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The efficiency of vancomycin powder and rifampicin for deep surgical site infections in spinal instrumentation surgery

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Abstract

Objective: Infection after spinal surgery always increases the hospital stay in the clinic and can cause serious patient morbidity. This study aimed to show the difference between sprinkling vancomycin powder and washing with rifampicin during debridement surgery in deep infections seen after spinal instrumentation surgeries.

Material and methods: This present study was conducted on 179 cases of infection after spinal instrumentation surgeries. The patients were divided into three groups: those receiving topical vancomycin, rifampicin irrigation, and only normal saline irrigation. The preoperative and postoperative CRP levels, hospitalization time, operation length, bone involvement, second operation for infection, impact removal surgeries, and mortality rates have been examined.

Results: The CRP decrease on the 5th day was faster in the rifampicin group ($p<0.001$). On the 30th day, vancomycin and rifampicin decreased CRP values and had a similar effect on hospitalization time but were more effective than the normal saline group ($p<0.001$). In patients with bone involvement, the rifampicin group was superior to vancomycin and reduced implant removal surgery ($p<0.001$).

Conclusions: Vancomycin powder and rifampicin application during debridement in deep spinal surgical site infections can reduce hospital stays and prevent secondary surgeries. In addition, rifampicin can be effective in infections with bone involvement.

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Introduction

Surgical site infections (SSI) are prevalent consequences following surgical procedures and account for approximately 20% of all infections associated with healthcare (1). The reported prevalence of surgical site infections following spine surgery ranges from 0.7% to 16.1% (2). The occurrence of a deep infection subsequent to spine surgery is a potentially catastrophic consequence. The presence of a deep spinal infection is correlated with increased morbidity, death, and medical costs. Within the existing body of literature, there is mention of mild infections following spinal surgery, specifically pertaining to superficial wound infections, suture responses, and erythema (3). These types of infections can be effectively managed by implementing local drainage techniques or administering oral antibiotics. Nevertheless, deep spinal infections encompass illnesses that may additionally affect intramuscular, osseous, and neurological tissues. These factors can lead to significant rates of both death and morbidity. The standard therapies include intravenous antibiotics, surgical debridement, and washout with normal saline irrigation for deep infections (4). The spectrum of spinal surgeries comprises a variety of techniques, ranging from minimally invasive procedures like lumbar disc surgery to more complex stabilization operations requiring multiple levels of implants. There have been documented instances of deep infections that can disseminate to osseous and neurological tissues, particularly in situations involving the placement of implants (5).

Neurosurgeons commonly use vancomycin as a preventive intravenous antibiotic following spinal surgical interventions. It exhibits efficacy against gram-positive bacteria, the primary causative agent of surgical infections. Its use during the operation is based on a recent history of only 10 years (6). The prevailing microorganisms responsible for surgical site infections are Staphylococcus aureus and Staphylococcus epidermidis (7). With the increasing use of antibiotics day by day, vancomycin resistance is increasing even more. For this reason, there are publications recommending the use of rifampicin in vancomycin-resistant surgical wounds (8).

This study aimed to compare the effects of treating deep surgical site infections after spine surgery with vancomycin powder, rifampicin rinse, and normal saline infusion.

Materials and methods

This study included 179 cases with deep surgical infection following 2005 instrumented spinal surgery cases performed between 2015 and 2022. The written informed consents were obtained from the patients or their guardians. The patients were operated on for surgical debridement and drainage due to deep infection. Our study did not include individuals who had immunodeficiency, rheumatic illness, were under 18 years of age, were undergoing oncological treatment, had other organ infections, had severe kidney and liver failure, or had allergies to vancomycin and rifampicin. The patients were diagnosed with contrast-enhanced lumbar MRI taken after fever, increased infection parameters, and sensitivity in the surgical field. Bone involvement was determined by contrast-enhanced lumbar MRI. Various antibiotics and local treatments were administered to the patients for local infection before surgery, but they were unsuccessful. The first group received irrigation with normal saline during the debridement process. After rinsing with normal saline, 450 mg rifampicin (3 ampoules x 150 mg per ampoule) was administered inside the soft tissue in the second group. In the case of the third group, 1 gram of vancomycin powder was administered inside the soft tissue after irrigation with normal saline. All patients were followed up with a wound drain for three days after the operation. Preoperative cultures of the patients were taken, but culture results were excluded from the study because of inconsistent results, the patients were under antibiotics before. The patients' preoperative C-reactive protein (CRP) values, postoperative CRP values on the fifth day, length of hospital stay, bone infection, mortality, and reoperation for infection were recorded. The typical protocol involved administering intravenous vancomycin (30 mg/kg/day) and meropenem (3 gr/day) therapy to all patients for at least six weeks following the surgical procedure.

