

Individualized antibiotic prophylaxis reduces surgical site infections by gram-negative bacteria in instrumented spinal surgery

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Abstract

Purpose Surgical site infection (SSI) can be a challenging complication after posterior spinal fusion and instrumentation (PSFI). An increasing rate of SSI by gram-negative bacteria (GNB) has been observed. Current guideline recommendations have not been effective for preventing infection by these microorganisms.

Methods Retrospective cohort study comparing two consecutive groups of patients undergoing PSFI at a single institution. Cohort A includes 236 patients, operated between January 2006 and March 2007, receiving standard preoperative antibiotic prophylaxis with cefazolin (clindamycin in allergic patients). Cohort B includes 223 patients operated between January and December 2009, receiving individualized antibiotic prophylaxis and treatment based on preoperative urine culture. Cultures were done 3–5 days before surgery in patients meeting one of the following risk criteria for urinary tract colonization: hospitalization longer

than 7 days, indwelling catheter, neurogenic bladder, history of urinary incontinence, or history of recurrent urinary tract infection.

Results Twenty-two (9.3%) patients in cohort A developed SSI, 68.2% due to GNB. 38 (17%) patients in cohort B were considered at risk for GNB colonization; preoperative urine culture was positive in 14 (36%). After adjusted antibiotic prophylaxis, 15 (6.27%) patients in cohort B developed SSI, 33.4% due to GNB. A statistically significant reduction in GNB SSI was seen in cohort B (Fisher's exact test, $p = 0.039$).

Conclusion Higher preoperative GNB colonization rates were found in patients with neurogenic bladder or indwelling catheters. Preoperative bacteriological screening, treatment for bacteriuria, and individualized antibiotic prophylaxis were effective for reducing GNB SSI.

Keywords Antibiotic prophylaxis · Surgical site infection · Gram-negative bacteria · Urinary tract infection · Spine surgery

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Introduction

The incidence of surgical site infection (SSI) after short lumbar instrumentation ranges from 2 to 4% [14, 29]. In high-risk patients undergoing major surgery and receiving long instrumentation, infection rates may rise up to 8–15% [1, 27]. Published data show that SSI increases the morbidity, mortality, and healthcare costs associated with spinal surgery [17].

The great majority of SSIs following spinal surgery are caused by gram-positive bacteria, particularly *Staphylococcus aureus* [20]. However, a growing rate of infection due to gram-negative bacteria (GNB) has been observed

[22]. Contamination by GNB should not occur during the operative procedure, as these microorganisms are not usually present among the patient's skin flora. Previous studies have suggested that GNB contamination could be secondary to hematogenous seeding originating in the urinary tract or to local skin contamination in incontinent patients, especially those undergoing surgery at the lumbosacral level [13].

Prevention of SSI is of utmost importance, and perioperative antibiotic prophylaxis is a key measure to avoid this complication [9, 30]. The recommended standard perioperative antibiotic prophylaxis in spinal surgery [2, 30] is cefazolin. This first-generation cephalosporin has a long half-life in bone and serum, excellent activity against gram-positive microorganisms and some activity against GNB, including *Proteus* spp. and certain strains of *Escherichia coli*. Isolated reports have shown that broader-spectrum prophylaxis may be necessary in patient subpopulations more prone to acquiring polymicrobial SSI, such as those with neuromuscular deformities or spinal cord injury [11, 26].

The recently published North American Spine Society (NASS) evidence-based guidelines on antibiotic prophylaxis in spinal surgery [30] have pointed out that potential subgroups of patients requiring effective prophylaxis against GNB may exist, but have not yet been identified. It has been shown that patients with incontinence, neurogenic bladder, or indwelling catheters are more prone to urinary tract colonization (UTC) and infection [15], and may therefore be at higher risk of SSI by GNB. Since the indications for spinal fusion, and the complexity and comorbidities of our patients are progressively increasing, the percentage of patients requiring broad-spectrum antibiotic prophylaxis may also be rising. Oncologic patients, polytrauma patients with indwelling catheters in intensive care units, and incontinent patients undergoing lumbosacral surgery are likely to have UTC, and therefore, may benefit from broad-spectrum antibiotic prophylaxis.

