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ORIGINAL ARTICLE

Effect of preoperative *Staphylococcus aureus* screening / decolonization on surgical site infection following major orthopaedic operations: a prospective study

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Abstract

Carriers of *Staphylococcus aureus (S. aureus)* have a higher likelihood of having surgical site infection (SSI). The aim of this study was to evaluate the impact of preoperative *S. aureus* screening and decolonization on the rate of SSI after major orthopaedic surgical operations.

A prospective observational study was conducted on 400 patients scheduled for major orthopaedic surgical procedures at our institution between December 2013 to December 2014. The enrolled patients were divided into: intervention group (250 patients) who underwent the screening / decolonization protocol, and a control group (150 patients) with no implementation of the protocol. All patients were followed up for 3 months for postoperative *S. aureus* SSI.

Of the 250 patients screened, 70 (28%) had positive nasal swabs for *S. aureus*. Among screened patients, 58 (23.2%) were identified as MSSA carriers, and 12 (4.8%) were identified as MRSA carriers. On post operative follow up, there were a total of 5 *S. aureus* SSI in the control group (3.3%, 95% CI 1.1-7.6%) and 3 in the intervention group (1.2%, 95% CI 0.25- 3.5%). There was 2 MRSA infection in the control group (1.3%, 95% CI 0.2-4.7%), one MRSA infection in the intervention group (0.4%, 95% CI 0.01-2.2). Screening and decolonization lowered the *S. aureus* SSI rate to 1.2% in screened/decolonized (intervention) versus 3.3% in those unscreened (control) patients.

In Conclusion**,** preoperative screening / decolonization of MRSA and MSSA carriers among patients undergoing major orthopaedic surgical operations using a combination of mupirocin and chlorhexidine is a safe protocol for reducing *S. aureus* SSI.

Key Words: *Staphylococcus aureus*; decolonisation; surgical site infection; orthopaedics

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Introduction

Orthopaedic surgical site infections (SSIs) are a major adverse outcome for the patients and their surgeons as they cause substantial morbidity, lower quality of life, and inevitably result in prolonged recovery, prolonging hospital stay by a median of 2 weeks, doubling re-hospitalisation rates, and causes resource utilization.[1-5]

Staphylococcus aureus is a major pathogen implicated in orthopaedic surgical site infections (SSIs).[6,7] Previous studies have shown that 20-30% of the population are carriers for meticillin-sensitive *S. aureus* (MSSA),[8,9] and 1–5% are carriers for meticillin-resistant *S. aureus* (MRSA).[10] The increasing incidence of antibiotic-resistant staphylococci (MRSA) threatens the outcome of implant.[11]

The ecologic niche of *S. aureus* is the anterior nares, and 25 to 30 percent of the population is colonized at a given time.[12-14] Patients who are colonized are at 2 to 9 times higher risk to develop SSI than those who are non colonized,[15,16] most patients who develop a *S. aureus* surgical site infection are carriers of the strains causing the infection. It has been shown that 85% of SSIs can be traced to endogenous colonization of the patients.[8,17-20]

Colonization with *S. aureus* has been identified as a risk factor for SSI among orthopaedic patients.[11,21] Evidence indicating an association between nasal *S. aureus* carriage and subsequent *S. aureus* infection has led to the development of decolonization programs aimed at decreasing the *S. aureus* infection rate in dialysis or clean-surgery patients.[14,19,21]

Several eradication regimens have been used. Topical agents alone or in combination with oral antibiotics have been used for the elimination of both nasal and extranasal MRSA carriage.[22-24]

Mupirocin is a topical antistaphylococcal antibiotic with an FDA-approved indication for decolonization of the anterior nares.[19,25] Intranasal mupirocin has been shown to be the most effective means of treating and eradicating intranasal MRSA and MSSA and has become part of many preoperative protocols for prevention of infection.[4,26-28] Chlorhexidine baths have been added to intranasal mupirocin in an effort to eradicate carriage of MRSA[29,30] and to reduce nosocomial infections caused by MRSA in the intensive care unit.[31] Although many hospitals use oral vancomycin in combination with topical agents for the eradication of MRSA colonization, there is no data available on the effectiveness and safety of eradication regimens with oral vancomycin.