Statistical analysis

The sociodemographic and clinical characteristics of individuals were calculated as frequencies and percentages for categorical data using descriptive statistical methods. Numerical data were expressed as mean ± standard deviation or median (minimum-maximum) values. To find out whether there was a relationship between categorical variables, the Chi-square or Fisher's Exact Test was used. The normality distribution of numerical data was assessed using the Shapiro-Wilk test. Mean differences between two groups with normally distributed were compared by

Student's t-test, whereas the Mann–Whitney U test was applied for comparisons of the not normally distributed data. the Kruskal-Wallis H test was used in the comparison of the measurement values of three or more independent groups. The statistical significance of differences between groups was determined by Kruskal-Wallis followed by post-hoc Mann Whitney U-Test Bonferroni adjusted. The relationship between the parameters was evaluated at the spearman statistical significance. SPSS (Statistical Package for the Social Sciences, SPSS Inc., Chicago, IL, USA) version 25.0 package program was used for the data analysis. $p<0.001$ were considered statistically significant.

Results

The total number of patients consisted of 179 cases. 45.2% of them were women and 54.8% were men. The number of cases who were irrigated with normal saline was 60 (33.5%), cases were applied rifampicin was 59 (32.9%) and cases were applied topical vancomycin was 60 (33.5%). Demographic and clinical characteristics of normal saline irrigation, rifampicin applied or topical vancomycin applied groups are compared in **Table 1**. The individuals in the three groups had similar characteristics in terms of their mean age, gender, preoperative CRP, and bone involvement distribution ($p>0.001$).

The postoperative 5th day CRP values in the cases which were irrigated with normal saline were 57.3 [37.2 - 132.1], applied rifampicin was 39.2 [32.6 - 134], and applied topical vancomycin powder was 47.5 [32.6 - 144.6] ($p<0.001$). The reason for the statistical difference on the postoperative 5th day was due to the difference between the rifampicin applied groups and the normal saline group. The postoperative 30th-day CRP values in the cases which were irrigated with normal saline were 30.1 [17.2 - 52.1], applied rifampicin was 9.2 [4.2 - 20.1], and applied topical vancomycin powder was 8.9 [4.0 - 21.1] ($p<0.001$). The statistical difference on the postoperative 30th day was due to the difference between the groups administered normal saline and the other groups. No statistical difference was observed between the operation length of the groups ($p=0.305$). Also, the second operation for infection rate for infection in the normal saline irrigation group was 25% (15 cases) and it was significantly higher than the other two groups ($p<0.001$). The implant removal surgery rate was higher in the normal saline irrigation group (4 cases). Only one patient in the group irrigated with normal saline died due to sepsis.

Bone involvement was observed in all cases operated on for the second time due to infection. The relationship between implant removal surgery, day of hospital stay, and death was compared in patients who were operated on for the second time due to infection (**Table 2**) (**Figure 1**). The incidence of implant removal surgery was 26.6% (4 cases) in the normal saline group and 14.2% (1 case) in the vancomycin powder group, there was no statistically significance ($p=0.578$). The hospitalization day was 202 in the normal saline group, 95 in the rifampicin applied group, and 98 in the vancomycin powder applied group. The hospitalization day increased significantly in the normal saline group, which was operated for the second time due to infection ($p<0.001$). There was no statistically significant difference in terms of hospital stay in those who were not taken to the second operation due to infection ($p>0.001$) (**Table 3**) (**Figure 2**).

In cases with bone involvement, hospital stay, implant removal surgery, and mortality rates were examined between groups (Table 4). A statistically significant difference was observed in the rifampicin group compared to the other groups in terms of both hospitalization time and implant removal surgery when bone involvement was present ($p<0.001$) (**Figure 3**) (**Figure 4**).

