Antibiotic prophylaxis in obese patients submitted to bariatric surgery. A systematic review[1]

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ABSTRACT

PURPOSE: To review the use of cefazolin in prophylaxis of surgical wound infection (SSI) in bariatric surgery (BS).

METHODS: A systematic review was performed from October to November, 2013 using the following databases: The Cochrane Library, Medline, LILACS, and EMBASE. The inclusion criteria were randomized clinical trials and observational studies that were evaluated by two independent reviewers.

RESULTS: Nine hundred and sixty one titles were recovered after preliminary analysis (title and abstract), seven studies remained for final analysis. There were three clinical trials (one with SSI, and two with antibiotic levels as the outcome), and four were observational studies (three cohorts and one case-control, all had SSI as the outcome). After administration of 1g or 2 g, levels of cefazolin in serum and tissue were suboptimal according to two studies. Results from observational studies indicated that different antibiotics were used for prophylaxis of SSI in BS and that use of other drugs may be associated with higher rates of SSI.

CONCLUSION: The use of cefazolin for surgical wound infection prophylaxis in bariatric surgery is recommended, however further studies are needed in order to refine parameters as initial dose, redose, moment of administration and lasting of prophylaxis.

Key words: Bariatric Surgery. Antibiotic Prophylaxis. Obesity. Cefazolin. Review.

Introduction

Obesity is considered a chronic disease and is reaching epidemic proportions in developed and developing countries[1,2]. It represents an important burden of disease from clinical and public health perspective[3]. A long term strategy is required for its prevention and it must be managed with a comprehensive approach[1]. Obesity is associated to increase mortality and morbidity[1,4], and this condition is frequently not controlled by diet and pharmacologic therapy. Bariatric surgery, however, is being shown to be more effective in sustained weight reduction[5] which increases the demand for surgical intervention in these patients[6].

Although obesity is considered a risk factor for nosocomial infections[4,7] particularly surgical site infection (SSI), there were few studies that have evaluated this specific factor among patients submitted to bariatric surgery[7,8]. It is considered one of the most common complications in bariatric surgery[5,9], and its magnitude may be underestimated[5]. The frequency of SSI in obese patients ranges from 1–21.7% after bariatric surgeries[4,5,7,10,11], depending on the surgical technique applied[7]. It is important to consider that in these studies there is a poor standardization of antibiotic agents and its posology.

The factors that have been associated to an increase in the risk of post-surgical infections are usually identified as the evaluation of individual risk of the patient, the trans-operatory period and procedures that are carried out[9]. Surgical site and prevailing microorganisms drive the antibiotic choice for prophylaxis[9]. The most frequent species isolated from post-surgical infections in bariatric surgery are *Staphylococcus* spp[10,12] and S*treptococcus species*[7,10].

First generation cephalosporin's, due to spectrum, safety and experience of use, are the choice in the prophylaxis of most of surgeries[4]. A recent guideline issued by the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, the Surgical Infection Society and the Society for Health Care Epidemiology of America recommends cefazolin for procedures involving entry into lumen of gastrointestinal tract (as in bariatric surgery), with strength of evidence "A"[13]. This drug is, indeed, widely employed[4,5,8,11,14,15].

Despite the recommendations indicating the use of cefazolin, other drugs and regimens are also employed. In a large observational study, a total of 37 different antibiotic regimens were found for prevention of SSI in bariatric surgery[7], indicating that, although cefazolin is the most recommended drug, other options are widely used.

Cefazolin presents a half-life of two hours, giving protection for longer surgeries. It has anti-staphylococcal activity and is the preferred agent in gastrointestinal surgeries in high risk patients (i.e. obesity)[4]. Besides, it is a low cost drug. According to some authors, 2g of cefazolin should be administered in morbidly obese patients; however there is a concern if this dose is sufficient for all patients, considering that average corporal weight is variable as it has increased in the last years[4,7,14,15].

There is a need of qualified information not only about the agent to be employed, but also about dosage, moment of administration, posology and pharmacokinetic profile of the drug. The present scenario permits to observe the use of different antimicrobial agents, with different posology without consistent evidence, promoting conditions to an increase in bacterial resistance and related costs[4].

The objective of this study was to review the use of cefazolin in the prophylaxis of surgical wound infection in bariatric surgery.