Although some researchers studied the effect of decolonization protocols and their subsequent effect on rate of SSI, controversy exists on the use of such screening and treatment programs.

This is a prospective observational study of patients undergoing major orthopaedic surgical operations at our institution, with a control group to compare the effect of *S. aureus* screening / decolonization protocol on the rates of SSIs in patients who underwent elective major orthopaedic surgical operations versus those patients who did not follow this protocol.

Subjects and Methods

Patient population & study design

A prospective observational study was conducted on 400 patients (293 males, 117 females), average age 48.4 years (range 23-79 years) scheduled for major orthopaedic surgical procedures at our institution (orthopaedic surgery department, Mansoura University Hospital) in the period between December 2013 to December 2014. Eligible procedures included arthroplasty, spine, and sports medicine procedures i.e. elective orthopaedic patients who can undergo screening and decolonization before surgery. There were no bilateral procedures for a total of 400 patients; 75 Primary total hip arthroplasties, 15 revision total hip arthroplasties, 62 primary total knee arthroplasties, 8 revision total knee arthroplasties, 55 spinal surgery, 85 knee ligaments injuries, 100 internal fixation of non / malunited fractures.

Patients with risk factors were excluded; uncontrolled diabetes, renal failure, chronic vascular disorders or immunosuppressive therapy.

The enrolled patients were randomly assigned into 2 groups; intervention group (250 patients) who underwent the screening / decolonization protocol, and

a control group (150 patients) with no implementation of the protocol.

Screening

Two to three weeks before the intended surgery, patients in the intervention group were screened for nasal MRSA/MSSA colonization. Participants were educated about the rationale for nasal cultures. Informed consent was obtained from all individual participants included in the study.

Specimen Collection & Microbiological Processing

Samples were collected from both nares by swabbing a sterile saline solution moistened Dacron swab for five seconds along the interior walls of each nares to obtain adequate sampling.

Specimens were inoculated onto CHROMagar MRSA and CHROMagar SA plates (CHROMagar, France; Indomedix), which were incubated for 24 hours at 35°C to 37°C. After 24 hours, we interpreted mauve colonies present on both plates as MRSA and on only the CHROMagar SA plate as MSSA.[32,33] Negative plates were incubated for an additional 24 hours. Mauve colonies present on either medium after 48 hours were verified as *S. aureus* and identified by standard procedures, including colony morphology, Gram stain, catalase reaction, tube coagulase test, and API STAPH (bioMérieux S.A., Lyon, France).[34]

Intervention

One week before surgery, patients with nasal cultures positive for MSSA or MRSA were educated about the rationale for the decolonization protocol. Patients were instructed to apply intranasal 2% mupirocin ointment twice daily to both nares and bathe with 2% chlorhexidine body wash once daily for 5 days, including the day of surgery. The chlorhexidine body wash was applied by washcloth to the entire body, with special attention paid to the surgical site. Patients who were negative for MRSA and MSSA colonization did not receive any decolonization treatment.

During preoperative admission, we asked about compliance with the decolonization protocol to determine whether patients had followed instructions, completed the decolonization protocol, and experienced any adverse effects.

At the operation day, patients who were MRSA-negative were administered standard perioperative antibiotic prophylaxis with 1 g cefuroxime at least 30 minutes before incision, intraoperative, and for 24 hours postoperatively. On the other hand, patients who were MRSA-positive received 1g vancomycin intravenously at least 30 minutes before incision followed by 1 g every 12 hours for 24 hours.

Outcome

All patients were followed for 3 months for postoperative infection. SSIs were classified using the Centers for Disease Control criteria.[35] Only deep incisional SSIs were considered clinically relevant and considered in the analysis. A SSI was considered to be present if one of the following findings was noted during the follow up period: (1) the wound drained purulent material, (2) the wound drained serosanguineous material, the edges of the wound and surrounding tissues were erythematous, and the wound culture yielded a pathogen, or (3) a physician stated in the medical record that the surgical site was infected. Stitch abscesses were not considered to be SSIs.