Table 1: Comparison of demographic and clinical results of groups

Data	Normal Saline irrigation only (n=60) [a]	Rifampicin applied (n=59) [b]	Vancomycin powder applied (n=60) [c]	
	n (%) / M[Q1 - Q3]			p-value
Female	27 (45)	23 (38.9)	31 (51.7)	0.665
Male	33 (55)	36 (61.01)	29 (48.3)	
Age	35 [18 - 72]	39 [19 - 80]	41 [18 - 78]	0.205
Preoperative CRP	61.3 [50.6 - 150.5]	60.8 [45.7 - 170.2]	57.1 [45.7 - 170.2]	0.213
Postoperative 5th day CRP	57.3 [37.2 - 132.1]	39.2 [32.6 - 134]	47.5 [32.6 - 144.6]	<0.001*
Postoperative 30th day CRP	30.1 [17.2 - 52.1]	9.2 [4.2 - 20.1]	8.9 [4.0 - 21.1]	<0.001#
Operation length (min)	28 [22 - 45]	34 [24 - 47]	27 [22 - 50]	0.305
Hospitalization (day)	150 [80 - 200]	65 [60 - 100]	70 [62 - 103]	<0.001#
Second operation for infection	15 (25)	2 (3.4)	7 (11.6)	<0,001*
Bone involvement	16 (26.6)	15 (25.4)	16 (26.6)	0.435
Implant removal surgery	4	0	1	
Exitus	1	0	0	

M: median, Q1: percentile25, Q3: percentile75. CRP: C-reactive protein. *Difference was between b/a #Difference was between a/b and a/c

Table 2: The relationship between implant removal surgery, length of hospital stay, and death in patients undergoing second surgery due to infection

	Second operation for infection			
	Normal saline irrigation only (n=15) [a]	Rifampicin applied (n=2) [b]	Vancomycin powder applied (n=7) [c]	
	n (%) / M [Q1-Q3]			*p*-value
Bone involvement	15 (100)	2 (100)	7 (100)	
Implant removal surgery	4 (26.6)	0	1 (14.2)	*0.578*
Hospitalization (day)	202 [100 - 220]	95 [90 - 100]	98 [92 - 120]	***<0.001****
Exitus	1 (6.66)	0	0	

M: median, Q1: percentile 25, Q3: percentile 75. *Difference was between a/b and a/c

Table 3: Comparison of groups according to the length of hospital stay in patients who were not undergoing second surgery due to infection

	No second operation for infection			
	Normal Saline irrigation only (n=45) [a]	Rifampicin applied (n=57) [b]	Vancomycin powder applied (n=53) [c]	
	n (%) / M [Q1-Q3]			*p*-value
Hospitalization (day)	66 [62 - 103]	45 [36 - 54]	49 [40 - 56]	*0.345*

M: median, Q1: percentile 25, Q3: percentile 75

Table 4: The distribution of findings based on different groups in cases of infections with bone involvement

	Bone involvement			
	Normal Saline irrigation only (n=16) [a]	Rifampicin applied (n=15) [b]	Vancomycin powder applied (n=16) [c]	
	n (%) / M [Q1-Q3]			*p*-value
Implant removal surgery	4 (25)	0	1 (6.25)	***<0.001****
Hospitalization (day)	180 [123 - 202]	56 [45 - 102]	90 [82 - 120]	***<0.001****
Exitus	1 (6.66)	0	0	

M: median, Q1: percentile 25, Q3: percentile 75

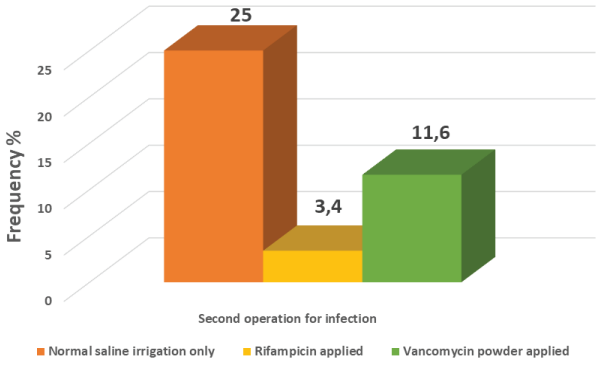

Figure 1: Distribution of patients who underwen surgery for the second time due to infectio according to groups

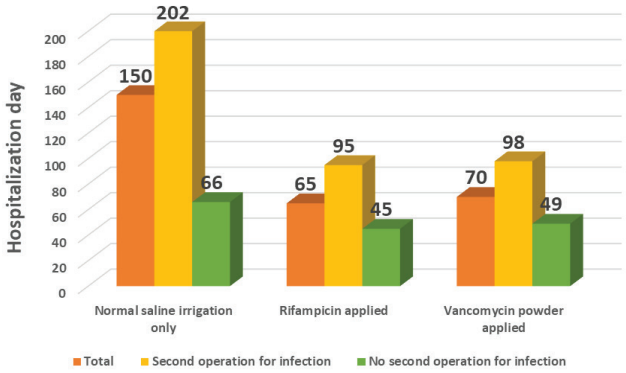

Figure 2: Showing the duration of hospital stay according to the groups of those who had and did not have a second operation due to infection.

