

## THE USE OF ORAL ANTIBIOTICS TO PREVENT SURGICAL SITE INFECTION ON POSTOPERATIVE MODIFIED RADICAL MASTECTOMY PATIENTS IN DR. SOETOMO GENERAL HOSPITAL, SURABAYA

**Norman Hadi, Hantoro Ishardyanto**

Departement of Surgery, Dr. Soetomo General Hospital, Faculty of Medicine, Universitas Airlangga, Surabaya, Indonesia

### ABSTRACT

*Surgical operations on modified radical mastectomy are considered clean procedures by the Centers for Disease Control and Prevention (CDC) wound classification system. Despite this, higher than expected Surgical Site Infection (SSI) rates are reported, varying from 1 % to 26 % across the literature. Some surgeons also prescribe postoperative prophylaxis for postoperative modified radical mastectomy patients to prevent infection despite its lack of proven efficacy. The aim of this study is to analyze the use of oral antibiotics to prevent Surgical Site Infection (SSI) on postoperative modified radical mastectomy patients in Dr. Soetomo General Hospital. This study was double-blinded randomized control trial of 60 postoperative modified radical mastectomy patients (2 groups) during the period of December 2017 to March 2018. Samples were prospectively divided into two groups (random sampling), in group A (n=30) patients received single dose prophylactic antibiotics and continued with oral antibiotics postoperative (Cefadroxil 2 x 500 mg) during 7 days and in group B (n=30) patients received single dose prophylactic antibiotics and continued without postoperative antibiotics (placebo). Both groups were evaluated clinically for surgical site infection up to 30 days. There was no statistically significant difference in both groups { $p=1$  ( $p>0.05$ )}. There was no incidence of surgical site infection in both groups during the 30-day follow-up period (days 3, 7, 14 and 30). There was no difference in the surgical site infection rate among those who received oral postoperative antibiotics prophylactic and without antibiotics (placebo) on postoperative modified radical mastectomy patients in Dr. Soetomo General Hospital. Because of the potential adverse events associated with antibiotic use, further evaluation of this practice is required.*

**Keywords:** Oral antibiotics; surgical site infection; postoperative modified radical mastectomy patients

### ABSTRAK

*Operasi bedah pada mastektomi radikal yang dimodifikasi dianggap prosedur yang bersih oleh sistem klasifikasi luka Centers for Disease and Prevention (CDC). Meskipun demikian, tingkat infeksi situs bedah (SSI) yang lebih tinggi dari yang diharapkan dilaporkan, bervariasi dari 1% hingga 26% di seluruh literatur. Beberapa ahli bedah juga meresepkan profilaksis pasca operasi untuk pasien mastektomi radikal termodifikasi pasca operasi untuk mencegah infeksi meskipun tidak terbukti kemanjurannya. Tujuan dari penelitian ini adalah untuk menganalisis penggunaan antibiotik oral untuk mencegah Infeksi Situs Bedah (SSI) pada pasien mastektomi radikal modifikasi pasca operasi di Rumah Sakit Umum Dr. Soetomo. Penelitian ini adalah uji coba acak tersamar ganda dari 60 pasien mastektomi radikal modifikasi pasca operasi (2 kelompok) selama periode Desember 2017 hingga Maret 2018. Sampel dibagi secara prospektif menjadi dua kelompok (pengambilan sampel acak), dalam kelompok A (n = 30) pasien menerima antibiotik profilaksis dosis tunggal dan dilanjutkan dengan antibiotik oral pasca operasi (Cefadroxil 2 x 500 mg) selama 7 hari dan pada kelompok B (n = 30) pasien menerima antibiotik profilaksis dosis tunggal dan dilanjutkan tanpa antibiotik pasca operasi (plasebo). Kedua kelompok dievaluasi secara klinis untuk infeksi tempat operasi hingga 30 hari. Tidak ada perbedaan yang signifikan secara statistik pada kedua kelompok { $p = 1$  ( $p > 0,05$ )}. Tidak ada insiden infeksi tempat operasi pada kedua kelompok selama periode tindak lanjut 30 hari (hari 3, 7, 14 dan 30). Tidak ada perbedaan dalam tingkat infeksi situs bedah di antara mereka yang menerima profilaksis antibiotik pasca operasi oral dan tanpa antibiotik (plasebo) pada pasien mastektomi radikal modifikasi pasca operasi di Rumah Sakit Umum Dr. Soetomo. Karena potensi efek samping yang terkait dengan penggunaan antibiotik, evaluasi lebih lanjut dari praktik ini diperlukan.*

