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Rapid Colonization with Methicillin-Resistant Coagulase-Negative Staphylococci After Surgery

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Abstract
Background Antimicrobial resistance may compromise the efficacy of antibiotic prophylaxis before surgery. The aim of this study was to measure susceptibility and clonal distribution of coagulase-negative staphylococci (CoNS) colonizing the skin around the surgery access site before and after the procedure.
Methods From March to September 2004, a series of 140 patients undergoing elective major abdominal surgery were screened for CoNS colonization at admission and 5 days after surgery. All isolates were tested for antibiotic susceptibility and genotyped by pulsed-field gel electrophoresis (PFGE).
Results Colonization rates with CoNS at admission and after surgery were 85% and 55%, respectively. The methicillin-resistant CoNS rate increased from 20% at admission to 47% after surgery ($P = 0.001$). The PFGE pattern after surgery revealed more patients colonized with identical clones: 8/140 patients (8/119 strains) and 26/140 patients (26/77 strains), respectively ($P < 0.001$).
Conclusions Our results suggest rapid recolonization of disinfected skin by resistant nosocomial CoNS. Larger studies, preferably among orthopedic or cardiovascular patients, are required to clarify whether standard antibiotic prophylaxis with first- or second-generation cephalosporins for CoNS infections may be compromised if the patient requires an additional intervention 5 days or more after the initial surgery.

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Introduction

Surgical site infection (SSI) is an important factor that interferes with a successful surgical outcome and is potentially associated with repercussions on the patient's future quality of life and extra costs generated by extended hospitalization. The incidence of SSI depends on the surgery class and its risk index [1]. Currently, coagulase-negative staphylococci (CoNS) are the second most frequent isolates identified after *Staphylococcus aureus* in the field of surgery [1–3].

Together with surgical asepsis, antimicrobial prophylaxis is the recommended strategy to prevent SSI for most clean and clean-contaminated surgical procedures [3, 4]. A first- or second-generation cephalosporin is still the antibiotic of choice, either used alone or, when necessary as in colorectal surgery, combined with an active agent for anaerobes [3–5]. Routine vancomycin use is not recommended [6]. There appears to be no evidence at present for the increasing role of CoNS in SSIs, in particular for procedures where they are most prevalent (e.g., cardiac, orthopedic, and vascular surgery) [7–9].

Given the high reported rate of methicillin-resistant CoNS (MR-CoNS)—up to 80% in the literature—this is surprising. A possible reason is that most surgical

procedures are carried out in patients entering the hospital from the community, either for an elective procedure or as an emergency case, and that the CoNS rate in the community is much lower than in the hospital where most information about CoNS susceptibility is obtained. The Sentinel Surveillance of Antibiotic Resistance in Switzerland (SEARCH) study (http://www.search.ifik.unibe.ch) has begun recently to report MR-CoNS rates. The rate of oxacillin-resistant CoNS in the outpatient setting was 35% for 2008. However, this proportion may be overestimated as the database contains only results from microbiology laboratories, and there is no information on whether patients found with MR-CoNS were hospitalized recently. Data are lacking on the colonization process of CoNS in the health care environment, and it remains unknown whether recolonization of disinfected skin occurs from the patients' intrinsic flora or the hospital environment.

In the present study, a cohort of elective surgery patients were screened for CoNS colonization at the site of skin incision at admission and 5 days after surgery. The aim was to assess the process of skin recolonization with CoNS around the surgery access site after intervention by measuring both susceptibility and clonal distribution in an unselected population of general surgery patients.

Methods

Setting and study population

This prospective cohort study was conducted from March to September 2004 at the department of visceral and transplant surgery of the University Hospital of Zurich, a 960-bed, tertiary-care, teaching hospital in northern Switzerland, in collaboration with the hospital epidemiology team. Consecutive adult patients (>16 years of age) admitted for elective major abdominal surgery were screened for CoNS skin colonization at admission and 5 days after surgery (or at the time of hospital discharge in case of a shorter stay). Patients scheduled for the following elective surgical procedures were included.

