

THERE IS NO DIFFERENCE OF SURGICAL SITE INFECTION BETWEEN SINGLE-DOSE AND MULTIPLE-DOSE OF PROPHYLAXIS ANTIBIOTIC IN OPEN APPENDECTOMY OF NON-PERFORATED ACUTE APPENDICITIS

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Objective: Acute appendicitis is the most common surgical emergency encountered compared with other non-traumatic acute abdomens. Sanglah General Hospital recorded there were 470 cases of acute appendicitis in the year 2006. This study aims to determine the effectiveness of a single-dose antibiotic prophylaxis in prevention of surgical site infection in open appendectomy of non-perforated acute appendicitis. **Method:** A single blind randomized controlled trial in 110 non-perforated acute appendicitis patients that underwent open appendectomy at Sanglah General Hospital emergency operating theatre from April to June 2012 was conducted. Cefazolin 1 g and Metronidazole 500 mg were administered intravenously prior operation. Samples were divided into two groups by permuted block. Following operation, the single-dose group was administered placebo, while the multiple-dose group received two additional doses of antibiotics. Surgical site infection (SSI) of both groups in every week for one month was evaluated. Surgical site infection was determined based on Hulton's criteria. Risk of surgical site infection of both groups was analyzed with Relative Risk (chi-square). **Results:** In the single-dose group 49.1% were males and 50.9% were females with a mean age of 28.71 years old, and in the multiple-dose group 40% were males and 60% were females with a mean age of 29.07 years old. Risk of SSI in single-dose group was 7.3% and multiple-dose group was 5.5% with Relative Risk (RR) = 1.33% (95% CI RR: 0.31-5.68, p= 1.000). **Conclusion:** There is no difference of SSI risk between single and multiple-dose antibiotic prophylaxis in open appendectomy of non-perforated acute appendicitis. **Keywords:** Antibiotic prophylaxis, single-dose, multiple-dose, non-perforated acute appendicitis, open appendectomy, SSI.

INTRODUCTION

Acute appendicitis is the most common surgical emergency encountered compared with other non-traumatic acute abdomens. Sanglah General Hospital recorded there were 470 cases of acute appendicitis in the year 2006.¹ A retrospective study that conducted in one hospital in India in 2002-2004 obtained the majority of acute appendicitis patients (91%) are non-perforated and only 9% are perforated.² Non-perforated acute appendicitis requires appendectomy to avoid perforation because perforation will lead to further complications.^{3,4} Open appendectomy of non-perforated acute appendicitis is classified as clean-contaminated surgery.^{5,6} Surgical Site Infection (SSI), which is a major complication following surgery, was reported about 9-30% in non-perforated

appendicitis patients who did not receive antibiotic prophylaxis. Antibiotic prophylaxis administered before, during and after surgery is effective to prevent postoperative infection. Antibiotic prophylaxis reduces SSI to 1-5%. It is recommended to administer prophylactic antibiotic routinely in appendectomy.^{7,8}

A single dose antibiotic prophylaxis is sufficient for clean-contaminated surgery. During prolonged operation, antibiotic prophylaxis should be readministered every 3 hours, but the duration should not exceed 24 hours. In daily practice, additional 2-3 doses of antibiotics after surgery and some even administered up to five days after surgery, are often found.^{11,12,13,14}

A randomized controlled trial study in non-perforated acute appendicitis patients in Hong Kong who underwent open appendectomy obtained SSI was not significantly different among the three groups, ie: a single-dose (6.5%), a multiple-dose antibiotic prophylaxis (three doses for a day) (6.4%), and multiple day (for five days after surgery) (3.6%).¹¹ Another retrospective study also

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showed that antibiotic prophylaxis that continued after surgery still had incidence of SSI 10%, and no significant difference from the single preoperative dose of antibiotic.¹³ Antibiotics that were continued after appendectomy did not reduce complication of SSI but rather extended length of stay, increased medical costs, increased morbidity and worsen patients outcome.^{13,14} In Sanglah General Hospital, patients with non-perforated acute appendicitis that underwent open appendectomy receive multiple doses of prophylaxis antibiotic, and there has not been a study to determine the effectiveness of a single-dose versus multiple-dose of prophylaxis antibiotic in prevention of surgical site infection in open appendectomy of non-perforated acute appendicitis.