Methods

A systematic review was carried out from October to November, 2013searching the following databases: The Cochrane Library, Medline, LILACS and EMBASE. The first choice in terms of type of publication was randomized clinical trial and then quasi-experiment. Observational studies were also searched in order to identify those articles that had less risk of bias. After a preliminary recovery, titles and abstracts were examined by two independent reviewers. Cases of disagreement were evaluated by a third reviewer.

To evaluate the quality of reporting in observational studies and clinical trial studies STROBE[16] CONSORT statements[17] were respectively employed.

Terms employed (Chart 1):

Mesh terms: bariatric surgery, gastric bypass, antibiotic prophylaxis, surgical site infection, cefazolin, and as free term, surgical wound infection – access: October 2013

DeCS terms: bariatric surgery, gastric bypass, antibiotic prophylaxis, cefazolin, surgical wound infection – access: October 2013

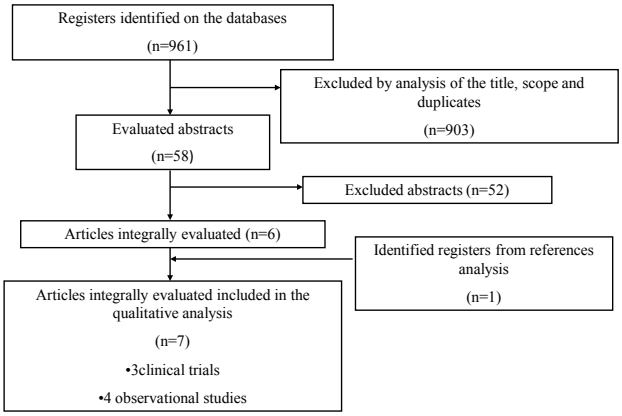
EMTREE terms: bariatric surgery, antibiotic prophylaxis, cefazolin – access: November 2013

CHART 1 – Databases strategy search.

DATABASE	TERMS	RESULTS
The Cochrane Library (Bireme)	Bariatric surgery and antibiotic prophylaxis	0
	Bariatric surgery and cefazolin prophylaxis	0
	Bariatric surgery and surgical site infection	10
	Bariatric surgery and surgical wound infection	17
	Gastric bypass and antibiotic prophylaxis	10
	Gastric bypass and cefazolin prophylaxis	0
	Gastric bypass and surgical site infection	11
	Gastric bypass and surgical wound infection	26
	Subtotal	74
LILACS	Bariatric surgery and antibiotic prophylaxis	1
	Bariatric surgery and cefazolin prophylaxis	0
	Bariatric surgery and surgical wound infection	1
	Gastric bypass and antibiotc prophylaxis	0
	Gastric bypass and cefazolin prophylaxis	0
	Gastric bypass and surgical wound infection	2
	Subtotal	4
MEDLINE	Bariatric surgery and antibiotic prophylaxis	29
	Bariatric surgery and cefazolin prophylaxis	5
	Bariatric surgery and surgical site infection	266
	Bariatric surgery and surgical wound infection	248
	Gastric bypass and antibiotic prophylaxis	13
	Gastric bypass and cefazolin prophylaxis	5
	Gastric bypass and surgical site infection	124
	Gastric bypass and surgical wound infection	117
	Subtotal	807
EMBASE	Bariatric surgery and antibiotic prophylaxis	62
	Bariatric surgery and cefazolin prophylaxis	14
	Subtotal	76
Total		961

No limits were applied in the search. We also analyzed references included in articles selected (Chart 2).

CHART 2 - Flow chart of databases search.



Results

Nine hundred and sixty one (961) titles were identified using the search strategy. The preliminary analysis of title and scope excluded 903 studies. After analysis of the abstract of the 58 remaining studies, 52 were considered inadequate. The remaining six studies, together with one additional included by the references analysis, were integrally analyzed. Among the three clinical trials, one had SSI as the outcome. SSI was the outcome of the four observational studies.

Clinical trials

The use of cefazolin for antibiotic prophylaxis in BS was for the first time supported by a study published more than thirty years ago by Pories *et al*.[11]. It was a double blind prospective randomized clinical trial with two arms: one group of patients received cefazolin intravenously, 1g 2 hours prior to surgery, at induction of anesthesia, and then 0.5g every 6 hours for 48 hours while the other group received a placebo. The study was interrupted previously than planned due to evidence that SSI was significantly less frequent in the group that received cefazolin (1/27=4% in the cefazolin group versus 5/23=21% in the placebo group, $p<0.05$). The study became a state of the art on the antibiotic prophylaxis for BS and since this study cefazolin is being widely used on this procedure. We have not identified any new article since the Pories' one, in which cefazolin was confronted to placebo.