- Upper gastrointestinal surgery: gastric or esophagus resection for cancer; major liver and pancreas resection for malignancy
- Colorectal surgery: right and left colectomy; rectum resection for cancer
- Various indications: mainly living donor nephrectomy

Surgical site disinfection was standardized according to institutional rules and performed with povidone–iodine solution; antibiotic prophylaxis was performed according to internal guidelines with cefazolin within 1 h before skin incision. The anesthetists' protocols were checked to ensure correct performance of surgical prophylaxis.

Only patients with a complete set of screening tests preoperatively and postoperatively were included in the final analysis. The study was approved as a quality improvement project by the institution's ethics committee, and patients were informed of the study's objective.

Screening and culture procedures

The screening test at admission was performed with a skin swab according to our standardized surgical approach (laparotomy or laparoscopy) based on a standardized frame. Skin swabs after surgery were performed within the same area. Patient demographic characteristics, operative procedures, length of stay, previous hospitalization within the last 12 months, and selection of preoperative antibiotic prophylaxis were recorded for risk analysis.

Bacterial culture and CoNS identification were done according to the protocols of the Clinical and Laboratory Standards Institute. Colonies of different morphology on the agar plate were subtyped. Susceptibility testing for oxacillin was performed using a disk diffusion technique with disks of 1 μg oxacillin on Mueller–Hinton agar (Oxoid, Basingstoke, UK). For cefalothin, cefuroxim, ciprofloxacin, and vancomycin, minimal inhibitory concentrations (MIC) were performed using Etest (AB Biodisk, Solna, Sweden). All CoNS isolates were genotyped by pulsed-field gel electrophoresis (PFGE) as previously described [10, 11]. Banding patterns of the PFGE results were analyzed using GelCompar II software (Applied Maths BVBA, Sint-Martens-Latem, Belgium).

Statistical analysis

Continuous variables were summarized by means or medians (interquartile range). Nonparametric statistical tests were used as appropriate. Continuous variables were compared with the Mann–Whitney *U*-test or Kruskal–Wallis analysis of variance, whereas discontinuous variables were compared with the χ^2 test. Risk factor analysis for colonization with CoNS exhibiting reduced susceptibility at either admission or discharge was conducted using univariate logistic regression. All tests were two-tailed, and $P < 0.05$ was considered statistically significant. All statistical analyses were conducted using Stata 10 (Stata, College Station, TX, USA).

Results

In all, 140 patients were included in the study. Patient demographics and characteristics are summarized in

Table 1. Cefazolin was the most frequently used antimicrobial agent for antibiotic prophylaxis (92.9%, 130/140) followed by amoxicillin-clavulanate (1.4%, 2/140). Two patients were under treatment with piperacillin/tazobactam and one patient with ciprofloxacin. Five patients had no documentation of receiving any antibiotic prophylaxis (3.6%). Sixteen patients undergoing colorectal surgery received metronidazole in addition to cefazolin.

At admission, CoNS was found in 119 patients (85%) in the area of the planned surgical access site. After surgery, 77 (55%) patients were positive for CoNS at the surgical site. No bacterial growth was found in 10 patients (8%) at admission, but it was observed in 56 (40%) after surgery (Table 2). On the basis of a different morphology on the agar plate, 168 CoNS strains were identified at admission and 108 after surgery. A total of 65 patients were colonized with CoNS both at admission and after surgery.

