar to imipenem and ertapenem. Meropenem is bactericidal except against *Listeria monocytogenes*, where it is bacteriostatic. It inhibits bacterial wall synthesis like other β -lactam antibiotics. In contrast to other beta-lactams, it is highly resistant to degradation by β -lactamases or cephalosporinases. In general, resistance arises due to mutations in penicillin-binding proteins, production of metallo- β -lactamases, or resistance to diffusion across the bacterial outer membrane. The spectrum of action includes many Gram-positive and Gram-negative bacteria (including *Pseudomonas*) and anaerobic bacteria. The overall spectrum is similar to that of imipenem, although meropenem is more active against Enterobacteriaceae and less active against Gram-positive bacteria. It is also very resistant to extended-spectrum β lactamases, but may be more susceptible to metallo- β -lactamases.[16] Meropenem is frequently given in the treatment of febrile neutropenia. This condition frequently occurs in patients with hematological malignancies and cancer patients receiving anticancer drugs that cause bone marrow suppression. It is approved for complicated skin and skin structure infections, complicated intra-abdominal infections, and bacterial meningitis.

Cefoperazone is a third-generation cephalosporin antibiotic, It is one of few cephalosporin antibiotics effective in treating *Pseudomonas* bacterial infections which are otherwise resistant to these antibiotics. Cefoperazone exerts its bactericidal effect by inhibiting the bacterial cell wall synthesis..Cefoperazone has a broad spectrum of activity and has been used to target bacteria responsible for causing infections of the respiratory and urinary tract, skin, and the female genital tract. The following represents MIC susceptibility data for a few medically significant microorganisms. *Haemophilus influenzae*: 0.12 - 0.25 $\mu\text{g/ml}$,*Staphylococcus aureus*: 0.125 - 32 $\mu\text{g/ml}$, *Streptococcus pneumoniae*: ≤ 0.007 - 1 $\mu\text{g/ml}$.

We compared two drugs meropenam and cefoperazone in patients having similar demographic profile and comorbidities, besides operating time between these two groups was comparable. Cefoperazone group included 242 patients and meropenam had 210 patients. Surgical site infection developed in 48 patients (19.8%) of cefoperazone group and in meropenam group 19 patients developed SSI (9.0%). This result was statically significant (p-value 0.001). Hence we infer that meropenam is superior than cefoperazone in prevention of surgical site infection in patients following elective colorectal surgery

Conclusion:

From our work we concluded that:

1. Overall incidence of SSI in our study was 18.2%. In elective surgeries incidence of SSI was 14.8% while in emergency procedures it was 36% and the results were statistically significant.
2. Surgical site infection was observed in 67 cases, of which superficial SSIs developed in 46 (68.65%) cases, deep SSI developed in 11(16.4%) and organ space SSI developed in 10 (14.9%) cases. There was no significant difference between these three groups with relation to the infection site.
3. Meropenem and cefoperazone were used for antibiotic prophylaxis. Surgical site infection developed in 19.8% in the cefoperazone group while as in meropenam group 9% of the cases developed surgical site infection. Hence meropenam was superior to cefoperazone in prevention of surgical site infection in patients following elective colorectal surgery.

Declarations

Ethic Approval & consent to participate

Ethical approval was sought from institutional ethical committee of Sheri Kashmir Institute of Medical Sciences, Srinagar, India. However, the committee decided that the study may be exempted from ethical clearance.

Patient consent was not required in our study as it did not involve any intervention on them or revealing their personal identity in any form.

Consent to publish

All the authors have agreed to publish this research

Availability of data & material

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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TABLE 1					
Comparison of two drugs based on age and duration of operation in patients with elective surgery					
Variable	Cefeparozone		Meropenem		P-value
	Mean	SD	Mean	SD	
Age (years)	47.7	15.86	44.9	15.27	0.060
Operating time (Hours)	2.23	1.23	2.17	1.29	0.571

TABLE 2						
Comparison of two drugs based on gender and BMI in patients with elective surgery						
Characteristic		Cefeparozone		Meropenem		P value
		No %	No %	No %	No %	
Gender	Male	148	61.2	116	55.2	0.203
	Female	94	38.8	94	44.8	
BMI	<25	159	65.7	134	63.8	0.674
	>25	83	34.3	76	36.2	

TABLE 3					
SSI rate as per mode of surgery in patients					
Mode of Surgery	SSI		NO SSI		P Value
	NO	%	NO	%	
Elective	67	14.8	385	85.2	<0.001
Emergency	31	36.0	55	64.0	
Total	98	18.2	440	81.8	

Comparison of two drugs based on comorbidities in patients with elective surgery					
Comorbidities					
Comorbidities	Cefoperazone		Meropenem		P value
	No	%	No	%	
CVD	51	21.1	49	23.3	0.564
Diabetes	30	12.4	19	9.0	0.253
COPD	10	4.1	12	5.7	0.436
Hypothyroidism	25	10.3	15	7.1	0.234

CVD = cardiovascular disease; COPD = chronic obstructive pulmonary disease

Comparison of two drugs based on SSI in patients with elective surgery					
SSI	Cefoperazone		Meropenem		P value
	No	%	No	%	
Present	48	19.8	19	9.0	<0.001
Absent	194	80.2	191	91.0	

FIG 1

