Prophylactic Versus Extended Antibiotics Regimen in Breast Cancer Surgery

Mazin A Shakir (FIBMS) [1] and **Husam H Ali** (MBChB) [2]

Abstract

Background: A single intravenous preoperative prophylactic dose of an antibiotic with antistaphylococcal activity represent standard care for breast and axillary surgical procedures. Some surgeons also prescribe postoperative extended regimen for all patients with breast and axillary surgery to prevent infection.

Objective: To evaluate the efficacy of using post-operative antibiotic (extended regimen) in breast cancer surgery to decrease surgical-site infections.

Patients and Methods: One hundred and five females suffering from breast cancer were enrolled in this study (from the 1st of January 2014 to the 30th of December 2015 in Al-Yarmouk Teaching Hospital admitted by multiple surgeons).They was divided into two groups. Group (1) received single prophylactic dose of ceftriaxone injection 1gm preoperatively and group (2) received extended doses postoperatively1 gram twice daily for 4days,then antibiotic changed to oral oute (cefixime 400 mg once daily for 7days). The patients in both groups discharged home in the2nd post-operative day and seen again after five days, then on the days, then on the day of removal of surgicalstitches (day10) and at day30.Allpatientshadclosedsuctionsurgicaldrainswhendischargedfromhospitalandremoved inday5. Second generation cephalosporin was not used because it is not available.

Results: During the period of this study, the incidence of wound infection was 7 (15%) in group1 and 6 (10%) in group2. The p value of the incidence of wound infection in these groups was 0.55, so it is statistically not significant.

Conclusion: No statistically significant reduction in surgical wound infection among those received postoperative extended doses of antibiotic prophylaxis (i.e.group2) compared with those who received preoperative single dose of antibiotic prophylaxis (i.e.group1).

Key words: Breast surgery, prophylactic antibiotic, surgical site infection.

Corresponding Author: Drwaleedarifalani@yahoo.com.

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[1,2]Deparment of General Surgery-Al-Yarmouk Teaching Hospital-Baghdad-Iraq.

Introduction

The breast is composed of 15 to 20 lobes, each composed of several lobules. Fibrous bands of connective tissue travel through the breast (Cooper's suspensory ligaments), insert perpendicularly into the dermis, and provide structural support [1, 2]. Breast cancer was the leading cause of cancer-related mortality in women until 1987, when it was surpassed by lung cancer [3]. Human beings and bacteria normally live together in a symbiotic relationship. When homeostasis is lost and/or there is external contamination which has reached a variable critical level, bacteria claim for human hegemony and the symbiotic relationship becomes a parasitic one. Consequently, infection appears. Infection appears when microbial contamination overwhelms host's defense mechanisms [4, 5].

Each year, more than 18 million surgical procedures are performed in US hospitals [6,7]. The Center for Disease Control and Prevention (CDC) reports that 2.7% of these operations are complicated by surgical-site infections (SSI) which are the second most common cause of nosocomial infection, accounting for 14-16% of all hospital-acquired infections[8,9]. According to the CDC criteria defining SSI, two thirds were confined to the incision, and one-third involved organs or spaces [10]. Patients who develop SSI are twice as likely to die, 60% more likely to spend time in an ICU, and more than five times as likely to be readmitted to the hospital than their non SSI counterparts [11]. In August 2002, the Center for Medicare and Medicaid Services (CMS) and the CDC implemented the National Surgical Infection Prevention (SIP) Project. The goal of the SIP project is to decrease the morbidity and mortality attributable to SSI, by promoting appropriate selection and timing of prophylactic antimicrobial (PAM) agent administration [12].