Other trials had levels of antibiotic as the outcome. Forse *et al*.[15] investigated the effect of the mode of administration of cefazolin (1g intramuscular, subcutaneous or intravenous) on drug serum and adipose tissue concentration and found that for all morbidly obese patients levels were significantly lower when compared to those of control (non-obese patients). It was also evident that levels were below the minimal inhibitory concentration, independent of the mode of administration. Only when patients received intravenous 2g of cefazolin prophylaxis were both serum and adipose tissue levels achieved. In a subsequent segment of the study, morbidly obese patients received 2g of cefazolin and SSI rate dropped to 5.6% compared to the previous rate of 16.5%. Levels of cefazolin were measured by Edmiston Jr *et al*.[14] in patients receiving 2g of cefazolin preoperatively, followed by a second dose at 3 hours in patients assigned in three groups, according to BMI. Therapeutic tissue levels were achieved in 48.1% (BMI= 40-49), 28.6% (BMI= 50-59), and 10.2% (BMI≥60), indicating that the dosing strategy may fail to provide adequate prophylaxis.

A synthesis of all clinical trials included on this review are shown on Table 1, and quality of reporting studies is shown on Table 2.

TABLE 1 - Articles identified and selected – clinical trials.

Study	Design	n	SSI %	Outcome	Results	Observations
Edmiston, 2004	Clinical trial Cefazolin 2g + second dose in 3 hours	38 A:17 B:11 C:10	 17.6 9.1 30	Tissue and seric concentration of cefazolin	Dose regimens may fail to provide adequate prophylaxis	3 BMI groups Therapeutic tissue levels reached A 40-49: 48,1% B 50-59: 28,6% C ≥60: 10,2%
Forse, 1989	RCT 1st phase: 1g SC 1g IM 1g IV Control 1g IV 2nd phase: 2g IV	48 9 10 11 10 8	General=16.5	Tissue and seric concentration of cefazolin	Lower concentration of cefazolin in morbidly obese	Decrease in SSI if 2g were administered (5.6%, 5/89)
Pories, 1981	RCT; Double blind, Cefazolin 1g 2h before and 0.5 g 6/6 h for 48 hours placebo	50 27 23	General=12 4 21	SSI	Study was suspended by the evidence of difference between the two arms. Tissue levels measured by laboratory of the pharmaceutical industry	

RCT: Randomized clinical trial
SSI: surgical site infection

TABLE 2 - Evaluation of clinical trials quality parameters according Consort statement.

Study	Pories, 1981	Forse, 1989	Edmiston, 2004
Title	no identification as a RCT; not structured	no identification as a RCT; not structured	no identification as a RCT; structured
Abstract			

(cont.)

(cont.)

Introduction	Background Objectives	adequate, not clear	adequate adequate	adequate not clear
Methods	Trial design	Adequate	not well described	not well described
	Eligibility criteria settings and locations	adequate unclear	unclear unclear	unclear unclear
	Intervention	Adequate	adequate	does not have an intervention
	Outcomes	SSI	antibiotic levels	antibiotic levels
	Sample size	not described	not described	not described
	Randomization	no information about sequence generation, allocation and implementation	no information about sequence generation, allocation and implementation	not a RCT
	Blinding	details are not presented	not blinded	not blinded
	Statistical methods	not presented	adequate	adequate
Results	Participant flow	not presented	not presented	not presented
	Recruitment	unclear; trial was ended and reasons were specified	unclear	unclear
	Baseline data	Adequate	adequate	adequate
	Numbers analyzed	Adequate	adequate	adequate
	Outcomes and estimation	Adequate	adequate	adequate
	Ancillary analysis	not presented	not presented	not presented
	Harms	not presented	not presented	not presented
Discussion	Limitations	not presented	not presented	not presented
	Generalisability	Adequate	adequate	adequate
	Interpretation	Adequate	adequate	adequate
Other information	Registration	not presented	not presented	not presented
	Protocol	not presented	not presented	not presented
	Funding	not presented	not presented	not presented

RCT: randomized clinical trial
SSI: surgical site infection

Observational studies

Three cohort and one case-control studies have described the issue of antibiotic prophylaxis in BS. The first one, a retrospective cohort, was published as a letter[18]. It did not find significant differences in rates of SSI in patients receiving 1 or 2 g of cefazolin (rates of SSI = 7.69% in the group receiving 1g and 10.3% 2g of cefazolin). The authors emphasized that there was a lack of standardization in the prescribing, administration, and duration of antibiotic prophylaxis.

