

USE OF INTRAOPERATORY VANCOMYCIN IN SPINAL SURGERIES

O USO DA VANCOMICINA INTRAOPERATÓRIA EM CIRURGIAS DE COLUNA

USO DE LA VANCOMICINA INTRAOPERATORIA EN CIRUGÍAS DE COLUMNA

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ABSTRACT

Objectives: Despite the use of systemic antibiotic prophylaxis, infection is still a challenge for spine surgeons, with high morbidity and mortality, long hospitalization, delayed rehabilitation, and a greater number of interventions. The purpose of this cross-sectional retrospective case-control study was to compare the incidence of postoperative infection in individuals who received a systemic antibiotic as the sole prophylactic method with those who received vancomycin in the operative wound in association with systemic antibiotic prophylaxis in spinal surgery. **Methods:** We evaluated 2694 medical records of individuals submitted to posterior spinal surgery in the thoracolumbar segment in the period from January 2012 to June 2017, 1360 in the treatment group and 1334 in the control group. **Results:** Nineteen (1.39%) of the treatment group progressed with surgical site infection, compared to 42 (3.14%) of the control group. **Conclusions:** There was a significant reduction in the postoperative infection rate with the use of vancomycin ($p=0.0379$). **Level of Evidence III; Case-Control Study.**

Keywords: Vancomycin; Infection; Antibiotic Prophylaxis; Spine.

RESUMO

Objetivos: Apesar do uso de antibioticoprofilaxia sistêmica, a infecção ainda constitui um desafio para os cirurgiões de coluna, com alta morbimortalidade, longo período de internação, retardo na reabilitação e maior número de intervenções. O propósito deste estudo transversal retrospectivo tipo caso-controle foi comparar a incidência de infecção pós-operatória nos indivíduos que receberam antibiótico sistêmico como único método profilático aos que receberam Vancomicina na ferida operatória em associação com antibiótico sistêmico em cirurgias na coluna vertebral. **Métodos:** Foram avaliados 2694 prontuários de indivíduos submetidos à cirurgia de coluna por via posterior no segmento toracolumbar no período de janeiro de 2012 a Junho de 2017, sendo 1360 no grupo tratamento e 1334 no grupo controle. **Resultados:** Dezenove (1,39%) do grupo tratamento evoluíram com infecção do sítio cirúrgico, em comparação com 42 (3,14%) do grupo controle. **Conclusão:** Houve redução significativa na taxa de infecção pós-operatória com o uso da Vancomicina ($p=0,0379$). **Nível de Evidência III; Estudo de Caso-Control.**

Descritores: Vancomicina; Infecção; Antibioticoprofilaxia; Coluna Vertebral.

RESUMEN

Objetivos: A pesar del uso de profilaxis con antibióticos sistémicos, la infección todavía constituye un desafío para los cirujanos de columna, con alta morbimortalidad, largo período de internación, retraso en la rehabilitación y mayor número de intervenciones. El propósito de este estudio transversal retrospectivo tipo caso-control fue comparar la incidencia de infección postoperatoria en los individuos que recibieron antibiótico sistémico como único método profilático a los que recibieron vancomicina en la herida operatoria en asociación con antibiótico sistémico en cirugías de la columna vertebral. **Métodos:** Se evaluaron 2694 prontuarios de individuos sometidos a cirugía de columna por vía posterior en el segmento toracolumbar en el período de enero de 2012 a junio de 2017, siendo 1360 en el grupo tratamiento y 1334 en el grupo control. **Resultados:** Diecinueve (1,39%) del grupo de tratamiento evolucionó con infección del sitio quirúrgico, en comparación con 42 (3,14%) del grupo control. **Conclusiones:** Hubo reducción significativa en la tasa de infección postoperatoria con el uso de la vancomicina ($p = 0,0379$). **Nivel de Evidencia III; Estudio de Caso-Control.**

Descriptores: Vancomicina; Infección; Profilaxis Antibiótica; Columna Vertebral.

