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Research Article

Use of Vancomycin in the Prevention of Superficial and Deep Infections after Sternotomy

Helmgton JB Souza, Thiago do Amaral Cavalcante, Leonardo Jadyr Silva Rodrigues Alves, Rafael Ramos Amaral, Diogo Assis Souza, Felipe Bruno Santos da Cunha, Henrique Louzan Machado*, Isaac Azevedo Silva, Marcus Vinícius N Santos, Glauco Kalil Pina, Luiz Sérgio Alves-Silva and Ricardo Barros Corso

Department of Medicine, University Center of Brasília, Brasília, Brazil

***Corresponding Author**: Henrique Louzan Machado, Department of Medicine, University Center of Brasília, Brasília, Brazil.

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Abstract

Introduction: Mediastinitis and sternal dehiscence are serious complications in patients submitted to sternotomy, with increasing morbidity and mortality. The incidence varies (0.15 to 8%) and occurs between the 10th and 20th postoperative days. Topical vancomycin at the borders of the sternum seems to reduce the incidence of sternal infection but may favour the emergence of antibiotic resistance and nephrotoxicity.

Objective: To evaluate the topical use of vancomycin as prophylaxis for superficial or deep infection in patients submitted to median sternotomy.

Methods: A prospective study with retrospective data collection, where 196 patients submitted to median sternotomy were divided into two groups: group A (101 patients) did not use topical vancomycin and group B (95 patients) used topical vancomycin, applied to the sternal bone after sternotomy and before sternal closure. We define it as superficial infection when it does not reach the sternum and deep when it reaches steel wires, sternum or presents retrosternal fluid collection.

Results: The surgical characteristics of the groups did not differ. In group B, there was no superficial or deep infection. Seven patients from group A had sternal infection (7% - $p < 0.03$), with six cases of mediastinitis (6% - $p < 0.05$). In the series studied, there was no mortality.

Conclusion: In the series studied, use of vancomycin showed bacteriostatic and bactericidal ability to avoid sternal infection.

Keywords: *Mediastinitis, Vancomycin, Cardiovascular Surgery, Sternal Dehiscence, Sternal Infection, Prophylaxis*

Introduction

Mediastinitis and sternal dehiscence are serious complications in patients submitted to sternotomy, which significantly increases the morbidity and mortality of procedures that require this access [1-3]. Its incidence varies from 0.15% to 8% [4]. It usually occurs between the 10th and 20th postoperative days and mainly affects patients undergoing myocardial revascularization (50%), valve replacement (20%), aortic diseases (20%) and other surgeries (10%) [5].

Although the incidence of deep sternotomy wound infection has been reduced in the last 15 years [6], the mortality rate is high, reaching 47%. Gram-positive bacteria are the most commonly isolated in patients diagnosed with mediastinitis. *Staphylococcus aureus* and *epidermidis* correspond to 70 to 80% of the occurrences [7].

According to the Society of Thoracic Surgeons (STS) database, the following are considered as risk factors for wound infection in the postoperative period of adult cardiac surgery: age, weight, renal failure, diabetes mellitus, heart failure, peripheral vascular disease, COPD, female sex, cardiogenic shock, reduced ejection fraction, myocardial infarction, emergency surgery, steroid use and smoking [8,9]. High infection rates are related to increased morbidity and mortality, as well as hospital costs, for the patient and the whole society [10]. In this context, the recommended strategies to reduce the incidence of deep sternal wound infection include: use of antibiotics in the perioperative period, glycaemic control from continuous infusion of insulin and restriction to the use of bone wax [11-15].

The use of bone wax, despite its haemostatic capacity, decreases the vascularization of the sternum, besides being difficult to absorb by the organism. This prolongs sternal ischemia and makes it difficult to consolidate. When used abusively, it is another factor that adds up to the emergence of infection [16,17].

Several studies have demonstrated that the topical use of vancomycin at the borders of the sternum reduces and even eliminates the incidence of superficial and deep sternal infection in cardiac surgery [18-20]. Vancomycin is a bactericidal glycopeptide antibiotic with predominantly renal clearance (80 - 90%) if applied intravenously. It is known that up to 30% of the total clearance of vancomycin is non-renal [21].