In this study we would like to determine the effectiveness of single-dose versus multiple-dose prophylaxis antibiotic in open appendectomy of non-perforated acute appendicitis.

METHODS

This is a single blind randomized controlled trial in 110 non-perforated acute appendicitis patients within age range of 15-50 years that underwent open appendectomy at Sanglah General Hospital emergency operating theatre from April to June 2012. This trial was approved by the Regional Ethical Review Board in Indonesia by Ethical Commission of Sanglah General Hospital/Faculty of Medicine Udayana University, Bali-Indonesia. All patients recruited gave their informed consent to participate in this research.

Patients with obesity (relative body weight > 120%), diabetes mellitus (random blood sugar > 200 mg/dL), on steroid therapy, poor nutritional status (relative body weight < 70%), anemia (Hb < 11.5 g/dL for female and Hb < 12.5 g / dL for male), currently undergoing chemotherapy or radiation, allergic to cefazolin, or metronidazole, perforated appendicitis, and/or length of surgery more than 3 hours were excluded from this study. Variables include age, nutritional status, glucose levels of patients, length of surgery, length of stay, and operators that affect the incidence of SSI are controlled by design. Patients were administered prophylactic antibiotic cefazolin 1 g and metronidazole 500 mg IV at time of induction (prior surgery). Samples were divided into two groups by permuted block randomization. Single-dose group were administered a placebo after surgery, while multiple-dose group were administered two additional doses. Initial wound evaluation and care was performed in two days after surgery, then the patients were discharged. SSI were determined in both groups every week for a month in the surgical outpatient clinic. SSI is defined by Hulton's criteria. SSI risk that obtained from both groups were then analyzed by Relative Risk (chi-square) with 95% confidence interval.

RESULTS

The sample consisted of 49 males (44.5%) and 61 females (55.5%). Each group consisted of 55 subjects. In the single-dose prophylaxis antibiotic group, 49.1% were males and 50.9% were females with a mean age of 28.71. In multiple-dose prophylaxis antibiotic group, 40% were males and 60% were females with a mean age of 29.07 years. Table 1 presented the subject characteristic in this research.

Table 1
Baseline Characteristics of Single-dose and Multiple-dose of Prophylaxis Antibiotic Group

Characteristics	Single dose (n=55)	Multiple dose (n=55)
Sex		
Male	27 (49.1%)	22 (40.0%)
Female	28 (50.9%)	33 (60.0%)
Age (year old)	28.71±9.56	29.07±8.76
Relative Body Weight (%)	98.33±8.46	98.74±7.27
Hemoglobin (g/dL)	13.44±0.95	13.46±0.87
Random Blood Sugar (mg/dL)	108.49±13.06	101.77±13.72
Length of operation (minute)	93.36±29.17	100.27±23.87

Of the 110 subjects, 7 (6.4%) showed SSI. Of the 55 subjects in the single-dose group, 4 (7.3%) showed SSI, consisted of 3 (5.5%) first degree, and 1 (1.8%) second degree. Meanwhile, of 55 subjects in the multiple-dose group, 3 (5.5%) showed SSI, consisted of 2 (3.6%) first degree, and 1 (1.8%) second degree. Data of Surgical site infection observation were presented in Table 2. All events of SSI found at 7th day post-surgery.

Surgical site infection in single-dose and multiple-dose of prophylaxis antibiotic data were presented in Table 3. SSI risk were 7.3% in the single-dose antibiotic prophylaxis group and 5.5% in the multiple-dose antibiotic prophylaxis group with a relative risk (RR) = 1.33% (95% CI RR: 0.31 -5.68, $p = 1.000$). Thus, there is no difference of SSI risk between single-dose and multiple-dose of prophylaxis antibiotic in open appendectomy of non-perforated acute appendicitis.