INTRODUCTION

The use of systemic antibiotics as surgical prophylaxis is already a well-established routine in spine surgeries. Despite this, infection of the surgical site is still a major problem in our environment.¹⁻⁴

The incidence of deep infection in the surgical site decreases with systemic antibiotic prophylaxis, however, according to the literature, infection rates still reach values close to 10%.^{5,6}

The impact of infection in spine surgeries results from the necessity for a long period of hospitalization, as well as from the delay in postoperative rehabilitation.^{6,7}

The intraoperative prophylactic use of vancomycin has shown consistent results in recent years, with reduced rates of infection and, therefore, of the morbidity associated with procedures performed on the spine.^{8,9}

The objective of this study was to compare the incidence of postoperative infection in individuals who received systemic antibiotics as the only prophylactic method to those who received vancomycin in the surgical wound in combination with intravenous antibiotic prophylaxis in spine surgeries.

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METHODS

This was a longitudinal, retrospective, case-control study conducted through the analysis of the medical records of patients who underwent posterior approach surgical treatment of the thoracolumbar spine performed by the spine surgery group of the Hospital do Trabalhador and the Hospital de Clínicas UFPR (Curitiba, Brazil) during the period from January 2012 to June 2017. The study was approved by the Institutional Review Board as number 60655416.0.0000.5225. All participants signed the Informed Consent Form.

Included in the study were patients who underwent open posterior approach spine surgery indicated for trauma or degenerative diseases and who progressed with infection of the surgical site.

Excluded from the study were surgeries performed via minimally invasive approach, surgeries to correct scoliosis, revision surgeries, surgeries in segments other than the thoracolumbar segment, anterior or double approach surgeries, individuals who lost the segment following surgical treatment, participants with incomplete medical record data, patients previously treated for spondylodiscitis, and individuals who had already presented either local or distant infection at the time of surgery.

Two homogeneous groups were created according to the type of antibiotic prophylaxis instituted in the surgery. For the Treatment Group, we selected the patients submitted to spine surgery who received intravenous cefazolin 2 grams in the anesthetic induction, combined with vancomycin in powder form for topical use in the surgical wound, which was applied to the entire extension of the wound (subfascial and subcutaneous) just before plane closure, one gram being prescribed for surgeries up to 3 levels.⁷ In surgical procedures involving more than 3 levels, 2 grams of topical vancomycin was used, in accordance with the protocol proposed by O'Neil et al.¹⁰ The Control Group was comprised of the individuals who received intravenous cefazolin 2 grams in the anesthetic induction as the sole prophylactic method.

We analyzed parameters such as age, sex, number of levels surgically approached, type of germ observed in the cultures, time between the surgery and the diagnosis of postoperative infection, duration of hospitalization, and type of antibiotic prophylaxis instituted.

For the diagnosis of postoperative infection the following clinical parameters were considered: hyperemia in the surgical wound and fever, presence of fistula draining purulent contents, seroma with local phlogistic signs, cerebrospinal fluid fistula associated with phlogistic signs, or pseudoarthrosis associated with any of the clinical signs mentioned. The laboratory parameters of infection considered were elevated leukogram values (with or without deviation), elevation of the erythrocyte sedimentation rate (ERS) and C-reactive protein (CRP), in addition to positive blood cultures or cultures of surgical wound secretions, only the cultures having been included in this analysis. Neither complementary exams nor the management (clinical or surgical) of postoperative infection were analyzed in this study. Similarly, neither surgical time nor intraoperative complications were analyzed.

We analyzed the data assisted by the free Biostat 5.0 software with the application of the Kruskal-Wallis test by mean of the comparison of the groups using by the Student-Newman-Keuls test, which showed homogeneity between the groups studied. For the analysis of the independent samples, we conducted the t-test, considering a value of $p < 0.05$ to be statistically significant.

RESULTS

Of the thoracolumbar surgical procedures performed at the Hospital do Trabalhador and at the Hospital de Clínicas UFPR from January 2012 to June 2017, 2694 cases met the study inclusion criteria – 1360 for the treatment group and 1334 for the control group. This sample was divided homogeneously and with statistical representativity ($p < 0.05$). Nineteen individuals (1.39%) in the treatment group contracted infection of the surgical site as compared to 42 cases (3.14%) in the control group ($p = 0.037$), as shown in Figure 1.