We hypothesized that detecting UTC preoperatively and adjusting antibiotic prophylaxis according to urine culture results might lower the overall SSI rate, by reducing the number of GNB infections.

Materials and methods

A cohort study was designed to compare two groups of patients undergoing surgery at a single tertiary university hospital, which serves as a referral center for patients with acute spinal cord injuries, and all types of fractures, deformities, and degenerative conditions of the spine. All patients included in the study were treated with posterior spinal fusion and instrumentation (PSFI) at the thoracic or lumbar spine.

Cohort A included all patients undergoing thoracolumbar PSFI between 1 January 2006 and 31 March 2007. All received standard antibiotic prophylaxis with cefazolin (clindamycin in patients with known beta-lactam allergy), according to the guidelines in effect at that time.

Cohort B included all patients undergoing thoracolumbar PSFI between January and December 2009. Patients in this group received individualized antibiotic prophylaxis based on the more recent NASS guidelines and preoperative bacteriologic screening. To identify patients potentially at risk for postoperative GNB SSI, all those with at least one UTC risk factor underwent urine culture 3–5 days before surgery. Risk criteria were established based on literature review, guideline recommendations, and expert consensus, as follows:

- *Indwelling bladder catheter*, including chronic indwelling catheters (>30 days) and prolonged catheterization (>7 days) during hospital admission before spinal surgery. Pigrau and Rodríguez-Pardo [15] have reported a 20% colonization rate in patients with indwelling catheters.
- *Neurogenic bladder*, defined as bladder dysfunction resulting from central nervous system disease or dysfunction of peripheral nerves involved in control of miction. Patients with this condition present a higher risk of UTC due to incomplete voiding, elevated vesical pressure, and frequent catheterization [4]. Higher rates of urinary tract infection (UTI) by multiresistant microorganisms have also been described in these patients [24].
- *Urinary incontinence*, defined as involuntary urinary leakage and including stress incontinence (urinary leakage during exertion), urge incontinence (involuntary urinary leakage accompanied by or preceded by urgency), and mixed types (both symptoms present). Urinary incontinence has been related to asymptomatic bacteriuria in elderly patients [19], and was found to be an independent risk factor for developing SSI after spinal surgery [13].
- *Preoperative hospital stay longer than 7 days*.
- *Referral from long-term care facilities* (e.g., nursing home, convalescent home). In the elderly population, a higher rate of asymptomatic bacteriuria has been observed in patients staying at long-term care facilities [12].
- *Known history of recurrent UTI* at least three episodes during the last 12 months [16].

Positive cultures were defined as those showing bacterial growth $>10^5$ CFU/mL. Culture-positive patients received specific antibiotic prophylaxis and treatment for bacteriuria adjusted to the microorganism isolated and antibiogram. All patients with clinical symptoms of SSI

and positive cultures were identified; superficial and deep wound infections as classified by CDC/NISS [10] were both considered. All patients had a minimum postoperative follow-up of 9 months to determine whether further infection developed. Infection rates and the percentage of infections due to GNB were calculated in both groups and compared with Fisher's exact test. SPSS 13.0 (Chicago, IL) was used for the statistical analyses.

Results

Cohort A included 236 patients with the following diagnoses: 60 (25.42%) fractures, 107 (45.33%) degenerative conditions, 50 (21.18%) deformities, 10 (4.23%) tumors, and 9 (3.81%) other diagnoses. Twenty-two patients (9.32%) developed SSI, and 15 (6.2%) were due to GNB. There were ten deep infections and five superficial ones, with the following distribution of microorganisms: nine *E. coli*, two *Klebsiella pneumoniae*, two *Pseudomonas aeruginosa*, two *Enterobacter* spp., and one *Acinetobacter baumannii*.

Cohort B included 223 patients, with the following diagnoses: 44 (19.73%) fractures, 97 (41.63%), degenerative conditions, 44 (19.73%) deformities, 12 (5.38%) tumors, and 26 (11.65%) others. Thirty-eight patients (17%) had at least one UTC risk factor and underwent preoperative urine culture. Fourteen (36.6%) cultures were positive. The UTC criteria with the highest rate of positive cultures were neurogenic bladder (3 out of 5) and indwelling catheter (8 out of 14) (Table 1).