In another retrospective, single center cohort[5], with 269 individuals submitted to Roux-en-Y gastric bypass, the rate of SSI observed was 20%. Epidural analgesia and delayed antibiotic prophylaxis administration (after incision) increased the odds of SSI (1.6 and 1.9, respectively). Gender, age, BMI, duration of surgery, and diabetes, on the other hand, had no effect on SSI.

In a large (2,012 patients) prospective multicenter (nine community hospitals in the USA) cohort, with 82% of laparoscopic procedures, the overall rate of SSI was 1.4% in patients submitted to BS[7]. A total of 37 different antibiotic regimens were observed and SSI rate was higher in patients receiving vancomycin prophylaxis (relative risk = 9.4; 95% confidence interval = 3.1 – 26.1, p=0.005), when compared to patients that received other antibiotics. It is interesting to observe that cefazolin was administered as the single agent in less than half of the surgeries that had antimicrobial prophylaxis recorded (864/1,989; 43%).

Recently, a case-control study was used to identify factors associated to SSI in patients following Roux-en Y gastric bypass[9].

Each case of SSI (n=91) was matched with three controls (n=273) in the investigation. After multivariate analysis, use of prophylaxis with antibiotics other than cefazolin (OR, 4.2; 95% CI: 1.47-11.7) was identified as a risk factor for SSI. Other variables that had a significant association with SSI included duration of surgery and comorbidities as diagnosis of bipolar disorder and sleep apnea. The authors proposed a score to improve stratification of risk for SSI after BS.

Table 3 presents a summary of observational studies and Table 4 shows evaluation according to Strobe Statements.

TABLE 3 - Articles identified and selected – observational studies.

Study	Design	N	SSI rate (%)	Outcome	Results
Chopra, 2012	Case-control (1:3)	91 cases 273 controls		SSI	OR 4.2 for SSI Use of preoperative antibiotic other than cefazolin
Christou, 2004	Observational, retrospective Cefazolin 2g + 2 doses post-surgery Ticarcillin/clavulanic acid 3.1g	269	20	SSI	Epidural anesthesia and delayed antibiotic prophylaxis increase OR for SSI
Freeman, 2011	Prospective cohort 37 different regimens Cefazolin=43% Cefoxitin= 21%	2012	1.4	SSI	Higher rates of SSI with vancomycin. 82% laparospcopic surgery
Mehta, 1995	Retrospective review Cefazolin 1g Cefazolin 2g	55 26 29	 7.69 10.3	SSI	Significant differences were not observed

TABLE 4 - Quality reporting of observational studies, according Strobe checklist.

Parameters	Article 1 Christou et al., 2004 Observational	Article 2 Freeman et al., 2011 Cohort	Article 3 Chopra et al., 2012 Case-control	Article 4 Mehta,1995 Retrospective cohort
Title and abstract	Adequate	adequate	adequate	does not have an abstract (letter)
Introduction				
• Background	adequate	adequate	adequate	adequate
• Objectives	unclear	adequate	unclear	unclear
Method				
• Study design	unclear	adequate	adequate	unclear
• Setting	unclear	adequate	adequate	unclear
• Participants	eligibility unclear	adequate	adequate	unclear
• Variables	adequate	adequate	adequate	unclear
• Data sources / measurements	adequate	adequate	adequate	unclear
• Bias	adequate	unclear	adequate	unclear
• Study size	unclear	unclear	unclear	unclear
• Quantitative variables	unclear	adequate	unclear	unclear
• Statistical methods	adequate	adequate	adequate	unclear

(cont.)

(cont.)