Treatment group

Of the 1360 patients in the treatment group, nineteen had infection at the surgical site (9 men [47.3%] and 10 women [52.6%]).

The mean age was 47 years (26 to 70 years). Nine (47.3%) had undergone the surgical procedure for degenerative disease, while 10 (52.6%) had been operated for fracture (Figure 2).

Nine (47.36%) were operated at 1 level, 5 (26.31%) at 2 levels, 3 (15.78%) at 3 levels, and 2 (10.52%) at 4 or more levels. *Staphylococcus aureus* was identified in 7 cases (37%), other microorganisms in 6 cases (31%), and no organism was identified in the other 6 cases (31%). The other microorganisms isolated in this group were *Pseudomonas aeruginosa* (3), *Staphylococcus epidermidis* (1), *Streptococcus mitis* (1), and *Enterobacter* spp. (1). The mean time between surgery and a diagnosis of infection of the surgical wound was 53 days (7 to 200 days). The mean hospitalization time was 30 days (10 to 90 days). The symptoms that led to a diagnosis of postoperative infection in this group were hyperemia in the wound or fever in 6 (31%), fistula or purulent secretion draining from the wound in 8 (42%), cerebrospinal fluid fistula associated with superficial infection in 2 (10.5%), infected pseudoarthrosis in 2 (10.5%), and infected seroma in 1 (5.2%). Table 1

Control group

Of the 1334 individuals in the control group, forty-two presented infection at the surgical site, 23 of whom (54.76%) were men and 19 of whom (45.23%) were women, with no differences between the groups ($p = 0.814$). The mean age was 50 years (22 to 86 years), with no difference between the groups ($p = 0.863$). In our multivariate analysis comparing the individuals with postoperative infection who were operated for degenerative disease with those with infection following surgeries for trauma, we did not observe any statistical difference between the groups studied in terms of age (degenerative $p = 0.203$; trauma $p = 0.258$) or number of levels (degenerative $p = 0.299$; trauma $p = 0.157$), as can be seen in Figure 3. Similarly, there was no statistical difference between the groups for

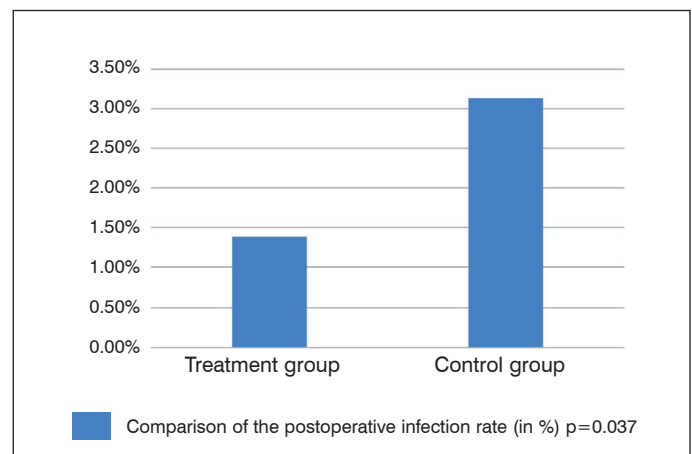


Figure 1. Comparison of the postoperative infection rate (in %), $p = 0.037$.

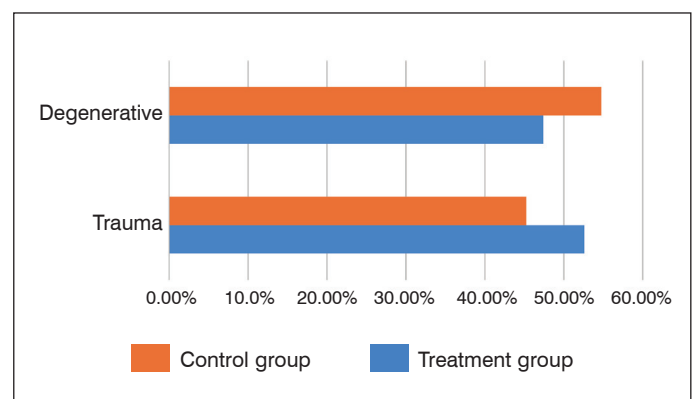


Figure 2. Postoperative infection rate by surgical indication (in %) $p = 0.065$.

the microbiotic profiles, in terms of postoperative infection in trauma ($p=0.272$) or in degenerative disease ($p=0.306$).