Cultures were obtained from surgical sites when signs and symptoms of infection were observed. Standard microbiologic methods were used to identify isolated *S. aureus*.[36]

Statistical analysis

Data were tabulated, coded then analyzed using the computer program SPSS (Statistical Package for Social Science) version 17.0. Descriptive statistics were calculated in the form of frequency (number/percent). Comparison was made between the rates of *S. aureus* SSI in the intervention and the control group. The significance of any differences in *S. aureus* SSI between the intervention group and the control group was performed using Fisher's exact test. P values $\leq$ 0.05 were considered to be statistically significant.

Results

Of the 250 patients screened, 70 (28%) had positive nasal swabs for *S. aureus*, of which 58 (23.2%) were identified as MSSA carriers, and 12 (4.8%) MRSA carriers.

Table I. *Staphylococcus aureus* surgical site infection (SSI) in the intervention and the control group

Patient group	Number of SSI/Number of Patients	SSI rate	p
Intervention group	3/250	1.2%	0.14
Control group	5/150	3.3%	

At the day of surgery, we asked about treatment compliance, and there was a self-reported 97.1% compliance rate with mupirocin nasal treatment and a 92.9% compliance rate with chlorhexidine shower. Non compliance was mainly due to poor understanding, and misperceptions about the prophylactic effect of the protocol used. Only one case reported skin rash and itching on using chlorhexidine shower.

On post operative follow up, there were a total of 5 *S. aureus* SSI in the control group (3.3%, 95% CI 1.1-7.6%) and 3 in the intervention group (1.2%, 95% CI 0.25- 3.5%) (Table I). There was 2 MRSA infection in the control group (1.3%, 95% CI 0.2-4.7%) and one MRSA infection in the intervention group (0.4%, 95% CI 0.01-2.2%); this patient was found to be a carrier of MRSA on initial screening and later developed a MRSA infection postoperatively. Other microorganisms were also isolated in addition to *S. aureus* but not considered in our study.

Of the 70 patients recognized as colonized with *S. aureus* and treated with decolonization protocol, one (1.4%, 95% CI 0.04- 7.7%) developed *S. aureus* SSI. Of the 180 screen negative patients, 2 developed *S. aureus* SSIs (1.1%, 95% CI 0.13-3.96%). Of the 150 unscreened and untreated (control) patients, 5 (3.3%, 95% CI 1.1-7.6%) developed *S. aureus* SSIs (Figure 1).

Overall, screening and decolonization lowered, but did not reached statistical significance (P= 0.14) the *S. aureus* SSI rate to 3 of 250 (1.2%, 95% CI 0.25-3.5%) operations in the total intervention group (both *S. aureus* carriers and non-carriers combined) versus 5 of 150 (3.3%, 95% CI 1.1-7.6%) in those unscreened (control) patients.

