



## Prospective Randomized Study on the Effectiveness of Oral Antibiotic Prophylaxis in Preventing Surgical Site Infection in Elective Colorectal Surgery (Research Article)

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### ABSTRACT

**Background:** Surgeries of the colon and rectum are categorized as clean-contaminated procedures. Increased incidence of surgical site infections associated with these procedures make antibiotic prophylaxis and bowel preparation an essential component in the preoperative preparation of the patients. While the role of intravenous antibiotics is well established, controversy still exists over the use of oral antibiotics for prophylaxis. This study was undertaken to evaluate the role of oral antibiotic prophylaxis in preventing/reducing the incidence of wound infection following elective colorectal surgeries.

**Methods:** 82 patients who underwent elective surgeries on the colon/rectum over 32 months were included in the study. They were randomized into two groups – Group 1 (with oral prophylaxis) and Group 2 (without oral prophylaxis). Postoperatively intravenous antibiotics were given for 2 days following which no antibiotics were given. Wound was inspected for evidence of infection.

**Results:** Overall incisional SSI rate was 31%. Infection rate was higher in females (33.3%) than in males (30%). Patients with higher ASA grade had high infection rates ( $p < 0.0001$ ) (Grade I – 14.3%; Grade II – 26%; Grade III – 50%). Patients in age group  $> 60$  yrs had increased infection rates ( $p < 0.0001$ ) (20 – 40 yrs – 14.3%; 40 – 60 yrs – 26.1%;  $> 60$  yrs – 50%). 5 patients from Group 1 ( $n=40$ ) and 8 from Group 2 ( $n=42$ ) developed incisional SSI without any statistically significant difference ( $p=0.514$ ). One patient developed urinary tract infection.

**Conclusion:** This study did not find any significant role for oral antibiotics in decreasing the infection rates. Hence oral antibiotics need not be administered preoperatively for colorectal surgeries.

**Keywords:** Antibiotic prophylaxis, Surgical site infection, Colorectal surgery.

## INTRODUCTION

Factors predisposing a patient to develop surgical site infections (SSI) are complex and related to the patient, the surgeon and the environment. Though modern surgical practices have greatly reduced the infection rates, the effect has been counter-balanced by debilitating diseases in the host, use of implants and immunocompromised state. Widespread antibiotic therapy has often made prevention and control of surgical infections more difficult. Contamination by bacteria from the contents of the large bowel suggests that risk of SSI in colorectal surgery is higher than other procedures. The use of antibiotic prophylaxis in patients who undergo elective surgery of the colon is now accepted universally and is effective for the prevention of SSI<sup>1</sup>. Surgeons have also adopted the routine use of mechanical bowel preparation prior to elective colorectal procedures as a widely established practice to reduce SSI<sup>2</sup>. Though many antibiotic regimens are currently in use, clear superiority of one above another is not present<sup>3,4</sup>. Added on to this controversy is the additional role of oral antibiotic prophylaxis. Local prevalence of pathogens and resistance profiles should be taken into account in order to achieve more cost-effective use of antimicrobial prophylaxis in colorectal surgery. Any prophylactic regimen chosen for should include broad spectrum cover for both aerobic and anaerobic organisms. Appropriate use of antimicrobial prophylaxis may help to reduce the development of antibiotic resistant bacteria<sup>1-5</sup>. This study aims at evaluating the role of oral antibiotic prophylaxis in reducing the incidence of surgical wound infection following elective colo-rectal surgeries.

## METHODS

The present study was a prospective study carried out over 32 months. Ethical clearance was obtained from the institutional ethics committee. All patients with diseases of colon and rectum who underwent elective surgery were considered for the study. Relevant demographic data was

collected preoperatively which included age, sex, risk factor (history of diabetes mellitus, immunocompromised states), diagnosis, American Society of Anaesthesiologists (ASA) grade. These patients had routine preoperative investigations for surgical fitness and to rule out infections. They were randomized into two groups – Group 1 and Group 2 based on computer generated randomization chart. Group 1 received preoperative oral antibiotic prophylaxis with Ciprofloxacin 500mg (bid) and Metronidazole 400mg (tid) for two days before surgery. Group 2 did not receive any oral antibiotic prophylaxis. Patients had their bowel prepared with sodium phosphate solution (Exelyte, Crest Pharma, India) on the day before surgery supplemented with enema in the night. Hair removal was done on the day of surgery. Both the groups received intravenous (i.v) antibiotic prophylaxis with Ceftriaxone 1g and Metronidazole 500mg at the induction of anaesthesia.