Parameters	Article 1 Christou et al., 2004 Observational	Article 2 Freeman et al., 2011 Cohort	Article 3 Chopra et al., 2012 Case-control	Article 4 Mehta,1995 Retrospective cohort
Title and abstract	Adequate	adequate	adequate	does not have an abstract (letter)
Introduction				
• Background	adequate	adequate	adequate	adequate
• Objectives	unclear	adequate	unclear	unclear
Method				
• Study design	unclear	adequate	adequate	unclear
• Setting	unclear	adequate	adequate	unclear
• Participants	eligibility unclear	adequate	adequate	unclear
• Variables	adequate	adequate	adequate	unclear
• Data sources / measurements	adequate	adequate	adequate	unclear
• Bias	adequate	unclear	adequate	unclear
• Study size	unclear	unclear	unclear	unclear
• Quantitative variables	unclear	adequate	unclear	unclear
• Statistical methods	adequate	adequate	adequate	unclear
Results				
• Participants	unclear	unclear	unclear	unclear
• Descriptive data	unclear	unclear	adequate	unclear
• Outcome data	adequate	adequate	presents outcomes for each group	unclear
• Main results	adequate	adequate (rate of SSI)	adequate (independent predictors of SSI)	adequate
Discussion				
• Key results	adequate	adequate	adequate	unclear
• Limitations	not presented	adequate	adequate	not presented
• Interpretation	adequate	adequate	adequate	adequate
• Generalizability	limited (one center)	limited to laparoscopic surgery in one center	limited to laparoscopic surgery	limited (one center)
Other information				
• Funding	not presented	presented	not presented	not presented

SSI: surgical site infection

Studies not involving cefazolin

Besides cefazolin, other antimicrobial agents were evaluated for prophylaxis of SSI in BS. Kanamycin was considered for the prevention of deep wound infection by infusion of the drug into the subcutaneous space at the time of wound closure[10]. The authors evaluated 410 patients submitted to bariatric surgery and none had an infection which started in the subcutaneous space or at the fascial level. The lack of a control group in the study, however, makes impossible a conclusion about the influence of this procedure. In another trial[19], patients were allocated in three groups for antibiotic prophylaxis (ampicillin/sulbactam, ceftriaxone or ertapenem) and the lower rate of infection was observed among patients receiving ertapenem (rates of SSI = 3.78%, 6.81%, and 1.99% for groups receiving ampicillin/sulbactam, ceftriaxone, and ertapenem, respectively). The study was not randomized, and a group receiving cefazolin was not included. Finally, in a recent study [20], with a rather limited number of patients submitted to BS, preliminary results were suggestive of the efficacy of ertapenem in the prophylaxis of SSI; however, the need of further studies to confirm these observations was acknowledged by the authors.

Discussion

Cefazolin has been routinely used in the prophylaxis of infection in bariatric surgery in guidelines of hospitals worldwide Even though, there are few well designed studies available in the scientific literature to provide support for issues such as initial dose, need and rational for redose, moment of administration and lasting of prophylaxis. Only one study was placebo controlled and had SSI as the outcome. Two studies[14,15] had levels of antibiotic as the outcome and both find that levels of antibiotic in tissues were suboptimal and this observation appears consonant with the recent recommendation of an increased dose (3g) for patients weighing ≥120 kg[13].

Observational studies were also rather heterogeneous. Mehta's study[18] has, among its limitations, a small sample size (26 and 29 for 1 or 2 g of cefazolin, respectively). The cohort by Freeman[7] points out the high diversity and lack of standardization in antibiotic prophylaxis. The study presented some weaknesses (observational design, low rates of SSI, patients were not directly contacted during post-discharge surveillance), however strengths like multicenter design, prospective and standardized collection of data must be considered. Finally, the case-control study which was included in this review indicated that, besides use of antibiotics other than cefazolin, other variables had a significant association with SSI (duration of surgery and comorbidities as diagnosis of bipolar disorder and sleep apnea)[9] The influence in SSI of variables that are not related to antibiotic use had been identified previously in Christou's cohort[5] that showed that use of an epidural catheter for analgesia increased the risk for SSI.

Currently it would not be reasonable a placebo controlled clinical trial in this context, as the 1981 Pories' study[11] showed a significant reduction of rates of SSI and there is no antimicrobial agent that presents the necessary characteristics to replace cefazolin with some potential advantage in bariatric surgery. There is a need to emphasize that two observational studies showed that prophylactic use of antibiotics other than cefazolin were significantly associated with SSI[4,7].

Conclusion

The use of cefazolin for surgical wound infection prophylaxis in bariatric surgery is recommended, however further studies are needed in order to refine parameters as initial dose, redose, moment of administration and lasting of prophylaxis.

