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The effectiveness of pedicle screw immersion in vancomycin and ceftriaxone solution for the prevention of postoperative spinal infection: A prospective comparative study

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ABSTRACT

Objective: The aim of this study was to evaluate the efficacy of the local application of vancomycin hydrochloride (HCl)–ceftriaxone disodium hemiheptahydrate onto implants before using them to prevent postoperative infection.

Methods: The study included 239 patients (153 women and 86 men; mean age: 48.23 ± 16.77 years) who had thoracolumbar stabilization with transpedicular screws. All surgeries were performed by the same surgeon. Patients were divided into two groups. In the group 1 ($n = 104$), implants were bathed in a solution of local prophylactic antibiotics for 5 seconds just before implantation. In the group 2 ($n = 135$), implants were not bathed before implantation. Local antibiotics used in the study was effective against gram positive bacteria (including methicillin resistant *Staphylococcus aureus*) and gram negative bacteria. The rate of surgical site infection and wound healing time were compared between the groups.

Results: A total of 10 patients (4.1%) had deep wound infection and 20 (8.4%) had superficial infection. The most common bacteria was Staphylococcus aureus. One patient died 21 days after the surgery because of sepsis. The wound healed in a mean of 9.66 ± 2.04 days in patients who had no infection and in 32.33 ± 19.64 days in patients with infection ($p < 0.001$). The patients in group 1 had significantly less deep infection than the patients in group 2 ($p < 0.05$). However, there was no statistically significant difference between the groups for superficial infection. Patients with vertebral fracture had significantly lower deep infection rate in group 1. The deep infection rate of group 1 patients with diabetes, with bleeding of more than 2000 mL, transfused with blood transfusions above 3 units and with dural injury was significantly lower than those in the group 2. None of the patients had allergic reactions to the drugs used for local prophylaxis.

Conclusions: This study shown that bathing implants in antibiotics solution was an effective local prophylactic method to prevent deep infections in spinal surgeries with instrumentation.

Level of Evidence: Level III, Therapeutic study.

Introduction

Surgical site infection (SSI) is a serious complication of spinal surgery. It is reported in 0.7%–14% of patients who undergo spinal surgeries involving instrumentation.[1–8] SSI can be either superficial or deep. If the infection extends under the paravertebral fascia, it is defined as deep SSI. Deep SSI involves long hospital stays, repeated surgeries, removal of the spinal implant and increased incidence of developing pseudoarthrosis, resulting in high hospitalization costs.[9]

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Microorganisms generally stick to the surface of spinal implants and are, thus, transferred to the surgical site during surgery; in addition, they may appear on implants in a case of permanent bacteraemia after the surgery. Spinal implant surgeries are associated with an increased risk of infection owing to the bacterial biofilm layer that grows on the surface of implants, which is resistant to antibiotics.[10] The gold standard in infection control is preventing the development of SSI, which can be achieved by various methods.

This study primarily aimed to evaluate the efficacy of the local application of vancomycin hydrochloride (HCl)–ceftriaxone disodium hemiheptahydrate onto implants prior to their use in surgeries to prevent postoperative infection.

Material and methods

This prospective study was approved by the local ethics committee of the hospital on 25 February 2006 (number B.02.1.VGM.2.03.01). Written informed consent was obtained from all patients. Patients who were treatment via posterior thoracolumbar stabilization with transpedicular screws and posterolateral fusion in our neurosurgery clinic were included in this study. Between March 2006 and June 2009, 260 consecutive cases were treated. Eighteen patients were excluded owing to a preoperative diagnosis of spondylodiscitis or because of a known allergy to some drugs, which were to be used in the study. In addition, three patients were excluded because they did not follow-up. Therefore, in total, 239 cases were included in this study.