The prevalence of oxacillin resistance increased from 20% of isolated strains (34/168 strains among 32 patients) at admission to 47% (51/108 strains among 43 patients) after surgery ($P = 0.001$). Altogether, 31 patients, either colonized with susceptible CoNS or not colonized, were found with oxacillin-resistant CoNS (MR-CoNS) after surgery. There was a significant reduction of susceptibility to cefalothin before and after surgery (MIC_{90} was 0.75 μg/ml before surgery and 3 μg/ml after surgery: $P < 0.001$), cefuroxime (MIC_{90} 4 μg/ml and 256 μg/ml, respectively; $P < 0.001$), and ciprofloxacin (MIC_{90} 1 μg/ml and 32 μg/ml, respectively; $P < 0.001$). This reduction was due not only to the higher proportion of MR-CoNS, 51% of MR-CoNS and 4% of oxacillin-susceptible CoNS showed reduced susceptibility to ciprofloxacin ($P < 0.001$). No reduced susceptibility to vancomycin was observed.

Table 1 Characteristics of patients with elective major abdominal surgery screened for coagulase-negative staphylococcus colonization—University Hospital of Zurich, March to September 2004

Characteristic	Result
Age (years), median (IQR)	52 (42–63)
Male sex (%)	69 (49.3%)
Length of hospital stay (days), median (IQR)	9 (7–14)
Hospitalization during preceding 12 months (%)	59 (42%)
Surgical procedures (%)	
Upper gastrointestinal surgery	50 (36%)
Colorectal surgery	27 (19%)
Various indications	63 (45%)
Preoperative antibiotic prophylaxis (%)	
Cefazolin	130 (93%)
Amoxicillin/clavulanic acid	2 (1%)
Piperacillin/tazobactam[a]	2 (1%)
Ciprofloxacin[a]	1 (1%)
Metronidazole added	16 (11%)
No prophylaxis	5 (4%)
Nosocomial infections	
Surgical site infections[b]	4 (3%)
Pneumonia	1 (1%)

IQR interquartile range

[a] Ongoing antibiotic treatment at the time of surgery

[b] The following pathogens were isolated: *Enterococcus faecalis* (1), *Enterobacter cloacae* (1), no growth (2)

Table 2 Findings of skin swabs among patients screened for coagulase-negative staphylococcus colonization at admission and after surgery—University Hospital of Zurich, March to September 2004

Culture results	No. of patients before surgery	No. of patients with culture results after surgery		
		CoNS	No CoNS[a]	No growth
CoNS	119	65	6	48
No CoNS[a]	11	7	1	3
No growth	10	5	0	5
Total	140	77	7	56

CoNS coagulase-negative staphylococci

[a] Bacteria other than coagulase-negative staphylococci

Significantly more patients were found with identical clones in the PFGE analysis after surgery than at admission: 8/140 patients (8/119 strains) and 26/140 patients (26/77 strains), respectively ($P < 0.001$). Only four clones colonizing 2 patients each were detected at admission, whereas seven clones colonizing 26 patients were identified after surgery. Of the latter, one particular clone was found to colonize 10 patients. Other clones colonized three (four clones) or two (two clones) patients, respectively. Six of the seven identified clones after surgery, including the predominant clone colonizing 10 patients, were methicillin-resistant. Eight patients (6%) were found with identical clones at admission and after surgery. The susceptibility of these clones did not change during hospitalization. All other patients were found with different clones at admission and after surgery.

Risk factor analysis for MR-CoNS colonization at admission did not reveal significant results regarding age, sex, or hospitalization during the previous 12 months. Length and choice of prophylactic antibiotic administration were not significant risk factors for MR-CoNS colonization at discharge. Four surgical site infections (3%) were found among our patients.

Discussion

This study shows that most of our patients scheduled for major elective general surgery were colonized with CoNS at the time of hospitalization. Despite a strict antibiotic

prophylaxis policy with a single-shot, second-generation cephalosporin, a significant postoperative increase in MR-CoNS was observed together with a significant decrease in cephalosporin susceptibility.

Preoperative antibiotic prophylaxis is clearly one of the most effective measures for SSI prevention [12–14]. Based on several well conducted studies, single-dose regimens with first- or second-generation cephalosporins are recommended for most surgical procedures unless methicillin-resistant *Staphylococcus aureus* is a concern [15]. The role of MR-CoNS colonization before surgery and its impact on the occurrence of SSIs is unclear, and there is a paucity of data on the prevalence of MR-CoNS in the community.