Three well accepted performance measures for national surveillance and quality improvement have been developed: [1] The proportion of patients who have parenteral PAM initiated within 1 hour prior to incision (within 2 hours for vancomycin or fluoroquinolone) [2].The proportion of patients who are given a PAM agent that is consistent with current published guidelines [3]. The proportion of patients where PAM is discontinued within 24 h of surgery [13]. SSI is a significant cause of morbidity and mortality. In the context of breast surgery, this can lead to significant psychological trauma and delay in receiving adjuvant chemotherapy or radiotherapy. SSI rates in breast surgery have been reported to be between 1.4% and 2.3% for excision biopsies; between 6.6% and 18% for breast conserving surgery and between 19% and 38.3% for mastectomies[14,15]. SSI rates for aesthetic breast surgery have been reported to be between 1% and 7%.[16-18]The role of antibiotic prophylaxis in the reduction of post-operative infection rate is well established in clean-contaminated procedures.[19] However, much controversy still surrounds the use of antibiotics for clean procedures such as elective breast surgery, as injudicious use can lead to development of microbial resistance, increased number of adverse reactions to antibiotics, unnecessary medical costs and also increased consumption of nursing staff resources in drug administration. [20] More importantly SSI can delay adjuvant treatment. [21] Surgical site infection (SSI) of the breast is a source of postoperative complications includes predisposing patients to additional medical interventions (e.g.: surgical debridement or abscess draining), poor aesthetic results, and psychological trauma [22]. Certainly preventing SSIs in breast cancer patients is a necessary step for assuring high-quality surgical treatment [23].

Several investigators have found that patients undergoing definitive surgery for cancer had a lower risk for wound infection if the diagnosis had been established by prior needle biopsy rather than by an open surgical biopsy [24, 25], but one investigator found the opposite effect.[29] Nicotine and other components of cigarettes have well-known adverse effects on small vessels of the skin, resulting in a nearly fourfold increase in the risk of wound infection after breast surgery[27]. It has been experienced that wound infection after breast surgery is quite rare in cases where drains are not used and wires are not inserted [28]. Wound infection usually occurs between 5 and 21 days following surgery in approximately 10% of patients. The causative organism is often *Staphylococcus aureus* although

Staphylococcus albus and Coliforms or Bacteroides may be the cause. The presence of mammary duct ectasia is associated with an increased risk of wound infection. It is often not possible to make this diagnosis. [29] Non-invasive breast carcinoma is usually treated with wide local excision, without the need for axillary clearance. Wound infection occurs in approximately 10% of women undergoing curative surgery for breast carcinoma, and seems to be particularly common following axillary clearance. Wound infection is also common where definitive surgery follows a recent open biopsy. Despite the risk of morbidity the need for staging means that axillary clearance remains part of the management protocol for breast cancer [30].

Patients and Methods

One hundred and five female suffering from breast cancer were enrolled in a prospective study from the 1st of January 2014 to the 30th of December 2015, in AL-Yarmouk Teaching Hospital, in order to assess the exigency of postoperative extended doses of antibiotic in women undergoing definitive surgery for malignant breast disease. Patients enrolled in this study were divided into two groups. Group (1) received single prophylactic dose of intravenous ceftriaxone injection 1 g preoperatively. Group [2] received extended doses of the same antibiotic postoperatively,1 gram twice daily for 4 days, then antibiotic changed to oral route (cefixime 400 mg once daily for 7days).

Patients were 37-70 years of age. All patients had a diagnosis of breast cancer, based on previous histological evidence. No patient was entered into the study more than once. Patients known to have hypersensitivity to ceftriaxone or penicillin were excluded from this study, as well as patients who were taking concurrent antimicrobial therapy at the time of surgery and patients with active skin disease. Patients who were suffering from renal impairment, Peau d'orange disease of breast, mammary duct ectasia, recent biopsy procedure (within 30 days), diabetes, smokers, obese, old age patients, as well as those received neoadjuvant chemotherapy, breast size, prior radiation, prolonged operation and drain type were considered at high risk factors for wound infection. For group (1) patients (single dose antibiotic prophylaxis regimen), the anesthetist was instructed to administer the antibiotic (ceftriaxone 1 gm) as a single intravenous bolus injection through a peripherally placed 18-20 gauge intravenous cannula before the induction of anesthesia. The patient discharge home in the 2nd post- operative day and to be seen again after five days, day of removing of surgical stitches and day 30.Group (2) patients received ceftriaxone injection 1 gm twice daily through a peripherally placed intravenous cannula for 4 days after surgery. Then, the antibiotic was changed to oral cefixime 400 mg as a single daily dose for one week (duration of treatment 11 days). Patients in group two were discharged home in the 2nd post- operative day and seen after five days, day of removing of stitches, and day 30. All patients had closed suction surgical drains when discharged from hospital and removed in day 5.