**Kata kunci:** Antibiotik oral; infeksi bagian tubuh setelah pembedahan; pasien mastektomi radikal modifikasi pasca operasi

**Correspondence:** Norman Hadi, Departement of Surgery Dr. Soetomo General Hospital, Faculty of Medicine Airlangga University, Jalan Prof Dr. Moestopo 6-8, Surabaya 60286, Indonesia. Phone: +6281216543442. E-mail: dr.normanhadi@gmail.com

pISSN:2355-8393 • eISSN: 2599-056x • doi: 10.20473/fmi.v56i1.18449

• Fol Med Indones. 2020;56:36-40 • Received 22 Jun 2018 • Accepted 20 Dec 2018  
• Open access under CC-BY-NC-SA license • Available at <https://e-journal.unair.ac.id/FMI/>

## INTRODUCTION

Surgical operations on modified radical mastectomy are considered clean procedures by the Centers for Disease Control and Prevention (CDC) wound classification system. Despite this, higher than expected Surgical Site Infection (SSI) rates are reported, varying from 1 % to 26 % across the literature (Vilar-Compte et al 2004, Throckmorton et al 2009, Degnim et al 2013, Angarita et al 2011). Perioperative prophylactic antibiotics, given in accordance with Joint Commission SCIP (Surgical Care Improvement Project) guidelines, significantly reduce the risk of SSI after breast surgery but the value of postoperative prophylactic antibiotics is largely unknown (Sajid et al 2012, Bunn et al 2012, Felipe et al 2007, Specifications Manual for Joint Commission National Quality Core Measures 2010). Some surgeons also prescribe postoperative prophylaxis for postoperative modified radical mastectomy patients to prevent infection despite its lack of proven efficacy. The utility of routine or selective postoperative prophylactic antibiotics following modified radical mastectomy remains uncertain (Hedrick et al 2007).

According to the study by Felipe (2007) et al, the use of drains after breast and axillary surgery is one of the significant risk factors for the development of Surgical Site Infection. In 83 % of the cases, the microorganisms that cause SSI are the same as those on drains (Felipe 2007).

In a study by Brahmhatt et al (2012), 16 % of surveyed surgeons responded that they always or almost always prescribed postoperative prophylactic antibiotics while 76 % never or almost never prescribed antibiotics beyond the 24-hour postoperative period in the setting of no reconstruction.

Until now, there is no study that supports the use of oral antibiotics postoperative modified radical mastectomy routinely (Hedrick et al 2007). A recent study of the use of oral antibiotics postoperative modified radical mastectomy is a retrospective study by Throckmorton et al (2009), under the title Postoperative prophylactic antibiotics and surgical site infection rates in breast surgery. The study included 353 patients with 436 surgical sites who underwent breast surgery between July 2004 and June 2006 at the Department of Surgery Mayo Clinic. The study grouped patients into two groups: the first group received preoperative prophylactic antibiotics without postoperative antibiotics, and the second group received prophylactic antibiotics preoperatively as well as postoperative antibiotics. Throckmorton et al's (2009) study concluded that the rates of surgical site infection did not differ statistically ( $P = 0.67$ ) in the group of patients

receiving postoperative oral antibiotics and received no oral antibiotics postoperatively. The use of postoperative antibiotics also has potential side effects that require evaluation in practice. In the study, the surgeon used cefazolin for prophylactic antibiotics prior to surgery and used cephalexin (83.5%), levofloxacin (11.8%), and other antibiotics (4.7%) as oral antibiotics postoperatively. Whereas, another retrospective study conducted by Edwards et al (2014) Under the title Use of prophylactic postoperative antibiotics during surgical drain presence following mastectomy, concluded that the rates of surgical site infection differed significantly ( $P < 0.0001$ ) in the group of patients receiving postoperative oral antibiotics (SSI rate: 3.4%) and no oral antibiotic postoperative (SSI rate 7.3%), especially in smokers and old patients ( $> 60$ ).