Intraoperatively the skin was prepared with povidone-iodine solution (two scrubs) and a waiting period of two minutes was observed after the last scrub. Duration of surgery was calculated as the time between skin incision and skin closure. Bowel preparation was assessed by the operating surgeon as follows – clean, clear/mucoid liquid, liquid stools, and regular stools. Operative field contamination and blood loss were documented. Skin was closed either with non-absorbable suture material or staples. Wound was then cleaned Postoperatively all patients received i.v Ceftriaxone 1g twice daily and Metronidazole 500mg thrice daily for two days. No further antibiotics were given. Dressing was removed after 48hours. Surgical wound was monitored by a doctor from another unit who was blinded for the study protocol. He assessed the wound for evidence of infection like erythema, tenderness, discharge or dehiscence on successive days for 14 days. We adopted the Centers for Disease Control and Prevention (CDC) criteria for defining SSI<sup>3,4</sup>. Discharge present if any, was sent for culture to

identify the organism and its antibiotic sensitivity. Patients were then treated accordingly. Follow up for reassessment was done at 30 days.

#### **Inclusion criteria**

- All patients aged 18 years and above with diseases of colon and rectum requiring laparotomy
- All patients who have given consent for procedure

#### **Exclusion criteria**

- Pre-operative infectious diseases
- Patients posted for emergency surgeries
- Laparoscopic procedures
- Allergy to the antibiotics being used
- Antibiotic administration prior to prophylactic dose

#### **Statistical Analysis**

A hypothesis of no difference in the incidence of surgical site infection between the two groups was postulated. Statistical analysis for the study was performed using SPSS software (version 16.0, SPSS Inc, Chicago, IL). Fisher's exact test was used for analyzing categorical variables. Kruskal-Wallis one-way analysis of variance was used to compare the categorical variables between groups. Unpaired *t* test was used to analyze continuous variables between groups. All the values were expressed as mean  $\pm$  SD.  $p < 0.05$  was considered significant.

#### **RESULTS**

A total of 91 patients underwent elective colorectal surgery during the study period between of which nine patients were excluded due to various reasons (Table 1). Finally 82 patients were considered for the study. Of these, 40 patients received preoperative oral antibiotic prophylaxis (48.78%; Group 1). The 82 study cases included males – 50 (60.98%) and females – 32 (39.02%). The age of the youngest patient was 28yrs and the elder most patient was aged 80yrs (Mean =  $55.5 \pm 13.6$ ). Characteristics of the two groups are described in Table 2. There was no statistically