In cardiac surgery, the topical use of antibiotics has been widely used [22,23]. It has been described that the topical use of vancomycin may favour the appearance of pathogens resistant to this antibiotic [10]. However, studies have shown that the use of topical vancomycin, applied during sternal closure, showed a significant reduction in sternal infections [18].

Objective

The objective of the present study was to evaluate the topical use of vancomycin as prophylaxis for superficial or deep bacterial infection in patients submitted to median sternotomy in cardiac surgeries.

Methods

This study was approved by the Research Ethics Committee (number: 2.435.351). This is a prospective study with retrospective data collection. All patients submitted to cardiac surgery in the period between January 2015 and October 2016, who had as a common feature the median sternotomy access route, extracorporeal circulation aid and survival of at least 30 days were included.

The patients selected were divided into two groups. In group A, we related 101 patients who did not use topical vancomycin to prevent sternal infection. In group B, we assigned 95 patients who used topical vancomycin to prevent sternal infection. The patient allocation criterion was merely temporal, that is, the first 101 patients did not use vancomycin, while the subsequent 95 patients used this antibiotic.

Antibiotic prophylaxis was performed in all patients with cefuroxime 1.5g IV, 1 hour before the surgical incision, and the dose of 750 mg IV was repeated every 3 hours during the surgery and maintained every 6 hours until completing 24 hours of post-operative. In group B patients, we used topical vancomycin as follows:

1. 1g mixed with 1.0 mL of 0.9% saline solution (forming a consistent paste), applied to the sternum immediately after the median sternotomy;
2. 2g mixed with 02 mL of 0.9% physiological solution forming a consistent paste (Figure 1), The paste was applied to the sternum before the sternal closure with steel threads.

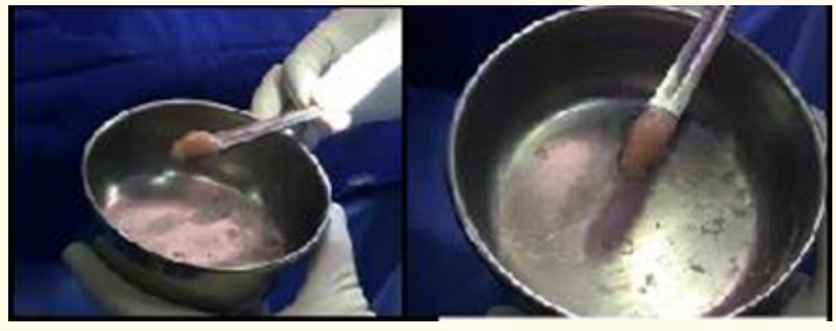

Figure 1: *Preparation of vancomycin paste.*

Total heparinization (5 mg/kg) and reversion at the end of extracorporeal circulation and volume replacement with protamine sulphate at the rate of 1.5:1 of the heparin dose were performed in all surgeries. The sternum was routinely closed with 5 or 6 wire strands (10 to 12 strands). Subcutaneous cell tissue and skin were approximated with absorbable monofilament yarns (Vicryl-0 and monocryl 4-0 - Ethicon).

All patients were evaluated daily by the surgical team, up to the date of hospital dis-charge and at least 3 times, in outpatient, until discharge. In these evaluations, skin integrity, presence of hyperaemic areas, signs of phlogosis or anastomotic dehiscence were observed. Patients diagnosed with superficial infection or deep sternal wound were promptly treated with surgical debridement and antibiotic therapy, according to the guidance of the Hospital Infection Control Committee, with daily dressing up to resolution of the infectious process.

According to the classification of Centers for Disease Control and Prevention, we de-fined as superficial sternal infection the wound that reaches the dermis, epidermis and subcutaneous cellular tissue, without involvement of the sternum. On the other hand, when the infection reaches the wire strand, the sternum, or the presence of retrosternal fluid collection is verified, we consider deep infection [18].