During the 1980s, Larson et al. reported 2.9% MR-CoNS skin colonization in the community [16]. More recent studies reporting on CoNS susceptibility were conducted in hospital settings, and CoNS susceptibility was not even the main outcome parameter. CoNS were predominantly isolated from nosocomial infections, mainly bloodstream or wound infections [7–9]; and not unexpectedly, MR-CoNS rates were high (>80% in some studies). Thus, the MR-CoNS colonization rate in the community cannot be deduced from such data, and that from Larson et al. dates too far back. In 2008, the Swiss SEARCH study reported a MR-CoNS rate of 35% among 1,009 clinical isolates in the community, indicating that most skin-colonizing CoNS are still methicillin-susceptible. However, as mentioned, the SEARCH data report only results obtained from microbiological laboratories without taking into consideration any patient data; thus, the MR-CoNS rate may be overestimated. The rate of MR-CoNS at admission in our study population was much lower (20% of all isolated CoNS). Given that 42% of our patients were hospitalized at least once during the preceding 12 months and therefore were potentially exposed to nosocomial MR-CoNS, the true rate of MR-CoNS among patients with no history of any contact with a health care institution is likely to be even lower. Knowledge of epidemiologic trends for community MR-CoNS is important because most patients scheduled for elective surgery enter the hospital directly from the community.

Five days after surgery, more than half (55%) of our patients were recolonized with CoNS at the incision site. One-third were found to be colonized with CoNS strains with a PFGE pattern identical to that of isolates found in other patients; the proportion of methicillin resistance among these strains was significantly higher than in non-identical strains after surgery ($P < 0.001$). The high prevalence of identical strains after surgery plus the high MR-CoNS rate strongly suggest that recolonization of the disinfected skin area after surgery originated from the hospital environment. Such recolonization may put the patient at risk when an additional surgical procedure is required and antibiotic prophylaxis is not adapted in consequence.

None of the oxacillin-susceptible CoNS showed reduced susceptibility to cefalothin or cefuroxim. Consistent with the published literature, half of the MR-CoNS showed reduced susceptibility to ciprofloxacin [17–20]. However, the overall resistance of oxacillin-susceptible CoNS against ciprofloxacin was low.

This study has some limitations. Abdominal surgery may not be the ideal cohort for studying the impact of reduced CoNS susceptibility because other microorganisms are more likely to be involved. However, postoperative recolonization of disinfected skin with nosocomial pathogens is a basic principle that is applicable to all surgical procedures and may include even multiresistant gram-negative organisms. SSI was not the primary endpoint of our study. Larger studies, preferably among orthopedic or cardiovascular patients, should address the question of whether the use of standard antibiotic prophylaxis is associated with more SSIs in patients who require an additional intervention after the initial surgery.

Conclusions

Our study shows that (1) the prevalence of skin MR-CoNS in the community is lower than in the hospital, (2) skin recolonization of the disinfected surgery field with CoNS occurs rapidly after surgery, and (3) such recolonization is likely due to nosocomial strains rather than to the endogenous flora of the patient. However, larger studies, preferably among orthopedic or cardiovascular patients, are required to clarify whether standard antibiotic prophylaxis with first- or second-generation cephalosporins for CoNS infections may be compromised if the patient requires an additional intervention at the same site 5 days or more after the initial surgery.