The use of postoperative oral antibiotics modified radical mastectomy routinely has no guidelines, and surgeons in practice have some use and some do not use. Surgeons using postoperative oral antibiotics modified radical mastectomy assume that will reduce the risk of surgical site infection events.

The aim of this study is to analyze the use of oral antibiotics to prevent Surgical Site Infection (SSI) on postoperative modified radical mastectomy patients in Dr. Soetomo General Hospital.

## MATERIALS AND METHODS

This study is double-blinded randomized control trial of 60 postoperative modified radical mastectomy patients (2 groups) during the period of December 2017 to April 2018. Samples were prospectively divided into two groups (random sampling), in group A ( $n=30$ ) patients received single dose prophylactic antibiotics and continued with oral antibiotics postoperative (Cefadroxil 2 x 500 mg) during 7 days and in group B ( $n=30$ ) patients received single dose prophylactic antibiotics and continued without postoperative antibiotics (placebo). Both groups were evaluated clinically for surgical site infection up to 30 days.

The study population included all female patients who had undergone modified radical mastectomy and have had neoadjuvant chemotherapy at Dr. Soetomo General Hospital during the period from December 2017 to April 2018. Data were collected for each patient by review of the data collector sheet, medical record, and existing paper charts. Patients undergoing immediate breast reconstruction, had a history of allergies with cefadroxil or other cephalosporins class or history of allergy to beta-lactam antibiotics, in elderly ( $\geq 60$ ), malnutrition, obesity ( $BMI \geq 30$ ), history of diabetes

mellitus, smoking, history of corticosteroid use, were excluded. Patients with missing documentation of postoperative evaluation were excluded due to inability to determine surgical site infection occurrence.

A diagnosis of surgical site infection entailed one of the following CDC criteria: 1) purulent drainage from the incision; 2) organisms isolated from an aseptically obtained culture of fluid or tissue; 3) deliberate opening of the incision by a surgeon in patients having either tenderness, localized swelling, redness, or warmth; or 4) diagnosis of surgical site infection by the surgeon or office nurse practitioner. Patients clinically diagnosed and documented with cellulitis were also categorized as having an surgical site infection (Mangram AJ 1999).

Information on patient clinical factors potentially relevant to surgical site infection risk was collected. Patient age and body mass index (BMI) at time of surgery as well as diagnosis of diabetes and current corticosteroid use were abstracted. Breast cancer-related therapies included prior ipsilateral breast surgery, receipt of neoadjuvant chemotherapy, and prior radiation therapy to the ipsilateral breast. Surgery type was defined as unilateral modified radical mastectomy. Procedure length was recorded in minutes from the start of the incision to completion of skin closure. Length of hospital stay (LOS) and drain duration was reflected in a number of days. BMI > 30 was chosen as the defining threshold for obesity. Age  $\geq$  60 was the defining threshold for patient age.

The association between surgical site infection following modified radical mastectomy and postoperative antibiotic use was assessed using Mann Whitney U Test. Patient clinical factors were assessed

using independent T-test. Statistical significance was attributed for  $p$ -value > 0.05. All calculations were performed with SPSS version 17 software.

## RESULTS

A total of 60 women who underwent modified radical mastectomy patients during the period of December 2017 to April 2018. Samples were prospectively divided into two groups (random sampling), in group A (n=30) patients received single dose prophylactic antibiotics consisting of one dose of cefazolin within 30 minutes prior to surgical incision and continued with oral antibiotics postoperative (Cefadroxil 2 x 500 mg) during 7 days, and in group B (n=30) patients received single dose prophylactic antibiotics cefazolin and continued without postoperative antibiotics (placebo). Both groups were evaluated clinically for surgical site infection up to 30 days. Patient characteristics for those who received only perioperative antibiotics were compared with those who received both perioperative and postoperative antibiotic prophylaxis (Table 1).