Patients with positive cultures received specific treatment for bacteriuria, and antibiotic prophylaxis was modified based on the antibiogram (Table 2). Urine culture isolated *E. coli* in ten cases (1 ESBL-producer), *K. pneumoniae* in two (1 ESBL), *A. baumannii* in one, and *Enterococcus faecalis* in one. Fifteen patients from cohort B developed SSI (6.72%), and five cases (33.3%) were caused by GNB. All five infections were superficial, and the isolated microorganisms were *E. coli* in one patient, *P.*

aeruginosa in three, and *Enterobacter* spp. in one. In two patients, superficial SSI was treated with wound dressings, whereas in three cases, surgical debridement was necessary. In two of these patients, opening was limited to superficial layers (above the fascia) and in one, the entire wound was opened for debridement of superficial layers and repositioning of a pedicle screw. Additionally, all five patients received specific antibiotic treatment during 8 weeks. None of them experienced any further infectious complication after a minimum follow-up of 9 months. Table 3 shows the characteristics of the patients that developed SSI in both groups.

The difference between the overall infection rates in the two groups (cohort A: 9.32%, cohort B: 6.72%) did not reach statistical significance ($p > 0.1$, statistical power 27.3%). However, the percentage of SSI due to GNB in cohort B (33.4%) was significantly lower than in cohort A (68.2%) ($p < 0.04$).

Discussion

Surgical site infection is a potentially devastating complication following instrumented spinal surgery. The most commonly implicated microorganism is *S. aureus* [20], but over the last years, infections due to more virulent microorganisms such as methicillin-resistant *S. aureus* (MRSA) and gram-negative rods have been increasing alarmingly [20, 22]. Prevention is a major issue and first-generation cephalosporins, especially cefazolin, are considered the most suitable antibiotics for perioperative prophylaxis [2]. However, recently launched evidence-based guidelines [30] point out that broad-spectrum antibiotics may be needed for some high-risk populations. Our study shows that preoperative detection of UTC in patients at risk and adjusting antibiotic prophylaxis to preoperative urine cultures significantly reduces the rate of postoperative GNB SSI.

The relevance of infections caused by microorganisms resistant to standard prophylaxis in institutions attending to high-risk populations, such as patients with neuromuscular scoliosis, complex deformities, acute spinal cord injury, and spinal tumors, is clearly shown by our data. Almost 10% of patients included in cohort A receiving standard perioperative cephazolin acquired SSI and 68.2% of cases were due to GNB. At least some of these patients were likely colonized by GNB before surgery [7]. Therefore, targeting patients who are more prone to be preoperatively colonized by cefazolin-resistant microorganisms is essential. Programs are being developed for screening and decolonizing MRSA in patients undergoing surgery [5, 6, 25], but measures to prevent GNB infection are still lacking, even though a link between preoperative UTC and spinal SSI has already been reported in myelomeningocele

Table 1 Patients meeting criteria for preoperative urine culture

	Total preoperative culture	Positive preoperative culture
Neurogenic bladder	5	8
Indwelling catheter	14	3
Preoperative stay >7 days	7	1
Urinary incontinence	7	1
Recurrent urinary tract infection	3	1
Preoperative stay at long-term care facility	2	0