Cefazolin sodium (1 gm) was intravenously injected in all the patients 30 min prior to the skin incision. Furthermore, 1 g of cefazolin sodium was postoperatively administered for 24 h (3 × 1, every 8 h") for routine prophylaxis. The surgeries were all performed by the same spinal surgeon. The fascia was closed with #1 polyglactin (MEDSORB PGLA®, Medeks, Istanbul, Turkey), the subcutaneous tissue was closed with #2/0 polyglactin (PEGESORB®, Dogsan, Trabzon, Turkey) and the skin was closed with #2/0 polypropylene (PROPİLEN®, Dogsan, Trabzon, Turkey) in all the patients. A drain was placed in each patient that was removed on the first postoperative day. In the hospital, the authors evaluated the wounds daily until complete closure of the wound. Superficial and deep infections were distinguished by a neurosurgeon along with a specialist in infectious diseases based on examination and MRI with contrast. In cases exhibiting flux from the surgery site, culture samples were collected from the wounds and were examined in our microbiology laboratory. Both before surgery and one week after surgery, blood glucose levels, white blood cell (WBC) counts, haemoglobin and haematocrit values, C-reactive protein (CRP) levels and erythrocyte sedimentation rates (ESRs) were examined for each patient. In addition, daily WBC, ESR and CRP levels were measured in patients diagnosed with an infection. All SSI cases were treated by the author, who is an infectious disease specialist. Each SSI case was followed from its diagnosis to wound healing, and the number of days to reach complete wound healing was prospectively recorded for all such cases. The patients were followed for an average of 1.2 years (range: 21 days–3.5 years) for SSI.

Study groups

The broad-spectrum antibiotics for the local prophylaxis solution were selected based on the microorganisms present at the infection site (gram-positive bacteria including methicillin-resistant *Staphylococcus aureus* and gram-negative bacteria). To prepare the solution, vancomycin HCl (Edicin i.v. 500 mg 1 Flakon; Sandoz, Istanbul, Turkey) powder and ceftriaxone disodium hemiheptahydrate (Cefaday i.v. 1000 mg 1 Flakon; Biofarma, Istanbul, Turkey) powder were dissolved in 250 ml of saline (Fig. 1a and b). The patients were divided into two groups. In group 1 (n = 104), the implants were bathed in the local prophylactic antibiotics solution for 5 s just before implantation (Fig. 1c). In group 2 (n = 135), the

Fig. 1. To prepare the solution, a) The antibiotics powder are unpacked and, b) Dissolved in 250 ml saline. c) Implants are bathed in the solution of local prophylactic antibiotics just before implantation.

implants were applied without bathing them in local prophylactic antibiotics solution. The patients were classified into the two groups according to their preference for using the local antibiotics solution during the operation. Patients who preferred local antibiotics comprised group 1, whereas patients who did not prefer the antibiotics solution comprised group 2 (control group).

Statistical analyses

The normality of the variables was assessed using a one-sample Kolmogorov–Smirnov test. Associations between SSI and potential risk factors were analysed using chi-square and Fisher's exact tests. Significant differences between continuous variables were determined with the *t*-test or the Mann–Whitney U test. A multivariate logistic regression analysis was used to identify independent risk factors for SSI. A p value of <0.05 was considered as statistically significant.

Results

This study included 239 patients (153 females and 86 males) aged 48.23 ± 16.77 years old. In 26 patients (10.8%), additional interventions were performed after the surgery for non-infectious reasons. Screw revision was performed in nine patients in group 1 and in 11 patients in group 2. External lumbar drainage was performed for cerebrospinal fluid (CSF) leakage in six patients (three in group 1 and three in group 2), and three of these patients (one in group 1 and two in group 2) underwent additional operation for duraplasty.

Among all the patients, 10 (4.1%) had a deep wound infection and 20 (8.4%) had a superficial infection. The average duration for the development of the infection was 13.26 ± 10.96 days. Wound debridement was performed in all patients with deep infection and in four patients with superficial infection. Instrumentation systems were removed in four cases with deep infection. One patient's wound was closed with a paravertebral muscle flap. One patient succumbed to sepsis after 21 days of the operation. Proper wound closure observed in 9.66 ± 2.04 days in patients without infection and in 32.33 ± 19.64 days in the patients with SSI ($p < 0.001$).

The postoperative WBC and ESR levels in the patients with and without SSI were not statistically different. However, the postoperative CRP levels in the patients with SSI were higher than those in the patients without SSI ($p < 0.001$).