The distribution of the sexes in this study consisted of 60 (100%) of women. The age range of the study sample was age 30 to 59 years. The age group of 50-59 years was the most age group in the cefadroxil group and the placebo group was 18 patients each. The Body Mass Index (BMI) distribution in the cefadroxil group had an average value of  $23.59 \pm 2.41$  kg/m<sup>2</sup>, while in the placebo group  $24.20 \pm 1.42$  kg/m<sup>2</sup>. Statistical test with independent T-test with 95% level of confidence showed that age distribution and Body Mass Index (BMI) in cefadroxil and placebo group did not differ significantly ( $p > 0.05$ ).

Table 1. Characteristics of patients

Characteristics Age (yr), mean $\pm$ SD	Mean ( $\pm$ SD) Cefadroxil group (n=60)	Mean ( $\pm$ SD) Placebo group (n=60)	<i>P</i> value	Significance*
Age (yr), mean $\pm$ SD	50.57 (7.19)	49.93 (8.448)	0.758	Not significant
Stage of cancer	-	-	0.690	Not significant
History of chemotherapy	-	-	1.000	Not significant
Procedure length (min), mean $\pm$ SD	116.0 (12.20)	119.67 (15.86)	0.320	Not significant
Bleeding at surgery (cc)	85.83 (41.64)	69.17 (28.22)	0.075	Not significant
Preoperative Hb level (g/dL)	12.56 (0.97)	12.49 (1.05)	0.780	Not significant
Praoperative Leukosit level (/cc)	6897.0 (2047.7)	7238.00 (2304.38)	0.547	Not significant
Praoperative GDA level (mg/dL)	105.73 (14.62)	111.00 (16.362)	0.194	Not significant
Praoperative Albumin level (g/dL)	3.85 (0.34)	3.87 (0.40)	0.838	Not significant
BMI (kg/m <sup>2</sup> ), mean $\pm$ SD	23.59 (2.41)	24.20 (1.42)	0.235	Not significant
Number of Chemotherapy Cycles (times)	-	-	0.376	Not significant

Note: With a limit of significance  $p > 0.05$  (data is homogeneous in both samples)

The distribution of operation duration in cefadroxil and placebo group did not differ significantly ( $p = 0.320$ ). The average duration of operation in the cefadroxil group was  $116.00 \pm 12.2$  minutes, with a range duration of surgery ranging from 100 minutes to 150 minutes. The average duration of surgery in the placebo group was  $119.67 \pm 15.86$  with a range duration of operation in the placebo group between 100 min and 180 min.

The mean value of Hb levels in the Cefadroxil group was  $12.56 \text{ g/dL} \pm 0.97$  with a range of  $10 \text{ g/dL} - 14.3 \text{ g/dL}$ . The mean value of Hb levels in the placebo group was  $12.49 \text{ g/dL} \pm 1.05$  with a range of  $10.5 \text{ g/dL} - 14.9 \text{ g/dL}$ . Statistical test with Mann Whitney U-Test results showed that the distribution of Hb levels in Cefadroxil and placebo groups did not differ significantly ( $p > 0.05$ ). Distribution of leukocyte, random blood sugar and albumin levels in cefadroxil and placebo groups did not differ significantly ( $p > 0.05$ ). Mann Whitney U-Test test results for the distribution of bleeding amounts in the cefadroxil and placebo groups did not differ significantly ( $p > 0.05$ ).

Cancer stage distribution in cefadroxil and placebo groups did not differ significantly ( $p = 0.690$ ). In the cefadroxil group were 87% of patients with stage IIIB and 13% with stage IIIA. In the placebo group as many as 90% of patients with stage IIIB and 10% with stage IIIA.

The history of chemotherapy type in cefadroxil and placebo group did not differ significantly ( $p = 1$ ). Distribution of total neoadjuvant chemotherapy cycles in cefadroxil and placebo groups did not differ significantly ( $p = 0.376$ ).