Table 2 Characteristics of patients with positive preoperative urine culture

Spine diagnosis	Sex	Age	Criterion for urine culture	Microorganism	Antibiotic prophylaxis administered	Urinary tract infection treatment
Fracture with SCI	F	64	Indwelling catheter	<i>E. coli</i> R to ciprofloxacin	Cefazolin	Amoxicillin-clavulanic acid
Fracture with SCI	F	57	Indwelling catheter	<i>S E. coli</i>	Cefazolin	Ciprofloxacin
Fracture with SCI	M	29	Indwelling catheter	<i>E. coli</i> R to cephalosporin	Meropenem	Meropenem 10 days
Fracture without SCI	F	79	Indwelling catheter	<i>E. coli</i> + <i>Providencia</i> spp	Cefepime	Cefepime
Fracture without SCI	F	82	Indwelling catheter	<i>E. coli</i>	Cefepime	Ciprofloxacin
Fracture w SCI	M	29	Indwelling catheter	<i>K. pneumoniae</i> R to ceftioxin cefuroxime and ampicillin and S to cefepime and ciprofloxacin	Cefepime	Ciprofloxacin
Metastasis	M	57	Indwelling catheter	<i>S E. coli</i>	Cefazolin	Cefazolin IV
Fracture without SCI	F	30	Indwelling catheter	<i>A. baumannii</i>	Meropenem	Meropenem 10 days
Spondylodiskitis by <i>S. aureus</i>	F	63	Preop stay >7 days	ESBL <i>E. coli</i>	Ertapenem	Ertapenem 7 days
Pseudoarthrosis after neuromuscular scoliosis	F	14	Neurogenic bladder	ESBL <i>K. pneumoniae</i>	Ertapenem	Ertapenem 7 days
Neuromuscular scoliosis	M	26	Neurogenic bladder	<i>E. coli</i>	Cefepime	Cefuroxime oral
Neuromuscular scoliosis	M	14	Neurogenic bladder	<i>E. coli</i> R to ciprofloxacin and cotrimoxazole	Cefepime	Amoxicillin clavulanic acid
Spinal stenosis	F	72	Recurrent UTI	<i>E. coli</i> R to ciprofloxacin and cotrimoxazole and S to ampicillin and cephalosporin	Cefazolin	Cefuroxime oral
Spinal stenosis	F	83	Incontinence	<i>Enterococcus faecalis</i>	Cefazolin	Ciprofloxacin

ESBL extended-spectrum beta-lactamase, R resistant, S susceptible, SCI spinal cord injury, UTI urinary tract infection

Table 3 Characteristics of patients that developed infection

	Cohort A	Cohort B
Sex	9 M, 13 F	7 M, 8 F
Mean age (SD)	49.3 (16.81)	48.4 (17.82)
Mean number of segments fused	5.8	5.6
Deep wound infection	18/22	5/15
Diabetes mellitus	3/22	2/15
Distribution by diagnosis		
Deformity	8	7
Degenerative	9	4
Fracture	4	2
Tumor	1	2

patients [7]. Other identified risk factors for SSI after instrumented spine surgery (diabetes mellitus, American Society of Anesthesiology risk index, body mass index, malnutrition, major bleeding, need for transfusion, and

long surgical time [18, 21, 23, 29]) may be difficult to modify.

Our results show that the proposed checklist to rule out preoperative UTC and identify patients more prone to develop GNB-SSI is effective. By using it, we were able to significantly reduce GNB SSI from 68.2% in cohort A to 33.4% in cohort B. *E. coli* was the most frequently identified microorganism (10 out of 14) in cohort B preoperative cultures, and *E. coli* was also responsible for 9 of the 15 SSIs in cohort A. The only patient in cohort B developing SSI by *E. coli* experienced postoperative UTI by the same microorganism. It seems reasonable that the decreased GNB infection rate observed in cohort B would be related to preoperative identification and treatment of these microorganisms. Nonetheless, although preoperative urine culture appears to be effective for preventing GNB SSI, in our setting routine culturing in every patient undergoing PSFI implies an unacceptable workload and cannot be considered. Limiting preoperative urine culture

to the smaller number of at-risk patients was both practicable and clinically effective.