Discussion

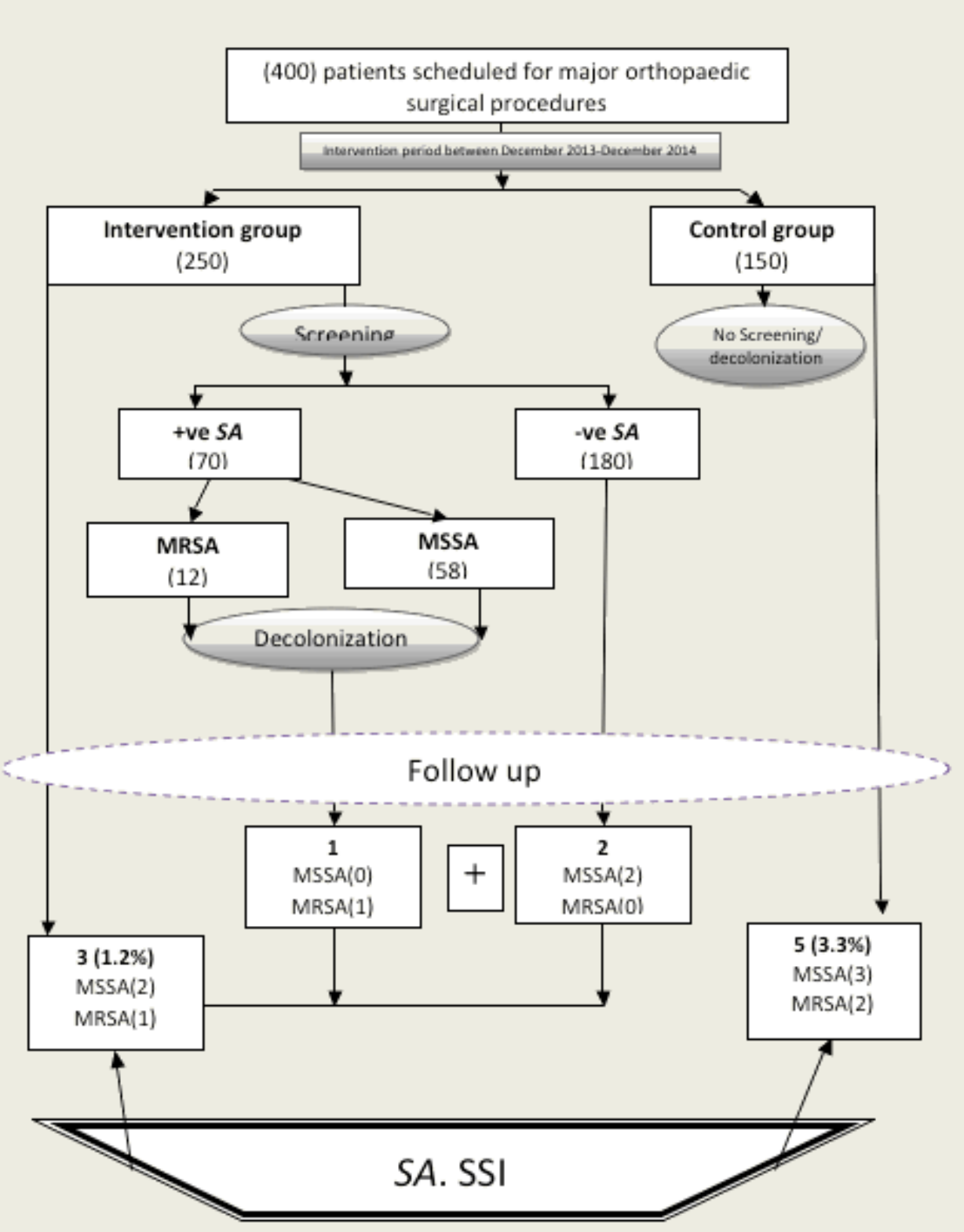
The causes of SSIs in orthopaedics are multifactorial, including surgical- and patient- related factors. *S. aureus* is considered to be the most important organism responsible for post-operative wound infections in orthopaedic patients.[4,37] Approximately 30% of the general population is colonized with *S. aureus*. Being a *S. aureus* carrier is a significant risk factor of developing SSI.[12,13,15,38] So, it is important to find ways to reduce *S. aureus* (MSSA/MRSA) colonization before orthopaedic surgical procedures to decrease the risk of SSIs. One method is preoperative screening and decolonization of *S. aureus*-positive carriers.

Mupirocin is a simple strategy for eradicating *S. aureus*, including MRSA, from the nares. Previous literature review and meta-analysis reported that perioperative intranasal mupirocin decreased the incidence of SSI and should be considered as routine practice in these settings.[39,40] However, it reduced *S. aureus* infections after orthopaedic surgery in some,[41] but not all studies.[21,42] Lack of statistically significant benefit may have been due to failure to eradicate *S. aureus* from extranasal sites such as skin, which can be achieved with chlorhexidine baths.[43] The combination of mupirocin and chlorhexidine is safe and well tolerated.

The objectives of this study was to assess the effect of a decolonization protocol (mupirocin ointment, chlorhexidine body wash plus prophylactic vancomycin in cases of MRSA carriers) on the rate of *S. aureus* SSI compared with a concurrent control group in patients elective for major orthopaedic surgical procedures in our institution.

Preoperative screening revealed that 28% of patients in the intervention group were nasal carriers of *S. aureus*, approximating the rate previously reported by other studies.[27,44-46]

The results of our study demonstrate that utilizing a current decolonization protocol was associated with a reduced rate of *S. aureus* SSI (1.2% vs 3.3%). With the numbers available in this study, we were unable



***SA**: S. aureus; **MSSA**: meticillin-sensitive S. aureus; **MRSA**: meticillin-resistant S. aureus; **SSI**: surgical site infection; +ve: positive; -ve: negative*

Figure 1. *Staphylococcus aureus* surgical site infection of the enrolled patient groups with and without screening and decolonization protocol

to detect statistically significant differences in SSI between the intervention and the control group. Our findings add to those of previous studies on the effect of screening and decolonization on SSI in patients undergoing orthopaedic surgery or mixed surgery including orthopaedic surgery.