DISCUSSION

Open appendectomy of non-perforated acute appendicitis is classified as clean-contaminated surgery. SSI was reported about 9-30% on non-perforated appendicitis in patients who did not receive antibiotic prophylaxis. Antibiotic prophylaxis has reduced SSI to 1-5%.^{8,9,15,16} Prophylactic antibiotic should be administered within an hour prior to incision. During prolonged

Table 2
Observation of Surgical site infection

Day after surgery	2 nd	7 th			14 th	21 st	28 th
		I	II	III			
Degree of infection	0	0	1	2	0	0	0
Single-dose	55	51	3	1	55	55	55
Multiple-dose	55	52	2	1	55	55	55
Total	110	103	5	2	110	110	110

Table 3
Surgical Site Infection in Single-dose and Multiple-dose Prophylaxis Antibiotic Group

Prophylaxis Antibiotic	SSI		Total
	Yes	No	
Single-dose	4 (7.3%)	51(92.7%)	55 (100%)
Multiple-dose	3 (5.5%)	52 (94.5%)	55 (100%)

operation, prophylaxis antibiotic should be readministered every three hours, but the duration should not exceed 24 hours.^{9,10} However, in some countries multiple-dose antibiotic (three doses in 24 hours) is still administered for non-perforated acute appendicitis.^{11,12,13,14} To prove the effectiveness of single-dose prophylaxis antibiotic in open appendectomy of non-perforated acute appendicitis, several studies have been conducted.

This study found that there is no difference of SSI between single-dose and multiple-dose antibiotic prophylaxis in open appendectomy of non-perforated acute appendicitis. The result of this study is similar to previous study that stated a single-dose of prophylaxis antibiotic is as effective as multiple-dose in open appendectomy of non-perforated acute appendicitis which indicated by the similar SSI outcome.¹³

A randomized controlled trial study in Hong Kong by Mui et al, in non-perforated appendicitis patients who underwent open appendectomy obtained SSI was not significantly different among the three groups, ie: the single dose antibiotic prophylaxis group (6.5%), the multiple-dose antibiotic prophylaxis group (6.4%), and the group who had got antibiotic for five days after surgery (3.5%).¹¹

Prospective cohort study conducted in Thailand by Kasapitbal et al on the incidence of SSI after open appendectomy in non-perforated acute appendicitis patients also found no significant difference of SSI risk between the single-dose and multiple-dose antibiotic prophylaxis compared with the group who did not receive antibiotic prophylaxis. SSI relative risk for single-dose,

multiple-dose or one day dose, and multiple-day antibiotic prophylaxis were 0.28 (0.09 to 0.90), 0.3 (0.11 to 0.88) and 0.32 (0.1-0.98), respectively.¹²

Many prophylactic antibiotics have been studied and evaluated their effectiveness in prevention of SSI in the case of non-perforated acute appendicitis. Second generation cephalosporins (cefoxitin, cefoxetan) and the third (cefotaxime) are effective to prevent SSI, which the incidence of SSI decreased to <5%, in numerous studies. Metronidazole alone is less effective than cefotaxime, which the SSI incidence is still above 10%, but when combined with ampicillin, cefazolin (first generation cephalosporin), or gentamycin, the effectiveness is similar to the second or third generation cephalosporin^{5,10,16} In Sanglah General Hospital, cexitin and cefoxetan are not available, while cefotaxime is not recommended as a prophylactic antibiotic. This study used cefazolin combined with metronidazole. On a single-dose combination of cefazolin 1 g and metronidazole 500 mg were obtained SSI of 7.3% and the multiple-dose (three doses) cefazolin 1 g and metronidazole 500 mg were obtained SSI of 5.5%.

CONCLUSION

This study found no difference of SSI risk between single-dose and multiple-dose antibiotic prophylaxis in open appendectomy of non-perforated acute appendicitis.

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