To compare the proportions between the groups studied, we used the chi-square test with Yates correction, while the means were compared by Student's t-test. We considered the level of significance at 5%. The numerical data are expressed as mean, standard deviation and minimum value-maximum value.

Results

The clinical characteristics of the patients studied are listed in table 1. The groups did not differ in relation to most of the variables tested, except male gender, which was more frequent among patients treated with topical vancomycin (group B).

Characteristics	Group A (n = 101)	Group B (n = 95)	p**
Male gender	60 (59%)	71 (75%)	< 0.04
Age (years)	59 ± 11 (23 - 82)	61 ± 13 (26 - 85)	0.99
SAH	60 (59%)	61 (64%)	0.59
DM	24 (24%)	31 (33%)	0.22
Dyslipidemia	16 (16%)	16 (17%)	1.00
Smoking	25 (25%)	14 (15%)	0.11
Reoperation	6 (6%)	5 (5%)	0.92

Table 1: *Clinical characteristics of groups A and B*.*

SAH: Systemic Arterial Hypertension; DM: Diabetes Mellitus.

* *Data expressed in n (%), except age = mean ± standard deviation (minimum value-maximum value).*

** *Chi-square test with Yates correction except age = Student's t-test.*

Regarding the surgical characteristics of the selected sample (Table 2), the groups did not differ regarding the type of surgery, the surgeries performed, the time of extracorporeal circulation and the time of aortic clamping, as well as the character of the surgery (elective, urgency or emergency).

Surgical characteristics	Group A (n = 101)	Group B (n = 95)	p**
MR	45 (45%)	56 (59%)	0.06
MR + Valvular surgery/multivalvular	9 (9%)	5 (5%)	0.46
MR + Valvular surgery with or without LV aneurysm	2 (2%)	2 (2%)	0.65
Valvular surgery	23 (23%)	16 (17%)	0.39
Multivalvular surgery	11 (11%)	4 (4%)	0.14
Aneurysm + valve	7 (7%)	8 (8%)	0.90
Aortic aneurysm	2 (2%)	2 (2%)	0.66
Others	2 (2%)	2 (2%)	0.66
ECC time (minutes)	106 ± 35 (8-180)	104 ± 34 (32 - 221)	0.45
Ischemia time (minutes)	86 ± 29 (0-150)	87 ± 33 (0 - 171)	0.18
Elective surgeries	41 (41%)	39 (41%)	0.94
Urgency surgery	47 (47%)	41 (43%)	0.74
Emergency surgery	13 (13%)	15 (16%)	0,70

Table 2: *Surgical characteristics of groups A and B*.*

MR: Myocardial Revascularization; LV: Left Ventricle; ECC: Extracorporeal Circulation

**Data expressed in n (%), except extracorporeal circulation (ECC) time and ischemia time = mean + standard deviation (minimum value-maximum value).*

***Chi-square test with Yates correction, except for ECC time and ischemia time = Student's t-test.*

In group B patients, no cases of superficial or deep sternal wound infection were observed (Figure 2), while seven patients in group A presented sternal wound infection (7%; $p < 0.03$), with confirmation of six cases of mediastinitis (6%, $p < 0.05$) (Figure 3), and surgical reintervention was necessary for debridement of the sternum and resuture. There were no deaths during the follow-up of the patients.

Figure 2: *Not infected sternotomy.*

Figure 3: *Infected sternotomy.*

Of the patients affected by sternal wound infection, only one had diabetes mellitus and three said they were smokers. Five patients underwent coronary artery bypass grafting surgery, using a left internal thoracic artery graft. The ECC time was greater than 120 minutes in one patient. Among the patients diagnosed with mediastinitis, four were older than 60 years and all were women.

Discussion

Although there was a statistically significant difference between the groups in gender ($p < 0.04\%$), this difference interfered in the results obtained. Mainly because, in the other characteristics of the groups, it was verified homogeneity between them.

Matros., *et al.* demonstrated in a retrospective study that the incidence of deep sternal infection has been reduced in the last 15 years. One of the factors responsible for this reduction is the perioperative use of intravenous insulin. Despite this, the mortality resulting from this complication remains high [6].