There have been previously reported studies of large institutional efforts to reduce the rates of *S. aureus* or MRSA SSI in patients undergoing surgery. Some studies failed to demonstrate a significant reduction in infection rates: 0.8% vs 1.7%,[42] 1.6% vs 2.7%,[21] 2.3% vs 2.4%,[19] and 0.9% vs 0.7%.[47] On the other hand, other studies reported significant reduction of *S. aureus* SSI after decolonization protocol: 0% vs 3.5%,[44] 0% vs 3.3%,[45] 1.3% vs 2.7,[48] 0.19% vs 0.45%,[27] 3.4% vs 7.7%[49] and for MRSA SSI: 0.7% vs 1.6%.[41]

Differences among studies were attributed to the differences in the study design, sample size, end point, decolonization protocol, and follow-up. For example; Hacek *et al.*[42] estimated that their protocol prevented eight infections in their cohort of 1495 patients. Kim *et al.*[27] were able to demonstrate the effectiveness of their institution's screening and decolonization program in a cohort of more than 7000 patients undergoing elective spine surgery and TJA. They found a decrease in SSI in their treatment group compared with historical controls and also among non carrier patients compared with patients colonized with MRSA. Hadley *et al.*[50] were able to show a reduction in SSI compared with a concurrent control group. However, unlike our study, where decolonization treatment was provided only to patients who proved colonized on testing, patients in the study by Hadley *et al.* were empirically treated, regardless of screening results.

Although our findings did not reach statistical significance, they represented a positive trend towards the efficacy of a decolonization protocol implementation in decreasing SSI rate. In the present study, only one patient developed MRSA SSI following the decolonization protocol. This could be a decolonization failure. Failure to demonstrate successful eradication of carrier status following treatment had been documented in several studies.[27,51] They reported that the two most likely factors associated with decolonization failure are patient noncompliance and the presence of resistant organisms. In our study, the majority of our patients reported compliance (97.1% compliance rate with mupirocin nasal treatment and a 92.9% compliance rate with chlorhexidine shower), so it is less likely cause of decolonization failure. The emergence of resistant organisms to intranasal mupirocin has been evaluated.[52-54] In one study, 19% of swab isolates demonstrated resistance to mupirocin.[55] Although it was not evaluated in our study, we believe that mupirocin resistance may in part explain the decolonization failures in this study.

Cephalosporins have been widely used as prophylaxis against SSI for decades, but with the emergence of MRSA and the clear relationship between the nasal carriage of MRSA and postoperative SSIs, clinicians used vancomycin as prophylaxis.[27] Several time-series analyses have evaluated the effectiveness of vancomycin for surgical prophylaxis in institutions with a high prevalence of MRSA. *S. aureus* resistance to glycopeptides such as vancomycin has led some authors not to recommend vancomycin for routine use in surgical prophylaxis but may be considered as a component of a MRSA prevention bundle for SSIs in selective circumstances.[56,57]

Our study had some limitations; first, the small sample size that may led to non statistically significant results. Second, this study also detects the presence of MRSA/MSSA by culture swab, and not by PCR,[27,42] which could increase sensitivity. Another limitation of this study is that we did not repeat nasal screening on the day of surgery to determine the efficacy of the decolonization protocol; however, It is reasonable to expect that *S. aureus* was eradicated on the basis of the success reported by others.[12,15,58] Furthermore, the individual components of the decolonization protocol (mupirocin ointment, chlorhexidine shower, and prophylactic vancomycin) were not individually tested. We hypothesize that there is a synergistic benefit to each of these steps, but further studies would be needed to determine their individual effect on the primary outcome.

Conclusion

The data from our study suggest that preoperative screening/ decolonization of MRSA and MSSA carrier status among patients undergoing elective major

orthopaedic surgical operations using a combination of mupirocin and chlorhexidine is a safe protocol for reducing *S. aureus* SSI.

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