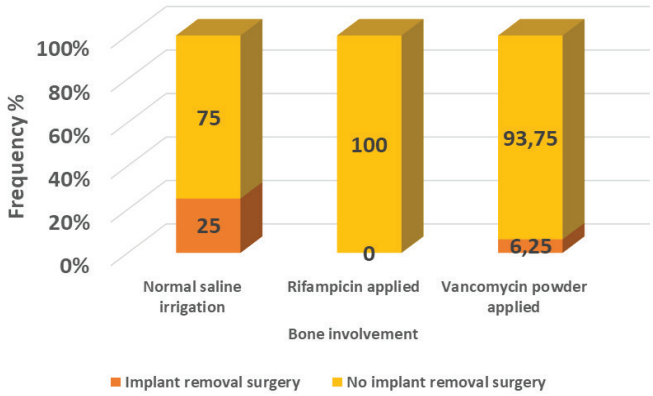

Figure 3: Distribution of implant removal surgery in patients with bone involvement according to groups

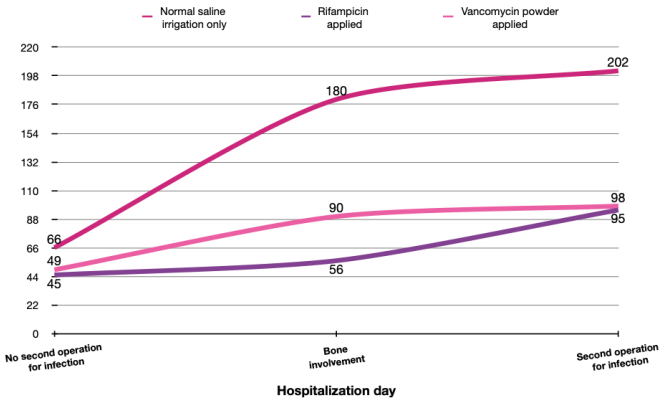

Figure 4: Distribution of hospitalization days according to groups, second surgery due to infection and bone involvement

Discussion

Surgical infection after spinal surgery is a significantly unfavorable complication that negatively impacts patients' overall health and can potentially increase the risk of morbidity and mortality. Surgical site infection following spine surgery has been shown in the scientific literature to develop in a range of 0.3% to 20% of patients (9). The infection, mainly once it infiltrates deep tissues, can lead to severe challenges such as osteomyelitis and meningitis, requiring repetitive surgical interventions and implant extraction procedures in individuals with implants (10). This puts an enormous cost on the healthcare industry (2).

Many reasons have been presented as risk factors for post-operative infection. The patient's body weight (11), diabetes (12), operation time, number of levels of surgery, and drain usage can be counted as the predisposing factors for spinal surgical infections (13). Moreover, smoking is a risk factor that increases the possibility of infection following spine surgery [2].

Prophylactic oral antibiotics can prevent post-surgical infections despite the lack of comprehensive evidence supporting their efficacy (14). In recent studies, evidence has emerged indicating that using antibiotic powders in the surgical field leads to a decrease in the incidence of postoperative infections (15,16). Vancomycin powder is widely used due to its efficacy in targeting gram-positive bacteria, the predominant pathogens responsible for surgical site infections (7). The possible side effects of vancomycin are red man syndrome, nephrotoxicity, colitis, and hearing loss. The local administration of the vancomycin powder prevents these systemic side effects (17).

Despite prophylactic oral and local precautions, infection can occur in spinal surgeries. The treatment of infection is a difficult struggle among clinicians. Although only oral antibiotics are used if the infection is superficial, oral antibiotics are insufficient in infections involving deep tissues. In patients with deep wound infections following spinal surgery, wound debridement and drainage are often recommended to remove accumulated purulent material within the surgical site (18). The studies have demonstrated the efficiency of washing with normal saline or povidone-iodine irrigation during debridement surgeries (19). In fact, it has been shown in a study that washing should be at least 1400 mL in order to prevent infections (20).