Twenty-three (54.7%) degenerative spinal pathologies were operated and 19 (45.2%) infections occurred following fixation of spinal fractures. There was a tendency towards significance in the increase of the postoperative infection rate for trauma as compared to that for degenerative pathologies ($p=0.065$). Twenty-one (50%) were operated

at 1 level, 11 (26%) at 2 levels, 7 (17%) at 3 levels, and 3 (7%) at 4 or more levels. There was no relationship between the number of levels involves and an increase in the rate of infection ($p=0.396$). In the control group, 24 (57%) of the infections were by *Staphylococcus aureus*, 8 (19%) by other agents, and 10 (23.8%) had no microorganism identified. The other microorganisms observed in the control group were *Escherichia coli* (2), *Staphylococcus epidermidis* (1), *Streptococcus*

Table 1. Comparison of the Treatment and Control groups.

Parameters	Treatment group, N		Control group, N		p-value
	9 (47.36%) M	10 (52.63%) F	23 (54.76%) M	19 (45.23%) F	
Sex	46.78 (26-70y.)		50.30 (22-86y.)		$p=0.814$
Age	46.78 (26-70y.)		50.30 (22-86y.)		$p=0.863$
Type of Surgery	Trauma -10 (52.63%)	Degenerative - 9 (47.36%)	Trauma - 19 (45.23%)	Degenerative -23 (54.76%)	$p=0.065$
Levels (in N)	1 - 9 (47.36 %) 2 - 5 (26.31 %) 3 - 3 (15.78%) ≥4 - 2 (10.52%)		1 - 21 (50.00%) 2 - 11 (26.19%) 3 - 7 (16.66%) >4 - 3 (7.14%)		$p=0.396$
Microorganism	Staphylococcus aureus - 7 (36.84%) Pseudomonas aeruginosa - 3 (15.78%) Staphylococcus epidermidis - 1 (5.26%) Streptococcus mitis - 1 (5.26%) Enterobacter spp. - 1 (5.26%) No agent - 6 (31.57%)		Staphylococcus aureus - 24 (57.14%) Escherichia coli - 2 (4.76%) Staphylococcus epidermidis - 1 (2.38%) Streptococcus epidermidis - 1 (2.38%) Streptococcus mitis - 1 (2.38%) Enterococcus fecalis - 1 (2.38%) Salmonella spp. - 1 (2.38%) Serratia marcescens - 1 (2.38%) No agent - 10 (23.80%)		$p=0.254$
Diagnosis time (in days)	52.84 (7-200)		69.26 (7-360)		$p=0.124$
Hospitalization time (in days)	30.47 (10-90)		25.76 (7-72)		$p=0.204$
Symptoms	Hyperemia + Fever - 6 (31.57%) Fistula + Purulent contents - 8 (42.10%) Cerebrospinal fluid fistula + Infection - 2 (10.52%) Infected seroma - 1 (5.26%) Infected PSA - 2 (10.52%)		Hyperemia + Fever - 11 (26.19%) Fistula + Purulent contents - 11 (26.19%) Cerebrospinal fluid fistula + Infection - 4 (9.52%) Infected seroma - 6 (14.28%) Infected PSA - 10 (23.80%)		$p=0.252$
Total	19		42		

Source: Electronic medical records - Hospital do Trabalhador and Hospital de Clínicas of UFPR.