In both of these groups, the incidence of Surgical Site Infection (SSI) was not obtained on wound surgery on days 3, 7, 14 and 30 performed in the Inpatient Installation and in the Outpatient Surgical oncology unit of Dr. Soetomo General Hospital. Mann Whitney U-Test results for Surgical Site Infection (SSI) incidence in cefadroxil and placebo group did not differ significantly with  $p = 1$  ( $p > 0.05$ ).

There was no statistically significant difference in both groups ( $p=1$  ( $p > 0.05$ )). There was no incidence of surgical site infection in both groups during the 30 days follow up period (day 3, 7, 14 and 30).

## DISCUSSION

The rates of surgical site infection in breast surgery including axillary procedures vary from 1.4% to 38.3% depending on the type of surgical procedure: 1.5% for

wide excision, up to 38% for mastectomy. The rates seem to be a higher rate of infection that might be expected after other types of "clean surgery". These high rates of post-operative infections provide the consideration of antibiotic prophylaxis even though breast surgery is considered "clean" procedure. On the other hand, there is no clear evidence from published data for the benefit of antibiotic prophylaxis in breast cancer surgery (Vilar-Compte 2004).

Surgical Site Infection are associated with significant costs and morbidity, yet consideration also must be given to the risk of complications associated with prophylactic antibiotics, including allergic reactions, medication intolerance, Clostridium difficile infection, and increasing microbial resistance. While drug-related complications are uncommon after a single dose of perioperative antibiotics, the risk of adverse events associated with prophylaxis are more frequent with prolonged courses of antibiotic administration. In a study by Throckmorton et al (2009) 5.5 % of patients receiving postoperative prophylactic antibiotics after breast surgery developed an antibiotic-related complication compared with 0 % of patients who had only received a single preoperative dose.

Routine antibiotic prophylaxis is not necessary for patients not at risk of Surgical Site Infection, because the rate of SSI in these patients is low (Throckmorton et al 2009). Some surgeons limit the use of antibiotic to high-risk patients. The factors associated with postoperative infection in breast surgery are as follows: obesity, neoadjuvant chemotherapy or radiation therapy, prolonged closed suction drainage, second drain placed, diabetes mellitus, immunodeficiency, steroid use, hematoma, seroma, length of surgery, type of surgery, immediate breast reconstruction, advanced age, and smoking (Vilar-Compte 2004).

Guidelines for the use of antibiotics Department of Surgery Dr. Soetomo General Hospital recommends a single dose of 2-gram cefazolin prophylactic antibiotic (class I generation cephalosporins) for modified radical mastectomy surgery with limited use up to less than 24 hours postoperatively (Pedoman Penggunaan Antibiotika di Bidang Bedah 2009). Similarly, the American Society of Breast Surgeons stated that postoperative antibiotic use was not provided without clinical indication Specific (The American Society of Breast Surgeons 2012).

The age range of this study sample was age 30 to 59 years, with the majority of patients aged between 50-59 years. The mean age of patients in the cefadroxil group was  $50.57 \pm 7.19$  while the mean age in the placebo group was  $49.93 \pm 8.48$ . Old age ( $\geq 60$  years) is at high

risk of increasing the incidence of surgical site infection associated with a declining immune system in the elderly (WHO 2009).

Increased blood sugar levels ( $> 200\text{mg/dL}$ ) in the postoperative period ( $<48\text{h}$ ) were associated with an increased risk of surgical site infection.<sup>12</sup> In this study, no random blood sugar levels  $> 200\text{ mg/dL}$  were found. The mean preoperative blood sugar levels in the cefadroxil group were  $105.73 \pm 14.62\text{ mg/dL}$  (with the lowest levels of 86 and the highest levels of 171). Mean random blood sugar levels in the placebo group were  $111.00 \pm 16.36\text{ mg/dL}$  (with the lowest grade 79 and the highest levels of 148).

