

# Efficacy of prophylactic antibiotic administration for breast cancer surgery in overweight or obese patients: research highlight

Rachel L. O'Connell, Jennifer E. Rusby

Department of Breast Surgery, The Royal Marsden NHS Foundation Trust, Down Road, Sutton, Surrey, SM2 5PT, UK

Corresponding to: Rachel L. O'Connell. Department of Breast Surgery, The Royal Marsden NHS Foundation Trust, Downs Road, Sutton, Surrey, SM2 5PT, UK. Email: roconnell@doctors.org.uk.

**Abstract:** The rate of surgical site infection (SSI) after breast surgery is higher than expected for a 'clean procedure'. There is currently no consensus on the use of antibiotics, and as a result there is variation in use. An infection may compromise cosmesis and delay the start of adjuvant therapy. This research highlight reviews a recent paper by Gulluoglu and colleagues investigating the use of antibiotics in overweight and obese patients undergoing breast cancer surgery and also reviews the current literature on this important topic.

**Key Words:** Surgical site infection (SSI); breast cancer surgery



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Breast surgery is regarded as a 'clean procedure' and as such the expectation of surgical site infection (SSI) is low. However, published rates of SSI in breast surgery are variable and often high, ranging from 0.8% to 26% (1-6). SSI following breast surgery can potentially compromise the aesthetic outcome, prolong hospital stay, be a cause of readmission and increase the overall cost of the procedure (7). Furthermore, it can delay the start of adjuvant therapy or interrupt the process of breast reconstruction (8). Conversely, antibiotic use has consequences other than simply the cost of the drug. In recent years increased and widespread antibiotic use has led to the public health issue of antibiotic resistance. To the individual there is risk of an adverse reaction, which at its worst can be fatal, as well as adverse effects such as clostridium difficile infection which can lead to significant morbidity and mortality. For all of these reasons SSI is an important consideration to breast surgeons, and strategies to reduce SSI are relevant and important.

Gulluoglu and colleagues recently published in *Annals of Surgery* (9) a randomized controlled trial to assess the impact of prophylactic antibiotics on the prevention of SSI in overweight or obese patients [defined as a body mass index (BMI) of greater than 25 kg/m<sup>2</sup>] undergoing breast

cancer surgery. This was a phase IV randomized, controlled, parallel-group efficacy trial. The prophylaxis group received 1 g ampicillin-sulbactam intravenously at induction of anaesthesia and the control group received no intervention. Both the patients and observers were blinded. A sample size of 360 patients was calculated to give 90% power to detect a statistically significant difference where P=0.05 in a 2 sided test. In total 369 patients were included in the final intention to treat analysis. There were several exclusion criteria, most importantly immediate breast reconstruction, but other exclusions were chronic renal disease, uncontrolled diabetes, low serum albumin and ASA III-V. On discharge all patients were instructed to contact the investigators in the event of any wound problems and patients were reviewed on postoperative days 7, 14, 21 and 30. SSI was defined as occurring within 30 days of surgery and according to the criteria of Mangram *et al.* (10). The groups were well matched in terms of basic comparisons except the control group had significantly more frequent open surgical biopsies.

Antibiotic administration significantly reduced the SSI rate to 4.8% in the prophylaxis group compared to 13.7% in the control group (relative risk 0.35; 95% CI: 0.17-0.73). There were no adverse reactions observed in patients

who received antibiotics. The mean SSI-related cost was significantly higher in the control group when compared with that of the prophylaxis group. Patients with a BMI of less than 25 (n=144) were also kept under surveillance as a third arm of the study and did not receive prophylactic antibiotics. SSI developed in 3.5% of these patients and this was significantly lower than patients in the control group (no prophylaxis, BMI of 25 or over). The authors concluded that antibiotic prophylaxis significantly decreased SSI incidence after breast cancer surgery and was cost-effective in overweight and obese patients.

The main limitations of this study were that although patients were randomised, those in the control group were found to undergo significantly more open biopsies, which may (11) or may not (12) be a risk factor for SSI, therefore this difference may have predisposed to a higher rate of SSI in the control group. The second limitation was that localization of occult cancers with wire placement was not a baseline comparison variable, yet this may also be a risk factor for SSI.

Several previous randomized controlled trials have investigated the use of antibiotics in breast surgery by means of randomized control trials and many retrospective studies have been undertaken to identify risk factors for SSI. An updated Cochrane review of prophylactic antibiotics in breast cancer surgery was recently published (13). Eight trials of preoperative prophylaxis were included and the review concluded that antibiotic administration reduces the risk of SSI [pooled risk ratio (RR) 0.11, 95% CI: 0.01-1.95]. Another meta-analysis (14) including 3,720 patients from nine randomized control trials of breast surgery, including malignant and benign, also supported the use of prophylactic antibiotics (RR 0.64, 95% CI: 0.5-0.83). When reviewing each trial separately, only one (15) demonstrated a significant reduction in risk in SSI, it was only once the data from each study was pooled in the meta-analyses that the relative risk reduction became significant. A third meta-analysis investigating risk factors for SSI by Xue *et al.* (16) included eight studies with a combined total of 681 cases of SSI and 2,064 controls. Data was combined if the risk factor was studied by at least two studies. The authors did not support the use of prophylactic antibiotic. The drawback of these meta-analyses is that, the conclusion depends on the detail of how papers were selected for inclusion and how the analysis was undertaken. Furthermore, amongst the studies included there is heterogeneity in the antibiotics used, the procedures undertaken and the duration of follow up. For example, in the meta-analysis by Sajid *et al.* the length of

follow up in the trials ranged from five to forty-two days, seven different antibiotics were used and the procedures ranged from axillary surgery to reconstructive breast surgery.

Knowledge of risk factors for SSI is important to identify patients at high risk and to optimise any modifiable risk factors. As well as obesity, high American Society of Anesthesiologists (ASA) score, prolonged use of surgical drains, re-operation including previous breast biopsy or operation, previous chest irradiation, smoking, increased age, hypertension, diabetes mellitus, haematoma, seroma and intraoperative bleeding have all been implicated in the risk of SSI (16-18). One recent study assessing independent risk factors for SSI in more extensive surgery reported that receipt of a sub-optimal dose of prophylactic antibiotics was associated with a 5.1 fold increased odds of breast SSI (17). In their multivariate analysis obesity did not have a strong association with SSI and was displaced in the regression model by the sub-optimal dose variable, implying that the risk associated with obesity may be somewhat reduced by correct dosing of prophylactic antibiotics to account for increased tissue mass.

There is currently no consensus on the use of antibiotics, and as a result there is variation in use. Unless there are local guidelines the decision is made by the surgeon responsible for the procedure. A British study (19) reported that up to 33% of surgeons who performed wide local excisions, mastectomies and axillary surgery routinely use antibiotics whereas in a Columbian (20) study up to 68.1% of surgeons used antibiotics for similar procedures.

In conclusion, breast surgery is associated with a higher than expected rate of SSI. Breast-related infection carries the universal consequences such as the cost of treating an infection, additional nurse and doctor time, potential hospital inpatient stay and time off work. As well as this there are specific potential consequences such as poor cosmesis and delay in subsequent adjuvant therapies. There is a paucity of evidence or specific guidelines for surgeons to use, despite pressures to be cost effective and the public health impact of antibiotic resistance. For those doctors that use antibiotics routinely for all breast surgery, Gulluoglu and colleagues' paper will have little impact. However for those who use antibiotics in selected patients, this paper provides evidence to support the use of antibiotics in breast surgery for overweight or obese patients.

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