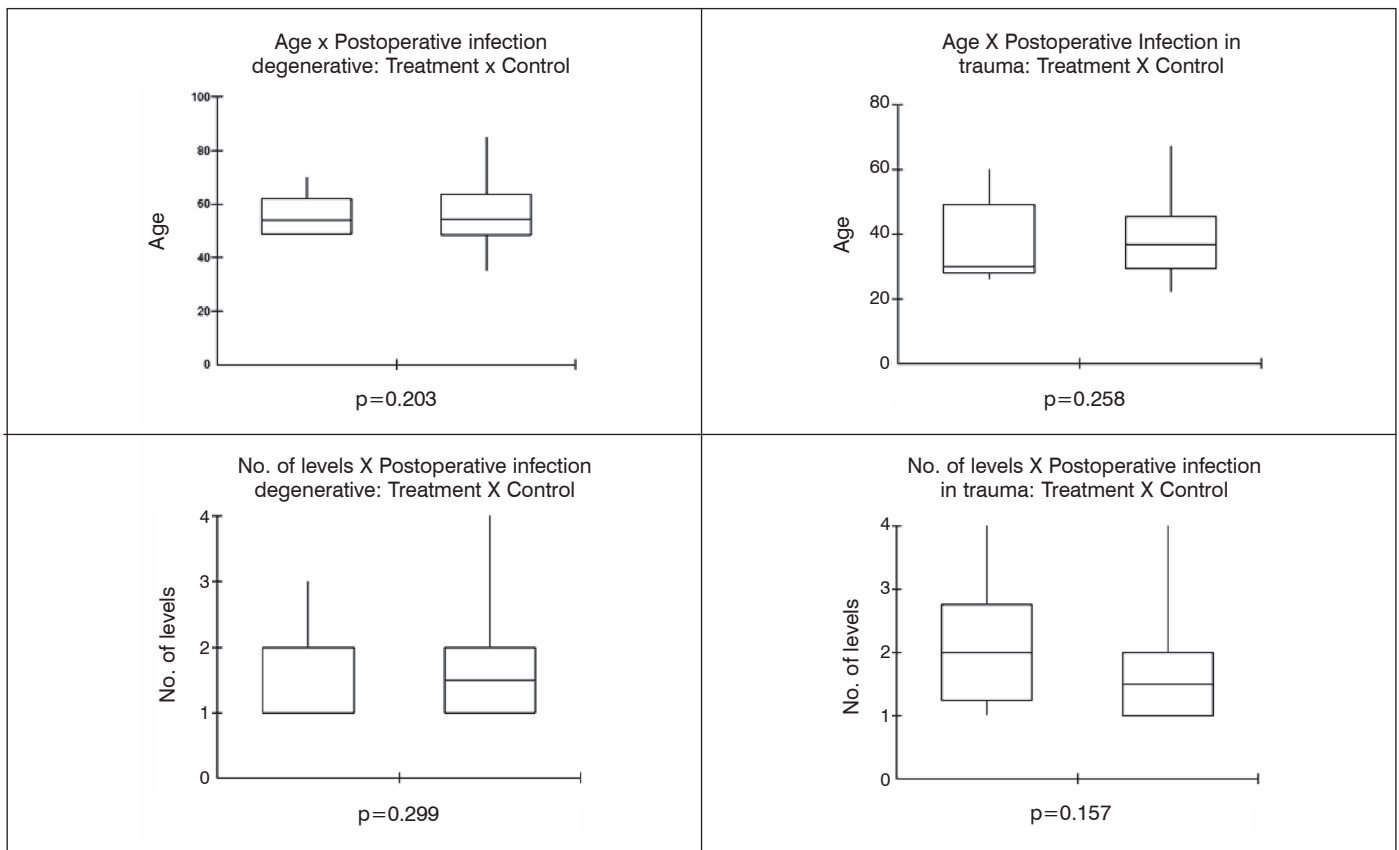


Figure 3. Multivariate analysis of both groups (treatment x control) in relation to postoperative infection of the spine after trauma in comparison to surgery for degenerative disease. Boxplots 1 and 2 do not show any difference associated with the age of the patients ($p>0.05$). Boxplots 3 and 4 do not show any difference in relation to the number of levels approached ($p>0.05$).

epidermidis (1), *Streptococcus mitis* (1), *Enterococcus faecalis* (1), *Salmonella* spp. (1), and *Serratia marcescens* (1). There was no difference in the profile of microorganisms isolated after the introduction of topical vancomycin to the surgical wound ($p=0.254$). The mean time between the surgery and the diagnosis of infection was 69 days (7 to 360 days), with no difference between the groups ($p=0.124$). The mean hospitalization time was 26 days (7 to 72 days), with no difference between the groups ($p=0.204$). The symptoms that led to the diagnosis of postoperative infection were hyperemia in the wound or fever in 11 cases (26.2%), fistula or purulent secretion draining from the wound in 11 cases (26.2%), cerebrospinal fluid fistula associated with superficial infection in 4 cases (9.5%), infected pseudoarthrosis in 10 cases (23.8%), and infected seroma in 6 cases (14.3%), with no difference between the groups ($p=0.254$).