In 22 of 30 patients (73.3%), microorganisms were isolated from the flux at the surgery sites. Multiple microorganisms were isolated from 12 patients. The most commonly isolated bacteria was *S. aureus* (n = 10), followed by (in order of frequency of isolation) *Coagulase negative Staphylococcus, Pseudomonas aeruginosa, Acinetobacter baumannii, Enterobacter cloacae, Escherichia coli, Proteus mirabilis, Enterococcus faecalis* and *Corynebacterium species*.

Comparison of study groups and effects of local prophylactic antibiotics

None of the patients demonstrated allergic reactions to the drugs used for local prophylaxis. Moreover, there was no difference between groups 1 and 2 regarding any of the studied characteristics (demographic data, primary diagnoses, presence of concomitant diseases, BMI, blood biochemistry and hospitalization and surgery factors) (Table 1).

Nine patients developed SSI (only one developed deep SSI) in group 1 (8.7%) and 21 patients developed SSI (nine with deep SSI) in group 2 (15.6%). The deep infection rate was significantly lower in group 1 (0.96%) than in group 2 (6.6%) (p = 0.04, OR = 7.36). However, there was no statistically significant difference between the two groups with regard to the development of superficial SSI (p = 0.81, OR = 1.17). All characteristics of the patients with deep SSI are shown in Table 2.

The study groups were also compared based on the presence of the following evaluated risk factors: primary diagnoses, presence of concomitant diseases, amount of intraoperative bleeding and blood transfusion and presence of an intraoperative dural injury. Patients with a vertebral fracture in group 1 had a significantly lower SSI rate than that in patients with a vertebral fracture in group 2 (p = 0.03). Patients with diabetes, those with >2000 ml of bleeding,

Table 1
Risk factors for infection in the study groups.

Risk factor	Group 1 (n = 104)	Group 2 (n = 135)	*p value*
Age (years)	50.8 ± 14.2	48 ± 14.9	0.13
Gender (F/M)	72(69%)/32 (31%)	81(60%)/54 (40%)	0.14
Primary diagnoses (traumatic/non-traumatic)	28(27%)/76(73%)	52(39%)/83(61%)	0.06
BMI	209 ± 5.4	27.9 ± 5.2	0.10
Diabetes mellitus (+/−)	10(10%)/94(90%)	19(14%)/116(86%)	0.29
Smoking (+/−)	15(14%)/89(86%)	28(21%)/107(79%)	0.20
Other concomitant diseases (+/−)	44(42%)/60(58%)	42(31%)/93(69%)	0.07
ASIA grade (A-B/C-D-E)	4(4%)/100(96%)	11(8%)/124(92%)	0.17
Preoperative glucose (mg/dl)	98 (58–246)	100 (56–383)	0.63
Preoperative Hb level (g/dl)	13 (4.6–16.8)	13.1 (8.2–17)	0.28
Preoperative hospitalization time (days)	9 (0–43)	11 (0–48)	0.51
Surgical category (emergent/elective)	10(10%)/94(90%)	13(10%)/122(90%)	0.99
Surgeryduration (h)	4 ± 1.1	3.8 ± 1	0.18
N of instrumented segments (<5/≥5)	91(88%)/13(12%)	121(90%)/14 (10%)	0.18
Transfusion (>3 unit bag/≤3 unit bag)	14(13%)/90(87%)	15(11%)/120(89%)	0.58
Dural injury (+/−)	15(14%)/89(86%)	19(14%)/116(86%)	0.93
Postoperative ICU stay (+/−)	16(15%)/88(85%)	12(9%)/123(91%)	0.12
Additional surgeries (+/−)	12(12%)/92(88%)	19(14%)/116(86%)	0.56
Postoperative WBC count	8.3 (3.4–25.1)	8.2 (1.7–19.5)	0.48
Postoperative CRP level	0.9 (0.3–19.4)	0.8 (0.3–19.3)	0.63
Postoperative ESR level	60.5 (2–401)	61 (2–120)	0.77

Age, BMI and surgery duration data are presented as means±standard deviations. Data of preoperative glucose and Hb levels; preoperative hospitalization stays and postoperative WBC, CRP and ESR levels are presented as medians (ranges) and others are presented as percentages. Significant p values are shown as bold characters.
N, number; SD, standard deviation; BMI, body mass index; ASIA, American Spinal Injury Association; Hb, haemoglobin; ICU, intensive care unit; WBC, white blood cell; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate.