In our study, there was no difference in the incidence of Surgical Site Infection postoperative modified radical mastectomy patients in Dr. Soetomo General Hospital who received oral postoperative antibiotics and who did not get oral antibiotics postoperatively. Our Surgical Site Infection Evaluation takes place on the 3rd day, on the 7th day, on the 14th day until the 30th postoperative day, and we do not get purulent drainage from the incision or drainage on the fascia, pain, swelling, or redness. In both of these groups, the incidence of Surgical Site Infection (SSI) was not obtained on wound surgery on days 3, 7, 14 and 30 performed in the Inpatient Installation and in the Outpatient Surgical Oncology unit of Dr. Soetomo General Hospital. Mann Whitney U-Test test results for Surgical Site Infection (SSI) incidence in cefadroxil and placebo group did not differ significantly with  $p = 1$  ( $p > 0.05$ ).

The use of postoperative oral antibiotics modified radical mastectomy requires further evaluation because of potential side effects associated with antibiotic use and the risk of resistance can occur if we do not use antibiotics wisely.

## CONCLUSION

There was no difference in the surgical site infection rate among those who received oral postoperative antibiotics prophylactic and without antibiotics (placebo) on postoperative modified radical mastectomy patients in Dr. Soetomo General Hospital. Because of the potential adverse events associated with antibiotic use, further evaluation of this practice is required.

## REFERENCES

Angarita FA, Acuna SA, Torregrosa L, Tawil M, Escallon J, Rui'z A (2011). Perioperative variables

associated with surgical site infection in breast cancer surgery. *J Hosp Infect* 79, 328-32

Brahmbhatt RD, Huebner M, Scow JS, et al (2012). National practice patterns in preoperative and postoperative antibiotic prophylaxis in breast procedures requiring drains: survey of the American Society of Breast Surgeons. *Ann Surg Oncol*. doi: 10.1245/s10434-012-2477-1

Bunn F, Jones DJ, Bell-Syer S (2012). Prophylactic antibiotics to prevent surgical site infection after breast cancer surgery. *Cochrane Database Syst. Rev*, CD005360. doi: 10.1002/14651858.CD005360

Degnim AC, Scow JS, Hoskin TL, et al (2013). Randomized controlled trial to reduce bacterial colonization of surgical drains after breast and axillary operations. *Ann Surg* 258, 240-7

Edwards BL, Stukenborg GJ, Brenin DR, Schroen AT (2014). Use of prophylactic postoperative antibiotics during surgical drain presence following mastectomy. *Annals of surgical oncology* 21, 3249-3255. doi:10.1245/s10434-014-3960-7

Felippe WAB, Werneck GL, Santoro-Lopes G (2007). Surgical site infection among women discharged with a drain in situ after breast cancer surgery. *World J Surg* 31, 2293-9

Hedrick TL, Smith PW, Gazoni LM, Sawyer RG (2007). The appropriate use of antibiotics in surgery: a review of surgical infections. *Curr Probl Surg* 44, 635-75

Pedoman Penggunaan Antibiotika di Bidang Bedah (2009). Department of Surgery, Faculty of Medicine, Universitas Airlangga/dr. Soetomo Hospital, Surabaya  
Sajid MS, Hutson K, Akhter N, Kalra L, Rapisarda I, Bonomi R (2012). An updated meta-analysis on the effectiveness of preoperative prophylactic antibiotics in patients undergoing breast surgical procedures. *Breast J* 18, 312-7

Specifications Manual for Joint Commission National Quality Core Measures (2010).

The American Society of Breast Surgeons (2012). Position statement on antibiotics and surgical site infection

Throckmorton AD, Boughey JC, Boostrom SY, et al (2009). Postoperative prophylactic antibiotics and surgical site infection rates in breast surgery. *Ann Surg Oncol* 16, 2464-9

Vilar-Compte D, Jacquemin B, Robles-Vidal C, Volkow P (2004). Surgical site infections in breast surgery: case-control study. *World J Surg* 28, 242-6. doi: 10.1007/s00268-003-7193-3

WHO guidelines for safe surgery (2009). Safe surgery saves lives