In the United States, the cost of patients with mediastinitis may increase the cost of hospitalization by up to $ 62,000 [24]. Several strategies have been proposed to pre-vent and treat superficial and deep sternal infections.

In a meta-analysis of 14 studies, Kowalewski., *et al.* showed a reduction in the risk of sternal infection, by up to 40%, with the use of gentamicin sponge. However, this benefit was less intense in the groups of patients who received bilateral internal thoracic artery grafts in myocardial revascularization surgeries [25]. For the treatment of patients with mediastinitis, the use of a gentamicin sponge has been advocated [10,23]. The topical use of gentamicin is attributed to the advantage of being less nephrotoxic and producing less bacterial resistance.

The use of titanium plates for sternal closure may also reduce complications related to the sternum in high-risk patients (manual workers, obesity, osteoporosis, intraoperative transverse fracture) [1].

The reduction of the incidence of infection has also been described from the use of topical vancomycin in spine surgeries [26], neurosurgery [27], dental implants [28] and re-duction of pocket infections in patients submitted to left ventricular assist devices [29].

The dose and dilution of vancomycin varies according to the publication. We found from the dilution of 500 mg of vancomycin in 10 mL of saline solution [30] to 500 mg in 1 mL [20] until the total dose of 5.0g diluted in 2 mL of saline solution. Likewise, use after sternotomy and before sternal closure varies according to the publication.

Lazar., *et al.*[19] showed that, in a series of 1,075 patients operated between 2007 and 2013, the use of topical vancomycin (2.5 g diluted in 2 mL of saline solution) applied to the borders of the sternum after sternotomy and prior to its closure (totalizing 5 g of vancomycin), associated with the use of cefazolin (2g) and vancomycin (1g) in anesthetic induction and maintained for 48 hours after surgery and continuous in-sulin infusion, with the goal of maintaining glycemia between 120 and 180 mg/dL, eliminated the occurrence of deep sternal wound infections when compared to a see-rise of 2,190 patients operated between 2003 and 2007, with similar characteristics but did not use topical vancomycin.

Despite the fear that topical use of vancomycin may cause persistence of elevated systemic levels and consequent bacterial resistance to the drug [31], Lazar., *et al.* demonstrated that the use of topical vancomycin, in addition to preventing the occur-renice of sternal infection, did not give rise to bacterial resistance or nephrotoxicity after one year of follow-up [19,32].

El Oakley*., et al.* attributes the fact that the topical use of vancomycin does not induce the increase of bacterial resistance to the drug to two factors: 1) because the drug is instilled in a confined space, this prevents the free movement of organisms into and out of the risk area; 2) it is believed that the topical use of vancomycin does not rep-resent a significant increase in its serum level [33]. In the follow-up of four patients who used 1g of vancomycin at the borders of the sternum at the time of chest closure, when serum levels of vancomycin were titrated within the first 48 hours postoperatively (preop, 1, 3, 6, 24 and 48 h) obtained a maximum serum dosage of 4.4 mg/L between 3 and 4 hours postoperatively.

Desmond., *et al.* demonstrated that vancomycin applied directly to the sternum was able to maintain significant systemic and urinary levels of vancomycin for more than 5 postoperative days. Despite this, this concentration is unable to inhibit *Staphylococcus aureus* growth, which would potentially be able to promote bacterial resistance to vancomycin [21].

We chose to use the total dose of 3g of vancomycin diluted in physiological solution, using 1g after sternotomy and 2g before sternal closure. This dosage provided the eradication of cases of superficial and deep sternal infection.

Although serum vancomycin levels were not measured in patients who used this drug, there was no change in the profile of infections accompanied by Hospital Infection Control Committee during the study period, suggesting that there wasn't induction to bacterial resistance. However, for a more accurate assessment, this verification would need to be carried out.

Conclusion

We can conclude that the topical use of vancomycin, in the dose prescribed in the study, has an easy preparation and bacteriostatic and bactericidal power capable of preventing superficial and deep sternal infection.

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