Patients were followed within five days after discharging by symptomatic history and physical examination focusing on the wound and surrounding area. Then we followed up the patients when they attended the outpatient clinic. Wound infection was defined as discharge from the wound or erythema indicative of cellulitis (>5mm from the wound) at any time during the study period. The wound infection when assessed, was termed as mild infection (erythema or redness around single stitch), moderate infection (erythema and redness around multiple stitches or along the wound) and severe infection (discharge from the wound, breakdown of wound edges or cellulitis).

Data were entered and analyzed using the available software packages of Statistical Packages for Social Sciences-Version 22 (SPSS-22). Data were presented as frequency and percentages with use of Pearson Chi-square test as test of significance with P value equal or less than 0.05 as the level of significance.

Results

During the period of this study (from the 1st of January 2014 to the 30th of December 2015), in AL-Yarmouk Teaching Hospital, one hundred and five females were enrolled in this study.

From 45 patients involved in group1, 13 (28.89%) had risk factors for wound infection such as diabetic, smoker, uremic, obese, old age, or mammary duct-ectasia. While 32 (71.11%) of them had no risk factors. Twenty six (43.33%) patients from 60 patients enrolled in group2 had risk factors for infection and 34 (56.67%) had no risk factors for wound infection, figure (1).

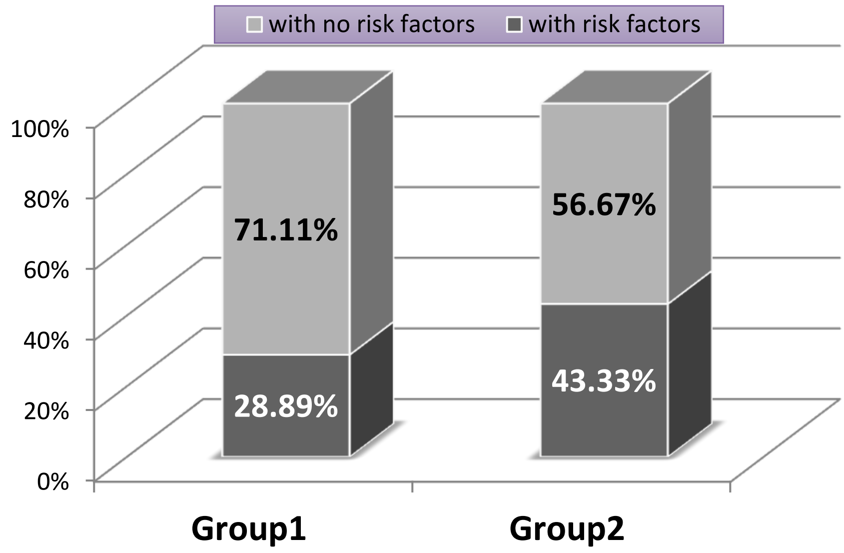

Figure (1): Number of patients had risk factors for wound infection.

The definitive treatment for the breast tumor was mostly modified radical mastectomy for 43 (95.56%) patients from group1 and 53 (88.33%) patients from group2. The remaining were treated by wide local excision (WLE) with axillary clearance, 2 (4.44%) from the group1 and 7 (11.66%) from group2. All procedures done by multiple surgeons. The incidence of wound infection regarding operative procedures was 7(15.55%) in group1, all patients underwent modified radical mastectomy, 5(11.10%) were with risk factors while the other 2(4.44%) were with no risk factors. No incidence of wound infection in those underwent (WLE) with axillary clearance in group (1).

The incidence of wound infection regarding operative procedures was 6(10.00%) in group2, 5(8.34%) patients underwent modified radical mastectomy, 3(5.00%) were with risk factors while 2(3.34%) patients were with no risk factors. Only one patient underwent (WLE) with axillary clearance suffered wound infection, and was with risk factor, Table (1).