significant difference in any of the baseline characteristics between the two groups. Majority of the patients had ASA grade II (52.4%). Majority of the patients had their bowel prepared adequately as deemed by the surgeon. There was no significant difference in intraoperative blood loss or blood transfusion between both the groups. Right hemicolectomy was the commonest procedure performed followed by abdomino-perineal resection. Characteristics of the patients with and without infection are listed in Table 3. 13 patients out of 82 developed wound infection accounting for an infection rate of 15.85%. All the wound infections were categorized as superficial SSI according to CDC criteria. Of the 13, males were nine and females were four. Overall wound infection rate in males was 18% and in females 12.5%. This difference was not statistically significant ( $p=0.738$ ). When compared with age, wound infection rates were high in the age group beyond 60 years (20 to 40 yrs – nil; 40 to 60 yrs – 9.5%;  $> 60$  yrs – 45%). This difference was statistically significant ( $p<0.0001$ ). Patients with ASA grade III had higher incidence of wound infection (58.33%) than compared with other grades (Grade I – nil; Grade II – 13.95%). This difference was statistically significant ( $p<0.0001$ ). The mean duration of the procedure in patients with wound infection was  $196.2 \pm 46.8$  min and in patients without wound infection was  $206.9 \pm 50.3$  min but this difference was not statistically significant ( $p = 0.89$ ). Of the 40 patients in Group 1, five patients developed wound infection as compared with eight patients out of 42 in Group 2 (Table 4). This difference was not statistically significant ( $p=0.514$ ). Of the eight patients with diabetes mellitus, three patients developed wound infection, of which two had received oral antibiotic prophylaxis. Klebsiella was the most common organism which was isolated as a single agent ( $n=4$ ) followed by Escherichia coli ( $n=3$ ). Other organisms included Citrobacter ( $n=1$ ), Pseudomonas ( $n=1$ ), Staphylococcus aureus ( $n=1$ ) and a mixture of these ( $n=3$ ). All the wound

infections were controlled with appropriate antibiotics. None of the patients had evidence of deep SSI or organ space SSI. UTI was documented in one patient and the isolate being *Escherichia coli*. No patients developed respiratory tract infection. No mortality was reported.

## DISCUSSION

Colorectal surgeries are classified as clean-contaminated procedures. Usually they are associated with an increased risk of wound infection due to high concentration of bacteria in the lumen. Elective colon and rectal surgeries differ in their risk factors for wound infection as demonstrated by Konishi T et al <sup>(6)</sup>. Independent risk factors in colonic surgery are colostomy closure and lack of oral antibiotics. In contrast, risk factors in rectal surgery are creation of colostomy, preoperative radiation, and preoperative use of steroids. Oral antibiotics distinctly did not have any advantage in rectal surgeries in that study. The overall wound infection rate among the study population is 15.85% which is almost similar when compared with other studies which ranges from 8 – 14% <sup>(4-6, 8)</sup>. As described by Reiping T et al <sup>(9)</sup> there are several factors affecting the incidence of wound infection following colorectal surgeries. The study has evaluated the role played by these factors such as age, ASA grade and duration of the procedure in wound infection following elective colorectal surgeries and the role of oral antibiotic prophylaxis in reducing the incidence of wound infection. Age group beyond 60 years had the highest incidence of wound infection and this difference is statistically significant ( $p < 0.0001$ ). Incidence was less among the age group 20 – 40 yrs. This finding is supported by several studies <sup>(9, 16)</sup>. Patients with higher ASA grade have increased risk of wound infection and this has been proved by the study. In this study patients with ASA grade III had the highest incidence of wound infection (58.33%). Wound infection rates appear

to be directly related to the duration of the procedure. However in the current study mean duration was less in those patients who had developed wound infection but with no statistical significance. Diabetes mellitus is associated with an increased risk of wound infection but this was not noted in the current study. Also the duration of antibiotics in the postoperative period is controversial with some advocating one or two doses <sup>(11)</sup>.

The role of oral antibiotics in reducing the incidence of wound infection is controversial. This practice is widely prevalent with American surgeons but being given up by the Europeans. Antimicrobial bowel preparation with oral antibiotics for elective colorectal surgery is strongly recommended in the National nosocomial Infections Surveillance (NNIS) guidelines for prevention of SSI <sup>(14)</sup>. Theoretically oral antibiotics reduce the bacterial load in the colon and thereby reduce the wound contamination. But their definitive role is debatable. A higher incidence of gastrointestinal intolerance has been noted following preoperative oral prophylaxis<sup>4</sup>. None of the patients who received oral prophylaxis in the study had gastrointestinal intolerance to the drugs used. Many of these trials had intravenous antibiotics repeated intraoperatively when the procedure went beyond 4 hours. But this was not practiced in the study. However it is recommended by NNIS <sup>(14)</sup>. Probably this may limit the number of doses required in the postoperative period. Perioperatively administered systemic antibiotics have an added advantage of minimising the risk of systemic infection <sup>(10, 12)</sup>. In the study only one patient developed UTI.