Table 2
Characteristics of 10 patients with deep infections.

Age/Gender	Primary Diagnosis	Concomitant disease	Surgery duration (hr)	N of segments	Study group	Blood loss (ml)	Implant removal
72/M	Trauma	+	5	5	2	1200	−
61/F	SL	−	4	3	2	1800	+
61/M	LSS	+	5	2	2	2200	−
37/F	SL	−	2	2	2	500	+
29/M	Trauma	+	3	5	2	2500	+
64/F	SL	+	5	3	2	1300	−
63/F	Tumour	+	8	5	2	2500	−
67/F	LSS	+	3	2	1	700	−
39/M	Tumour	−	5	3	2	2800	−
35/F	Trauma	+	4	5	2	1500	+

N, number; SL, spondylolisthesis; LSS, lumbar spinal stenosis.

those who were transfused with >3 units of blood and those with a dural injury had lower SSI rates in group 1 than in group 2 ($p = 0.03$, $p = 0.026$, $p = 0.016$ and $p < 0.001$, respectively). However, there were no intergroup differences with respect to low ASIA score, presence of chronic illnesses except diabetes mellitus and number of instrumented segments ($p = 0.17$, $p = 0.93$ and $p = 0.6$, respectively).

Discussion

Infection is the most common complication of spinal surgeries. SSI prolongs the patient's hospital stay and increases morbidity and mortality. Superficial infections typically progress mildly, but deep wound infections can lead to spondylodiscitis, osteomyelitis and meningitis.[11] Furthermore, the frequency of SSI is high after spinal surgeries that involve instrumentation.[9] Rechtine et al[12] ascertained that the rate of SSI for thoracolumbar trauma surgeries was 10% in 235 cases. Jutte and Castelein[13] reported a deep infection rate of 4.7% in 105 patients who were operated using underwent an operation involving pedicle screws. This rate was lower in our study. The treatment of patients with deep postoperative infections is expensive; moreover, the patient's length of stay in the hospital increases, preventing them from resuming work, and further increasing indirect costs.[14] Deep wound infections might also lead to sepsis and death, as shown in our research.[11]

According to this study, postoperative CRP levels were reliable indicators of infection. However, we could not identify a connection between high postoperative ESR levels and the presence of an SSI. CRP is more sensitive than ESR when evaluating the response to infection treatment.[15–17]

Reportedly, the most common causative microorganisms of SSI are *S. aureus* and other members of Staphylococcus species.[12,17,18] Chen et al[19] also reported that members of the Staphylococcus species were the most common causative agents of SSI and that they were isolated from 58.3% of cases. In our study, the most commonly isolated organism was also *S. aureus*. On the contrary, the rate of negative cultures in our study was high (26.7%), similar to that observed in the study by Gerometta et al[20] (0–31.4%).

Prophylaxis for infection and other protective procedures

Under the paravertebral fascia, foreign bodies and local tissue necrosis of paravertebral soft tissues, such as postoperative haematoma or intervertebral discs, create an optimum medium for microorganism growth. During surgery, microorganisms present in the air of the operating room can enter the wound and stick to the implants. In a prospective study that included patients who were operated in the same operating room and by the same surgeon, Gelalis et al[21] reported that the culture samples collected intraoperatively from the surgical wounds showed a 20% growth. Moreover, the development of biofilms on the surfaces of implants plays an important role in implant-associated infections because of the biofilm's protective effect on microorganisms against the host defence systems and antibiotics. This biofilm layer covers the surfaces of implants and neighbouring host tissues. The biofilm layer contains fibronectin, fibrinogen, collagen and other proteins. Glycocalyx-coated microcolonies are often protected from the host-tissue defences.[4] Extracellular DNA is a major structural component of the *S. aureus* biofilm matrix. Bacterial proteases cause the release of extracellular DNA, which is critical for the early development of biofilms.[22] Literature suggests that biocompatibility and physical/chemical properties of implants can be contributing factors for the differences in infection rates, especially with metal implants that have smooth and rough surfaces.[23,24] All of these studies showed the importance of intraoperative SSI prevention.