Table (1): Incidence of wound infection regarding operative procedures**.**

Operative procedures	Group 1			Group 2		
	Incidence of wou infection	Patients with risl factors	Patients without r factors	Incidence of wou infection	Patients with risk factors	Patients without risk factors
Modified radical mastectomy	7(15.55%)	5(11.1%)	2(4.44%)	5(8.34%)	3(5.00%)	2(3.34%)
(WLE) with axillary clearance	-	-	-	1(1.66%)	1(1.66%)	-

The final histopathological study after definitive treatment revealed that the main tumor stage was T2, 19 (42.22%) patients from group1 and 29 (48.33%) patients from group2. T1 stage was noticed in 8 (17.78%) patients from group1 and 6(10.00%) from group2, T3 in 15 (33.33%) patients from group1 and 8 (13.33%) from group2, T4 in 3 (6.66%) and 8 (13.33%) patients from group1 and group2, respectively. While L.N. involvements were found in 37 (82.22%) patients from group1 and 50 (83.33%) patients from group2. No patient seen with distant metastasis. Patients with T1 were presented with no wound infection in both groups. But those with T2 in group1, 4(8.88%) patients suffered from wound infection, 3(6.66%) with risk factors and 1(2.22%) without, while in group2, patients that developed wound infection were 2(3.34%) patients, one with risk factors and the other without. In group1, Patients with T3 were presented with wound infection as 3(6.66%) had risk factors and 1(2.22%) patient had no risk factors. But in group2, 2(3.34%) patients suffered from wound infection and both had risk factors. For patients with T4 histopathology, just 1(1.66%) patient in group2 suffered from wound infection and had no risk factors. All patients suffered from wound infection were with positive lymph nodes Table [2].

Table (1): The incidence of wound infection regarding to stages of breast cancer.

Stages of breast cancer	Group1			Group2		
	Incidence of wound infection	Patients with risk factors	Patients without risk factors	incidence of wound infection	Patients with risk factors	Patients without risk factors
T1	-	-	-	-	-	-
T2	4(8.88%)	3(6.66%)	1(2.22%)	3(5.00%)	2(3.34%)	1(1.66%)
T3	3(6.66%)	2(4.44%)	1(2.22%)	2(3.34%)	2(3.34%)	-
T4	-	-	-	1(1.66%)	-	1(1.66%)
Lymph node involvement	7(15.55%)	5(11.10%)	2(4.44%)	6(10.00%)	4(6.66%)	2(3.34%)

The incidence of wound infection was 7 (15.55%) in group1, five patients had mild infection, 4 of them (8.88%) had risk factors for infection and the remaining one (2.22%) had no risk factors. Two (4.44%) patients in group1 had moderate infection, one (2.22%) patient had risk factor and the other one had no risk factor. In group2, 6 (10.00%) patients had wound infection, 5(8.34%) patients had mild infection, 3 (5.00%) had risk factor and 2 (3.34%) patients had no risk factors. One patient (1.66%) suffered from moderate type of wound infection in group2.

No one suffered from severe type of wound infection. Figure 3&Table [3].

In our study the rate of wound infection after surgery for malignant breast diseases is 12.38% and p value of the incidence of wound infection in two groups was 0.55, so it is statistically not significant.

Table (1): Incidence of wound infection regarding to risk factors.