Neurogenic bladder was the UTC risk factor associated with the highest rate of positive cultures (3 of 5) followed by indwelling catheters (8 of 14). Both these criteria involve mechanical manipulation of the urinary tract: temporary catheter placement in patients with neurogenic bladder receiving intermittent catheterization, and permanent placement in patients with indwelling catheters. Preoperative hospital stay longer than 7 days, referral from long-term care facilities, and urinary incontinence were the factors associated with the lowest rate of positive cultures. Seven patients met the criterion *preoperative hospital stay >7 days* but only one of them (14.3%) was culture-positive. Two patients underwent culture because of prolonged stay and referral from a long-term care facility, but neither was positive. These two criteria have been used to identify patients with skin colonization by cefazolin-resistant microorganisms [3], [8], and they were included on our checklist hypothesizing that they might also be associated with UTC. Furthermore, Nicolle et al have shown that elderly patients staying in long-term care facilities have a high rate of asymptomatic bacteriuria [12]. Our results suggest that these two criteria could be ignored for identification of patients with UTC by cephalosporin-resistant microorganisms, but our small sample size does not allow a definite conclusion in this regard.

Urinary incontinence has also been related to asymptomatic bacteriuria in elderly patients [19] and is an independent risk factor for developing SSI after spinal surgery [13]. Asymptomatic bacteriuria is found in 22.4% of elderly women and 9.4% of men with incontinence, [19] and incontinence has been associated with UTC [19]; hence, it was included on our UTC risk criteria checklist. In our study, only 1 patient out of 7 with incontinence (14.3%) had a positive preoperative urine culture. However, incontinence may be difficult to objectify by simple interview unless loss of sphincter control is obvious. In our study, any patient with a history suggesting incontinence underwent urine culture, but the real number of incontinent patients is unknown. Some patients might not be willing to recognize minor incontinence and others may have been included in the group with no objective data certifying incontinence. Although there was one only positive culture in this group, we believe that incontinence should be included in the process of identifying patients with preoperative UTC, based on previous evidence.

Since five patients in cohort B had SSI by GNB, it can be argued that the proposed checklist was only partially effective. However, it should be noted that all GNB SSI in cohort B were superficial according to CDC/NISS criteria [10], suggesting that they may have been produced by local contamination during the postoperative course. All patients

healed and none required deep wound debridement. Furthermore, there is always a risk of postoperative GNB SSI. A large percentage of patients undergoing PSFI will have perioperative bladder catheterization. Catheter placement before surgery could elevate the risk of postoperative infection by GNB [28]. None of the patients who were treated and given individualized antibiotic prophylaxis sustained SSI by GNB. The difference in the overall infection rate did not reach statistical significance (>0.1), but the possibility of a type II error cannot be excluded: the statistical power was very low (27.3%) because of the comparison of small proportions in rather large samples.

All patients meeting at least one of the UTC risk criteria underwent urine culture 3–5 days before surgery. Identified urinary tract infections were treated appropriately and antibiotic prophylaxis was modified to cover the microorganisms isolated. However, spine surgery was not postponed until urine culture tested negative. This option was not available in our setting because fixed surgical dates had been assigned to patients. Notwithstanding, our results show that the proposed protocol for preoperative bacteriologic screening and individualized antibiotic prophylaxis is sufficiently effective to avoid GNB SSI, without the need to delay surgery.

This study has several limitations we would like to outline. Routine preoperative urine culture in every patient undergoing PSFI would likely enable a more valid analysis of the checklist UTC risk criteria, assessing the sensitivity and specificity according to each factor. Even though most acute SSIs appear within the first three postoperative months [14], our study, which had a minimum postoperative follow-up of 9 months, does not totally respect the 12-month postoperative period included in the CDC/NISS definition of deep SSI [10]. Finally, we cannot confirm that the significant decrease in GNB SSI observed in cohort B was exclusively due to preoperative bacteriologic GNB screening and individualized antibiotic prophylaxis. The high SSI rate observed in cohort A may have resulted in inadvertent increased surveillance of the surgical process that might have contributed to the final reduction in SSI rate.

Conclusions

A significant percentage of patients undergoing instrumented spine surgery (1 in 16, 6.72%) may have a positive urine culture before surgery.

Patients undergoing urinary tract manipulation are especially prone to UTC.

Preoperative urine culture and individualized antibiotic prophylaxis are associated with a significant decrease in SSI due to GNB in high-risk patients undergoing spinal surgery.

Conflict of interest D. Rodriguez-Pardo and C. Pigrau belong to the Spanish Network Research in Infectious Disease (REIPI RD 06/0008). None of the authors has any potential conflict of interest.

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