Again, local vancomycin powder can be used in patients who have been debrided due to infection, but the effectiveness of vancomycin powder decreases day by day as a result of increasing antibiotic resistance (21). Consequently, managing postoperative infections creates challenges owing to the presence of bacteria resistant to vancomycin.

The efficacy of rifampicin has been demonstrated in wound infections caused by gram-positive bacteria exhibiting resistance to vancomycin (8). Rifampicin, a bactericidal agent, is commonly utilized as a topical antibiotic in local infections (22). Therefore, research was conducted to examine the impact of this factor on preventing infection in spinal instrumentation procedures. In the study conducted by Karaarslan et al., rifampicin was used to cover the spinal implants during the surgical procedure. However, the researchers could not achieve a statistically significant outcome regarding infection prevention (23). The probable cause for this result can be attributed to the limited absorption of rifampicin on the implant surface, which has a smooth surface. Nevertheless, research has demonstrated that rifampicin can inhibit the formation of bacterial biofilm layers (24). Orthopedic surgery frequently utilizes it due to its beneficial impact on bone formation (21).

In our study, 179 patients were included with surgical site deep infection who have been operated on after spinal instrumentation surgery. The patients in our study underwent deep wound debridement surgery and were treated with different agents during surgery. The study results showed that the C-reactive protein (CRP) levels in the blood samples of the group given rifampicin dropped more quickly than in the group given vancomycin powder. However, after 30 days, the CRP levels in both groups reached similar levels. Our study demonstrated that using local antibiotics such as rifampicin or vancomycin powder during debridement surgery significantly reduced CRP levels compared to the control group that applied normal saline.

Sometimes, a second infection treatment surgery may be needed after debridement surgery. This Research has demonstrated that applying local antibiotics during debridement surgeries is necessary in all patients to decrease the need for subsequent surgical intervention caused by infection. The occurrence of a subsequent surgical procedure as a result of infection is associated with an extended duration of hospitalization.

Bone involvement after spinal surgeries is considered a poor prognosis and can be mortal (25). The bone involvement was present in nearly all patients who underwent a secondary surgical procedure due to infection in our study. For this reason, it is essential to consider that a secondary surgical intervention may be necessary in cases where bone involvement of infection is present. Bone involvement can give information about the depth of the infection and the difficulty of treatment. The presence of bone involvement additionally relates to a longer duration of hospitalization in our study. However, the patients with bone involvement demonstrated a notable improvement, particularly among those who applied rifampicin in our study.

Furthermore, the bone involvement of infection necessitated undergoing an extra surgical procedure to remove implants in our study. Imaging techniques revealed bone involvement in all individuals from whom implants were removed. It may be considered to individuals with bone involvement may undergo surgical procedures to remove implants. In contrast to vancomycin, rifampicin has been demonstrated to possess benefits in decreasing the duration of hospitalization and reducing the risk of surgical intervention for implant removal, particularly in individuals with bone involvement. Except for death due to infection and sepsis, no drug-related side effects were observed in the patients. Therefore, local use of vancomycin powder or rifampicin during debridement may be an effective method in deep surgical infections that develop after spinal implantations.

The study has limitations. Preoperative nasal cultures of the patients could not be taken. Since there was a surgical site infection and the patients were under prophylactic antibiotics, the blood cultures and surgical site cultures taken were evaluated as meaningless and were excluded from the study.

Conclusions

The use of vancomycin powder and rifampicin during debridement in deep spinal surgical site infections can be used to reduce hospital stay and to prevent secondary infection surgeries. In addition, rifampicin can be used in infections with bone involvement.

Conflict of interest:

The authors report no conflict of interest.

Funding source:

No funding was required.

Ethical approval:

The study was conducted in accordance with the Declaration of Helsinki and approved by the Institutional Review Board (or Ethics Committee) for studies involving humans.

Informed consent:

Informed consent was obtained from all patients or their guardians involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Acknowledgment:

No

Peer-review:

Externally. Evaluated by independent reviewers working in at least two different institutions appointed by the field editor.

Data availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Contributions

Research concept and design: **HSC, MSG**
Data analysis and interpretation: **YEO**
Collection and/or assembly of data: **YEO**
Writing the article: **HSC, YEO, MSG**
Critical revision of the article: **HSC**
Final approval of the article: **HSC, MSG**

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