When wound discharge culture reports are analysed it is seen that most of the isolates are Gram negative bacteria which are normal flora of the colon. *Klebsiella* and *Escherichia coli* are the most common organisms. This fact supports the evidence that wound infection following colorectal surgeries are caused by the luminal

organisms (endogenous) and reducing the bacterial count of the colon is very much essential in reducing the infection rates. This can be accomplished by mechanical preparation and addition of oral antibiotics. But both these practices have been debated<sup>(13,15,18,19)</sup>.

There are several limitations of the study. There are other known risk factors that were not evaluated but that could predispose a patient to SSI, including history of smoking, weight loss, intraoperative hypotension or hypothermia, postoperative glucose control, arterial oxygen levels. Wound infection rates among colon and rectal surgeries were not estimated separately. Also the infection rates among patients with malignancies and benign conditions should have been estimated separately.

## CONCLUSION

Surgical wound infections in colorectal surgeries appear to be high among age group beyond 60 years and those with higher ASA grade. Though

the role of oral antibiotic prophylaxis in reducing the bacterial load of colon and thereby reducing the rate of incisional SSI has been supported, this study did not find their significant role in decreasing the infection rates. Hence oral antibiotics need not be administered preoperatively for colorectal surgeries.

## DECLARATIONS

**Funding:** None

**Conflict of interest:** None

**Ethical approval:** Obtained from institutional ethics committee

**Table 1:** Reasons for exclusion after enrolling

Reason for exclusion	n
Bowel not entered	3
Allergy to ceftriaxone	1
Antibiotics changed in postoperative period	3
Violation of study protocol	2

**Table 2:** Baseline characteristics of individual groups

Characteristics (n=82)	Group 1 (n=40)	Group 2 (n=42)	p value
Age (yrs)	55.8±14.3	55.18±13.3	0.75*
Age group			
– 40 yrs	12	08	0.10**
41 – 60 yrs	15	27	0.315**
>60yrs	13	07	0.116*
Sex (M/F)	25/15	25/17	0.738**
ASA grade (I/II/III)	12/21/7	15/22/5	0.828**
Diabetes mellitus	03	05	0.998**
Serum albumin (g/dl)	4.1±0.6	4.0±0.3	0.901*
Duration of surgery (min)	199.5	207.3	0.50*
Bowel preparation			
clean	09	08	0.999**
clear/ mucoid liquid	27	30	0.790**
liquid stools	03	02	1.000**
regular stools	01	02	1.000**
Intraoperative blood loss (ml)	98±12.4	92±13.2	0.672*
Patients receiving blood transfusion	08	09	0.821**

\* Unpaired *t* test

\*\* Fisher's exact test



**Table 3:** Characteristics of patients with and without wound infection

Characteristics	With infection (n=13)	Without infection (n=69)	p value
Age (yrs)	59.3±11.4	53.7±14.3	0.134*
Age group			
– 40 yrs	00	20	-
41 – 60 yrs	04	38	0.095**
>60yrs	09	11	<0.0001**
Sex (M/F)	09/04	41/28	0.738**
ASA grade (I/II/III)	0/06/07	27/37/05	<0.0001**
Diabetes mellitus	03	05	0.132**
Serum albumin (g/dl)	4.1±0.6	4.0±0.3	0.901*
Duration of surgery (min)	196.2 ± 46.8	206.9 ± 50.3	0.89*
Bowel preparation			
clean	09	08	0.999**
clear/ mucoid liquid	27	30	0.790**
liquid stools	03	02	1.000**
regular stools	01	02	1.000**
Intraoperative blood loss (ml)	98±12.4	92±13.2	0.672*
Patients receiving blood transfusion	08	09	0.821**

\* Unpaired *t* test

\*\* Fisher's exact test

**Table 4:** Oral antibiotic prophylaxis and wound infection

Oral antibiotic	Wound infection		Total
	YES	NO	
YES	5	35	40
NO	8	34	42
Total	13	69	82

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