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References

1. Hidron AI, Edwards JR, Patel J et al (2008) NHSN annual update: antimicrobial-resistant pathogens associated with healthcare-associated infections: annual summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2006–2007. Infect Control Hosp Epidemiol 29:996–1011
2. Jarvis WR, Martone W (1992) Predominant pathogens in hospital infections. J Antimicrob Chemother 29(Suppl):19–24

3. Mangram AJ, Horan TC, Pearson ML et al (1999) Guideline for prevention of surgical site infection, 1999: Hospital Infection Control Practices Advisory Committee. Infect Control Hosp Epidemiol 20:247–278
4. Stratchounski LS, Taylor EW, Dellinger EP et al (2005) Antibiotic policies in surgery: a consensus paper. Int J Antimicrob Agents 26:312–322
5. DiPiro JT, Vallner JJ, Bowden TA et al (1985) Intraoperative serum and tissue activity of cefazolin and cefoxitin. Arch Surg 120:829–832
6. Anderson DJ, Kaye KS, Classen D et al (2008) Strategies to prevent surgical site infections in acute care hospitals. Infect Control Hosp Epidemiol 29:S51–S61
7. Wisplinghoff H, Bischoff T, Tallent SM et al (2004) Nosocomial bloodstream infections in US hospitals: analysis of 24, 179 cases from a prospective nationwide surveillance study. Clin Infect Dis 39:309–317
8. Cuevas O, Cercenado E, Vindel A et al (2004) Evolution of the antimicrobial resistance of *Staphylococcus* spp. in Spain: five nationwide prevalence studies, 1986 to 2002. Antimicrob Agents Chemother 48:4240–4245
9. Widerström M, Monsen T, Karlsson C et al (2006) Molecular epidemiology of methicillin-resistant coagulase-negative staphylococci in a Swedish county hospital: evidence of intra- and interhospital clonal spread. J Hosp Infect 64:177–183
10. Fleisch F, Zbinden R, Vanoli C et al (2001) Epidemic spread of a single clone of methicillin-resistant Staphylococcus aureus among injection drug users in Zurich, Switzerland. Clin Infect Dis 32:581–586
11. Tenover FC, Arbeit RD, Goering RV et al (1995) Interpreting chromosomal DNA restriction patterns produced by pulsed field gel electrophoresis: criteria for bacterial strain typing. J Clin Microbiol 33:2233–2239
12. Baum ML, Anish DS, Chalmers TC et al (1981) A survey of clinical trials of antibiotic prophylaxis in colon surgery: evidence against further use of no-treatment controls. N Engl J Med 305:795–799
13. Meijer WS, Schmitz PI, Jeekel J (1990) Meta-analysis of randomized, controlled clinical trials of antibiotic prophylaxis in biliary tract surgery. Br J Surg 77:283–290
14. Classen DC, Evans RS, Pestotnik SL et al (1992) The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. N Engl J Med 326:281–286
15. Wong ES (2004) Surgical site infections. In: Mayhall CG (ed) Hospital epidemiology and infection control, 3rd edn. Lippincott Williams & Wilkins, Philadelphia
16. Larson E, McGinley KJ, Grove GL et al (1986) Physiologic, microbiologic, and seasonal effects of handwashing on the skin of health care personnel. Am J Infect Control 14:51–59
17. Reynolds R, Potz N, Colman M et al (2004) BSAC Extended Working Party on Bacteraemia Resistance Surveillance. Antimicrobial susceptibility of the pathogens of bacteraemia in the UK and Ireland 2001–2002: the BSAC Bacteraemia Resistance Surveillance Programme. J Antimicrob Chemother 53:1018–1032
18. Karlowsky JA, Jones ME, Draghi DC et al (2004) Prevalence and antimicrobial susceptibilities of bacteria isolated from blood cultures of hospitalized patients in the United States in 2002. Ann Clin Microbiol Antimicrob 3:7–14
19. Kotilainen P, Nikoskelainen J, Huovinen P (1990) Emergence of ciprofloxacin-resistant coagulase-negative staphylococcal skin flora in immunocompromised patients receiving ciprofloxacin. J Infect Dis 161:41–44
20. Smith KR, Cobbs CG (1992) In vitro activity of sparfloxacin and three other fluoroquinolones against methicillin-resistant Staphylococcus aureus and Staphylococcus epidermidis. Eur J Clin Microbiol Infect Dis 11:55–58