DISCUSSION

Infections in spine surgeries have an incidence of 0.3 to 20% in the global literature.¹⁰ In our case series, the incidence of infection prior to the introduction of vancomycin was 3.14%. Despite the low frequency, the presence of infection in spinal surgeries, besides being devastating, worsens patient satisfaction regarding the surgical procedure and increases the cost of treatment, since it is associated with prolonged hospitalization, as seen in this analysis.¹⁰

Adverse systemic reactions, such as nephrotoxicity, ototoxicity, and skin rash are common with intravenous use of vancomycin. In contrast, the literature has shown the safety of topical vancomycin in the surgical wound, with rare reports of toxicity.¹¹⁻¹³

In the cases of spinal surgery for degeneration or trauma that involve up to three levels, the recommended dose of topical vancomycin is 1 gram. In approaches of more than three levels, 2g of topical vancomycin should be administered.^{6,7,14}

The literature points out a prevalence of infection in spinal surgeries for trauma when compared to surgical procedures for degenerative diseases of the spine.^{9,10} However, in our study we observed a tendency towards statistical significance in the increase in the rate of postoperative infection in trauma as compared to that

of postoperative infection in degenerative pathologies ($p=0.065$), as shown in Figure 2.

Hey et al.,¹¹ in their study of 389 individuals with postoperative infections in spine surgeries, observed a reduction in the rates of infection from 6.3% to 0.8% ($p=0.049$) after the introduction of vancomycin in the surgical wound as an adjuvant in the antibiotic prophylaxis. Similarly, in our study we observed a significant reduction ($p=0.037$) in infection rates, from 3.1% to 1.4%, applying the same prophylactic method.

The literature points out the prevalence of *Pseudomonas aeruginosa* when topical vancomycin is used, but there are no statistical data in our study to support this datum as significant.¹² Similarly, in our study this agent was not observed prior to the use of vancomycin and presented a frequency of 15.78% among the infected postoperative cases that had used the topical antibiotic in the surgical wound. Despite this, the change in the microbiotic profile did not have statistic representability ($p=0.254$) and *Staphylococcus aureus* still prevailed, with an incidence ranging from 36.8% to 57%. No case of local or systemic toxicity was noted after the introduction of topical vancomycin, corroborating the literature.^{13,14}

Despite the homogeneity of the samples, there is a bias in this study in terms of the intra-hospital microbiotic profile, which may have suffered impact changes in our analysis of microbial resistance with the introduction of vancomycin is taken into account.

CONCLUSIONS

In this study, there was a significant reduction in the indices of infection at the surgical site in those patients who received a combination of local vancomycin and systemic cefazolin as compared to the individuals who received only intravenous antibiotics, with no evidence of local or systemic toxicity associated with the topical use of vancomycin.

All authors declare no potential conflict of interest related to this article.

CONTRIBUTION OF THE AUTHORS: Each author made significant individual contributions to this manuscript. ETB (0000-0002-4096-642X)*, XSG (0000-0002-9636-9165)*, and ALK (0000-0002-0132-6083)* were the main contributors to the writing of the manuscript. ALK, XSG, MLB (0000-0002-2903-8550)*, and PGS (0000-0002-8326-4823)* performed the surgeries. ETB, ALK, and PGS followed-up with the patients and gathered the clinical data. XSG and MLB evaluated the statistical analysis data. ALK, ETB, and XSG conducted the bibliographical research and reviewed the manuscript. ALK and XSG contributed with the intellectual concept of the study. *ORCID (Open Researcher and Contributor ID).

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