Wound infection	Group 1		Group 2	
	With risk factors	Without risk factors	With risk factors	Without risk factors
Mild	4(8.88%)	1(2.22%)	3(5.00%)	2(3.34%)
Moderate	1(2.22%)	1(2.22%)	1(1.66%)	-
Severe	-	-	-	-

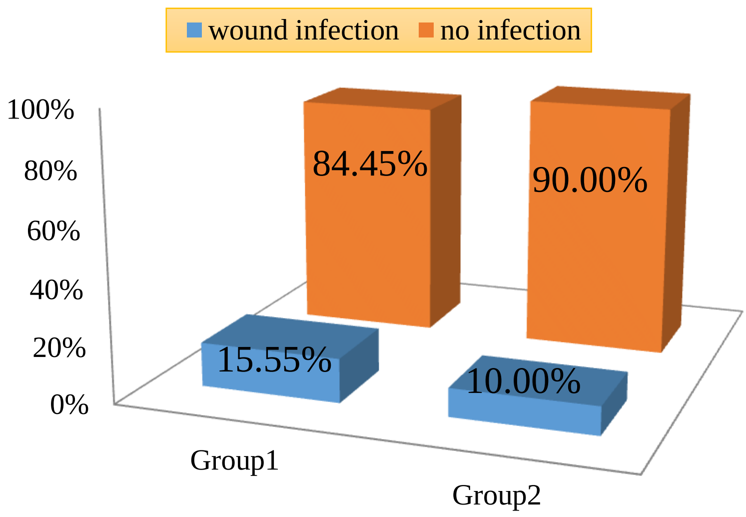

Figure (3): Incidence of wound infection (P=0.393).

Discussion

Globally Use of preoperative antibiotic coverage to minimize infection rates has been evaluated in multiple retrospective trials and in prospective, randomized, and controlled trials. These studies have yielded disparate results; many have shown that a single dose of a preoperative antibiotic (usually a cephalosporin, administered approximately 30 minutes preoperatively) effectively reduces wound infection rates by 40% or more [31][32]. Meta-analysis by Platt and colleagues, revealed that antibiotic prophylaxis reduced wound infection rates by 38%, despite the selection bias of antibiotics being used predominantly in higher-risk cases [33].

By comparing the incidence of wound infection of this clean surgery between two groups; in the single dose group the incidence of infection is 7 patients (15.55%). In the group 2, 6 (10.00%) patients had infection, in comparison between the incidences of infection rate in two groups we found that the p value was not statistically significant, so the extended doses regimen to the patients of breast surgery had no advantage over the single prophylaxis pre-operative regimen. In addition uncontrolled and injudicious use of antibiotics may lead to antibiotic resistance, adverse effects and increase medical costs.

The lowest reported rates of breast wound infections occurred in a phase III study of a long-acting versus a short-acting cephalosporin, revealing greater risk reduction with the former (0.45% versus 0.91%) [34]. In contrast, Wagman and colleagues found no effect of perioperative cephalosporin in a placebo-controlled, phase III trial involving 118 patients who had breast cancer (5% versus 8%), however, in the antibiotic arm the infections were delayed in onset (17.7 days versus 9.6 days) [35]. Gupta and colleagues reported similar rates of wound infection in a phase III study of prophylactic amoxicillin/clavulanic acid (17.7%) versus placebo (18.8%) and concluded that perioperative antibiotics are unnecessary in elective breast surgery [36].

In this study the rate of wound infection after surgery for malignant breast cancer is 12.38%. Mechanisms that have been postulated for this unanticipated rate include extensive dead space, the use of drains to manage the postoperative exudate, bacterial colonization of the drain, and concomitant nodal resection.

The accepted rate for wound infections after clean operations is approximately 1.5% [37]. But there are studies that have shown a higher incidence of wound infections after breast operations, ranging from 3% to 30%. [38].

The incidence of wound infection regarding operative procedures was 6(10.00%) in group2, 5(8.34%) patients underwent modified radical mastectomy, 3(5.00%) were with risk factors while 2(3.34%) patients were with no risk factors. Only one patient underwent (WLE) with axillary clearance suffered wound infection, and was with risk factor. Various studies demonstrated no consistent correlation between the risk of wound infection and mastectomy versus lumpectomy as definitive breast cancer surgery [34][35][36].

In conclusion: There was no statistically significant surgical wound infection reduction among those who received extended doses postoperative antibiotic prophylaxis compared with those with preoperative antibiotic prophylaxis. It is recommend to consider single prophylactic antibiotic and to avoid post-operative extended regimen, because the later need more nursing and more medical costs, and possibility of antibiotic resistance.

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