Ertapenem for the Prevention of Surgical Site Infection Following Colorectal Surgery

Gregory B. Tallman, PharmD1; David T. Bearden, PharmD1,2; James S. Lewis II, PharmD2; Miriam R. Elman, MPH1; Yoojin Kim, PhD2; Kevin Langstaff, BA2; Jessina C. McGregor, PhD1
1. Oregon State University/Oregon Health & Science University College of Pharmacy
2. Oregon Health & Science University

ABSTRACT (Updated)

Introduction: Recent data from randomized control trials suggest ertapenem prophylaxis may be superior to cefazolin for prevention of surgical site infections (SSIs) in colorectal surgery, however, these trials may have limited generalizability. The primary objective of this study was to compare the frequency of SSI in patients receiving ertapenem and other prophylactic regimens prior to colorectal surgery.

Methods: We conducted a retrospective cohort study of adult patients (age ≥ 18 years) undergoing colorectal procedures between Jul. 2012 and Sep. 2013. Patients with history of surgery in the prior 30 days, surgery due to trauma, or systemic antibiotics at the time of surgery were excluded. The primary outcome was surgical site infection within 30 days of surgery; outcome frequencies were compared between patients receiving ertapenem and other antibiotics for surgical prophylaxis using multivariable logistic regression to adjust for potential confounders.

Results: A total of 1,129 encounters were considered for inclusion; 767 were excluded. In the 362 encounters included in the study, 296 received ertapenem and 66 received alternative prophylaxis agent(s). Patients receiving ertapenem were younger (54.9 vs. 56.7 years), more likely to be male (52.7% vs. 36.4%), and have inflammatory bowel disease (26.4% vs. 6.1%). Cancer was significantly more common in patients not receiving ertapenem (83.3% vs. 69.2%). The median duration of surgery was significantly shorter among patients receiving ertapenem (179 minutes) compared to those receiving other antibiotics (198 minutes). SSI occurred in 16.4% of patients receiving ertapenem and 11.6% of patients receiving other antibiotics (OR 0.99, 95% CI 0.79 to 1.25). After adjusting for potential confounders, the adjusted OR for developing SSI after ertapenem use was 0.43 (95% CI 0.12 to 1.60).

Conclusions: After adjusting for confounding, ertapenem did not significantly reduce the risk of SSI following colorectal surgery compared to alternative agents, and routine use was not associated with a significant reduction in SSI risk.

INTRODUCTION

Risk of SSI is high after colorectal surgery

Antibiotic prophylaxis significantly reduces risk of SSI

Ertapenem has shown superiority to cefazolin prophylaxis in colorectal procedures; data indicate ertapenem is not superior to other regimens

National guidelines recommend against ertapenem use, except in institutions with high rates of third-generation cephalosporin resistance

Increased carbapenem use associated with increased prevalence of carbapenem-resistant Enterobacteriaceae

Despite low rates of cephalosporin resistance, our institutional policy includes ertapenem as an acceptable prophylactic agent

Public health risks of increased antibiotic resistance and CRE must be evaluated against individual benefits of ertapenem prophylaxis

OBJECTIVE

To evaluate the efficacy of ertapenem compared to other guideline-concordant antibiotic prophylactic regimens at preventing SSI after colorectal surgery

METHODS

Design

Retrospective cohort at Oregon Health & Science University hospital

Inclusion/Exclusion Criteria


Excluded patients < 18 years, admitted due to trauma, receiving systemic antibiotics at time of index procedure, received non-guideline prophylactic agents, or had previous surgery in 30 days prior to index procedure

Data

Demographics and covariates electronically extracted

Chart review performed for variables not captured electronically (e.g., surgeon, ASA classification, wound class)

Outcome data obtained from infection control surveillance and chart review

METHODS (Cont.)

Outcome

Primary outcome was SSI defined using NHSN surveillance definitions

SSI classified as superficial incisional, deep incisional, or organ/space SSI

Secondary outcomes include SSI by classification and pathogen

Analysis

Patients receiving ertapenem vs. other prophylaxis compared using descriptive statistics

Logistic regression performed to adjust for confounders of the relationship between ertapenem prophylaxis and SSIs

Forward selection with entry threshold of 20%, change in odds ratio 0.2, and included in model to assess for homogeneity between treatment groups

Post hoc sensitivity analysis comparing ertapenem to cefazolin only

RESULTS

Patient Population

1,129 patient encounters reviewed; 362 included in the study (Figure 1)

Heterogeneous selection of prophylactic antibiotic regimens (Table 1)

Many demographic and operative differences between groups (Table 2)

ASA classification, wound class not significantly different

Figure 1. Patient Selection

1129 Encounters Assessed

Table 1. Antibiotic Prophylaxis Regimens Used

Antibiotic regimens listed Frequency (% SSI)

Ertapenem 296 (76.3)

Other Antibiotics

Cefazolin 53 (13.7)

Ceftazidime + metronidazole 11 (2.8)

Cefotaxime + metronidazole 1 (0.3)

Ceftazidime + metronidazole 1 (0.3)

Non-guideline antibiotics 26 (6.7)

RESULTS (Cont.)

Table 2. Demographics and Operative Characteristics

Characteristic

Ertapenem (n = 296) Other Antibiotics (n = 66)

Mean Age, yr. (SD) 54.9 (16.6) 58.7 (14.4)

Male Sexa 150 (50.7) 24 (36.4)

Comorbidities

Diabetes Mellitus 41 (13.6) 9 (13.6)

COPD 38 (12.8) 7 (10.6)

IBDD 78 (26.7) 4 (6.1)

Malignancyb 205 (69.3) 55 (83.3)

ASA Classification 154 (52.0) 30 (45.5)

Other Surgeries 142 (48.0) 36 (54.5)

Wound Class

Clean-contaminated 211 (71.3) 54 (81.8)

Contaminated 55 (18.6) 7 (10.6)

Dirty/Infected 30 (10.1) 5 (7.6)

Median Duration Surgery, min. (IQR) 178 (121 to 240) 198 (140 to 295) (ICP)

Laparoscopic Approach 108 (36.5) 3 (4.6)

ASA, American Society of Anesthesiologists; BMI, body mass index; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; IQR, interquartile range; OR, odds ratio; SSI, surgical site infection; Staph, Staphylococcus.

† p < 0.05; ‡ p < 0.01

Table 3. Surgical Site Infections

Infection Classification

Ertapenem (n = 296) Other Antibiotics (n = 66)

Any SSI 16 (5.4) 11 (16.7)

Superficial Incisional SSI 11 (3.7) 7 (10.9)

Deep Incisional SSI 0 (0.0) 0 (0.0)

Organ Space SSI 5 (1.7) 4 (6.1)

All data are reported as n (%) unless otherwise indicated.

Table 4. Microbiology

Organism

Ertapenem (n = 16) Other Antibiotics (n = 11)

S. aureus 4 -

Enterococcus spp. 2 1

E. coli 2 -

P. aeruginosa 2 -

C. albicans 1 -

C. glabrata 1 -

M. fragilis 1 -

C. testosterone 1 -

All data are reported as n (%) unless otherwise indicated.

CONCLUSION

Ertapenem use was associated with non-significant protective effect against SSI after adjusting for measured confounders

In certain settings with low antibiotic resistance, routine ertapenem for colorectal prophylaxis may not be justified given risk of collateral damage

Further study needed to better explore the risks and benefits of ertapenem prophylaxis in colorectal settings of low resistance...