Many studies have evaluated the effects of local antibiotics or antimicrobials on the development of postoperative wound infections. In a study by Brennan et al,[25] the antimicrobial outcomes of silver-coated implants were good, with a low proportion of positive cultures and low rates of osteomyelitis. Similarly, another study observed that silver-coated titanium implants can be used to prevent implant-associated deep bone infections.[26] However, these types of implants are quite expensive and pose some risks due to silver intoxication.[27] Another cost-effective method involves bathing the implants in a povidone-iodine solution before implantation.[28]

Some studies demonstrated that the use of local antibiotics was less risky and cheaper treatment option. In a study conducted with 218 rats, Perdue et al[29] reported that they performed peritoneal lavage using a saline solution with ceftriaxone and successfully treated peritonitis. The most studied antibiotic for local prophylaxis is vancomycin, which is the effective against the most frequently cultured microorganisms from Staphylococcus species. Some clinical studies have reported that the rate of deep wound infection reduced following the use of local prophylactic intraoperative powdered vancomycin.[30,31] In addition, other antibiotics have been reported in the literature. In a rabbit model, Stall et al[32] cured twice as many infections using polylacticoglycolic acid microspheres saturated with gentamicin than using a placebo. Conversely, the local use of antibiotics and antimicrobials may cause serious complications. Blas et al[33] reported anaphylaxis due to bacitracin irrigation before closing the wound. In our study, a solution that contained broad-spectrum antibiotics, which were effective on the most common microorganisms causing SSI in our clinic, such as gram-positive bacteria including methicillin-resistant *S. aureus* and gram-negative bacteria, was locally applied on the implants before implantation. Thus, the surfaces of screws and other parts of instruments were coated with broad-spectrum antibiotics. A comparison between the patient groups demonstrated that bathing the implants in a prophylactic antibiotic solution prevented deep infections. This reliable method is cost-effective and easy to use.

Furthermore, in this study, none of the patients who received local antibiotic prophylaxis experienced an allergic reaction.

CSF leakage, smoking, obesity, diabetes, HT and blood transfusions are the risk factors associated with SSI.[2] In diabetic patients, local changes in the tissues increased the risk of infection. A previous study reported that diabetic patients had a 10%–20.9% rate of SSI.[4] However, in our study, diabetic patients were protected from deep SSI in group 2. Moreover, vertebral fractures lead to a high rate of SSI.[19] Moreover, excessive amount of blood loss and transfusions were reported as risk factors for infection development.[9] However, another study did not observe an increase in infection risk with a loss of $\geq$1500 ml of blood.[1] Reportedly, with the use of local antibiotics, the concentration of antibiotics at the operation site is higher than systemic application.[34] In our study, we observed that the local use of antibiotics had protective action against deep infections in patients with fractures and in patients who had too much blood transfused due to excessive bleeding. In a meta-analysis, Khan et al[35] defended the local use of vancomycin powder that might have a protective action against SSI; however, they recommended its use only in high-risk patients. By contrast, Suh et al[36] suggested that this method was not successful in preventing SSI. Conversely, in another study, vancomycin-impregnated fibrin sealant use was successful in preventing SSI.[37]

The limitations of this study include the high rate of infection, the fact that it was not effective in some high-risk groups and the simultaneous use of two antibiotics. In particular, the high rate of superficial infection relative to other studies may have affected the outcomes of this study. However, unlike our study, only deep infection rates were reported in most previous studies, and superficial infections were not mentioned.[2,13,30,35] Moreover, the efficacy might vary if the doses of antibiotics or the amount of saline changes.

Conclusion

This prospective study proposes a novel suggestion for the prevention of deep spinal infection. Bathing implants in vancomycin HCl and ceftriaxone disodium hemiheptahydrate solution before their application is an effective local prophylactic method in spinal surgeries with instrumentation. This method appears to be an interesting alternative that requires further prospective and randomized studies.

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