References

1. World Health Organization. Global database on body mass index 2012 [26 Oct 2012]. Available from: http://apps.who.int/bmi/index.jsp.
2. Padwal R, Klarenbach S, Wiebe N, Birch D, Karmali S, Manns B, Hazel M, Sharma AM, Tonelli M. Bariatric surgery: a systematic review and network meta-analysis of randomized trials. Obes Rev. 2011;12(8):602-21.
3. Kelly T, Yang W, Chen CS, Reynolds K, He J. Global burden of obesity in 2005 and projections to 2030. Int J Obes (Lond). 2008;32(9):1431-7.
4. Chopra T, Zhao JJ, Alangaden G, Wood MH, Kaye KS. Preventing surgical site infections after bariatric surgery: value of perioperative antibiotic regimens. Expert Rev Pharmacoecon Outcomes Res. 2010;10(3):317-28.
5. Christou NV, Jarand J, Sylvestre JL, McLean AP. Analysis of the incidence and risk factors for wound infections in open bariatric surgery. Obes Surg. 2004;14(1):16-22.
6. Santos LM, de Oliveira IV, Peters LR, Conde WL. Trends in morbid obesity and in bariatric surgeries covered by the Brazilian public health system. Obes Surg. 2010;20(7):943-8.
7. Freeman JT, Anderson DJ, Hartwig MG, Sexton DJ. Surgical site infections following bariatric surgery in community hospitals: A weighty concern? Obes Surg. 2011;21(7):836-40.
8. van Kralingen S, Taks M, Diepstraten J, van de Garde EM, van Dongen EP, Wiezer MJ, van Ramshorst B, Vlaminckx B, Deneer VH, Knibbe CA. Pharmacokinetics and protein binding of cefazolin in morbidly obese patients. Eur J Clin Pharmacol. 2011;67(10):985-92.
9. Chopra T, Marchaim D, Lynch Y, Kosmidis C, Zhao JJ, Dhar S, Gheyara N, Turner D, Gulish D, Wood M, Alangaden G, Kaye KS. Epidemiology and outcomes associated with surgical site infection following bariatric surgery. Am J Infect Control. 2012;40(9):815-9.
10. Alexander JW, Rahn R, Goodman HR. Prevention of surgical site infections by an infusion of topical antibiotics in morbidly obese patients. Surg Infect (Larchmt). 2009;10(1):53-7.
11. Pories WJ, van Rij AM, Burlingham BT, Fulghum RS, Meelheim D. Prophylactic cefazolin in gastric bypass surgery. Surgery. 1981;90(2):426-32.
12. Falagas ME, Karageorgopoulos DE. Adjustment of dosing of antimicrobial agents for bodyweight in adults. Lancet. 2010;375(9710):248-51.
13. Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Bolon MK, Fish DN, Napolitano LM, Sawyer RS, Slain D, Steinberg JP, Weinstein RA. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70(3):195-283.
14. Edmiston CE, Krepel C, Kelly H, Larson J, Andris D, Hennen C, Nakeeb A, Wallace JR. Perioperative antibiotic prophylaxis in the gastric bypass patient: do we achieve therapeutic levels? Surgery. 2004;136(4):738-47.
15. Forse RA, Karam B, MacLean LD, Christou NV. Antibiotic prophylaxis for surgery in morbidly obese patients. Surgery. 1989;106(4):750-6.
16. von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP. The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. J Clin Epidemiol. 2008;61(4):344-9.
17. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomized trials. Ann Intern Med. 2010;152(11):726-32.
18. Mehta U, Malone M, Alger S. Cefazolin use in clinically severe obese patients undergoing gastric restrictive surgery. Ann Pharmacother. 1995;29(9):935-6.

19. Ferraz AAB, Leão CS, Campos JM, Martins Filho E, Albuquerque AC, Ferraz EM. Profilaxia antimicrobiana na cirurgia bariátrica. Rev Col Bras Cir. 2007;34:73-7.
20. de Werra C, Di Micco R, Pilone V, Formato A, Montella E, Lambiase A, Cerbone D, Catania MR, Forestieri P. Serum in vivo and in vitro activity of single dose of ertapenem in surgical obese patients for prevention of SSIs. Obes Surg. 2013;23(7):911-9.

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