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Preventing Surgical Site Infections: A Randomized, Open-label Trial of Nasal Mupirocin Ointment and Nasal Povidone Iodine Solution

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Abstract

Background—Treatment of *Staphylococcus aureus* colonization prior to surgery reduces risk of surgical site infection (SSI). The regimen of nasal mupirocin ointment and topical chlorhexidine gluconate is effective, but cost and patient compliance may be a barrier. Nasal povidone iodine solution may provide an alternative to mupirocin.

Methods—We conducted an investigator initiated, open label, randomized trial comparing SSI after arthroplasty or spine fusion in patients receiving topical 2% chlorhexidine gluconate (CHG) wipes with either twice daily application of mupirocin 2% ointment for the 5 days prior to surgery

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Role of the Sponsor

3M had no role in the design and conduct of the study; collection, management, analysis and interpretation of the data; preparation, review or approval of the manuscript; or decision to submit this manuscript for publication.

Additional Contributions

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Presentations

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This trial was registered on ClinicalTrials.gov; registration identification number NCT01313182; URL http://clinicaltrials.gov/show/NCT01313182

Conflict of Interest Disclosures

M. Phillips, 3M corporation (research grant which funded this study); had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
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or two 30 second applications of povidone iodine 5% solution into each nostril within 2 hours of surgical incision. The primary study end point was deep SSI within the 3 months after surgery caused by any pathogen or *S. aureus*.

Results—In the intent-to-treat analysis, a deep SSI developed after 14 of 855 surgeries in the mupirocin group and 6 of 842 surgeries in the povidone iodine group; S. *aureus* deep SSI developed after 5 surgeries in the mupirocin group and 1 surgery in the povidone iodine group. In the per protocol analysis, *S. aureus* deep SSI developed in 5 of 763 surgeries in the mupirocin group and 0 of 776 surgeries in the povidone iodine group. Patients found to be *S. aureus* colonized before surgery were more likely to have a *S. aureus* deep SSI (OR 6.79; 95% CI 1.1–41.2; p=0.02).

Conclusions—Nasal povidone iodine may be considered as an alternative to mupirocin in a multifaceted approach to reduce SSI.

An estimated 290,000 surgical site infections occur after a procedure in the United States annually, accounting for 22% of all healthcare associated infections [1]. Deep surgical site infections (SSI) after arthroplasty or spine fusion surgery complicate up to 2% of cases, and result in revision surgery and prolonged antibiotic use [2, 3]. The patient morbidity and healthcare system cost is tremendous, with an estimated $566 million spent annually in hospital treatment costs for arthroplasty SSI alone [4]. *Staphylococcus aureus* is a frequent and feared cause of these infections, given its unique pathogenicity and ability to adhere to prosthetic material [5, 6]. Studies indicate *S. aureus* colonization prior to surgery is a risk of subsequent infection, with the nasal mucosa serving as a reservoir for *S. aureus* colonization and a source of secondary transmission to other body sites [7, 8].

Prevention of SSI by treatment of *S. aureus* colonization with intranasal topical mupirocin has been studied. A short-term suppression rate of 83% after multiple doses of nasal mupirocin was achieved in one randomized, placebo-controlled trial of 891 *S. aureus* colonized patients, resulting in a statistically significant reduction of invasive *S. aureus* infection [9]. Several controlled trials suggest a reduction in SSI with the use of pre-operative topical antiseptics [10, 11]. When nasal mupirocin was combined with use of chlorhexidine soap in a randomized, double-blind, placebo-controlled trial including 808 *S. aureus* colonized surgical patients, a significant reduction in deep *S. aureus* SSI was realized [12].

To reduce the risk of SSI after arthroplasty and spine fusion surgery at our institution, we historically provided a prescription for brand mupirocin ointment specifically formulated for application on intranasal mucosal surfaces twice a day for the five days prior to surgery, and instructions for the use of chlorhexidine soap the evening before surgery. After implementation of this protocol, we conducted an anonymous patient survey to measure compliance. Although 94% of patients used the chlorhexidine soap, only 86% applied the mupirocin ointment and 8% of patients stated they found it hard or very hard to purchase the mupirocin due to cost [13]. The brand nasal mupirocin ointment specifically produced for application on intranasal mucosal surfaces is only formulation currently available; although generic mupirocin ointment for topical use on skin is available at less cost, application of this formulation on mucosal surfaces may cause irritation. Our survey results, plus reports of

emerging mupirocin resistance, led us to search for alternatives [14–19]. Povidone-iodine solution is a broad-spectrum antiseptic suitable for suppression of *S. aureus* in nasal secretions [20]. In contrast to the application of nasal mupirocin antibiotic ointment to eradicate *S. aureus* in the nares before surgery, the application of povidone iodine is intended to transiently suppress *S. aureus* in the nares during surgery. Our hypothesis was a one-time application of nasal povidone iodine just prior to surgery would be as effective as twice daily applications of nasal mupirocin during the five days before surgery in preventing SSI, and provide a more convenient option for patients at lower cost.

Methods

Study treatment

We conducted an investigator initiated, prospective, open-label, randomized trial of twice daily application of mupirocin 2% ointment specifically formulated for use on intranasal mucosal surfaces into each nostril for the 5 days prior to surgery compared with a two 30 second applications of povidone iodine 5% solution formulated as a nasal antiseptic into each nostril (4 applications total) within 2 hours of surgical incision. Both treatments were combined with the application of six 2% chlorhexidine wipes on specific body surfaces from chin to toes the evening prior and morning of surgery. Patients received verbal and written instructions and had access to 24/7 telephone number in case of study treatment related questions.

Subjects

From March 2011 through March 2012, we recruited subjects at least 18 years old who presented to the pre-surgical assessment clinic prior to primary or revision arthroplasty and spine fusion surgery. Exclusion criteria included pregnancy, breastfeeding, allergy to mupirocin or povidone iodine, interval from pre-surgical assessment clinic visit to surgery of less than 7 days and an infectious indication for surgery. The need for nasal intubation (typically for cervical spine surgery) was added as an exclusion criterion shortly after study initiation. All subjects underwent the routine pre-operative evaluation appropriate for their planned surgery, including pregnancy testing, tobacco cessation education, nasal culture for *S. aureus*, and blood samples for hematology and serum chemistry testing.

Randomization, perioperative surgical prophylaxis and evaluation of S. aureus isolates

Subjects were stratified by arthroplasty or spine fusion surgery, and then randomized 50:50 to either mupirocin or povidone iodine treatment groups in blocks of 100. Research personnel evaluated subjects in the pre-operative holding area to determine chlorhexidine compliance and to either apply povidone iodine or assess compliance with mupirocin.

Subjects received routine antimicrobial prophylaxis, surgical site preparation and surgical draping. Primary antimicrobial prophylaxis was cefazolin 1 gm; subjects with reported β-lactam allergy received clindamycin 600 mg and those colonized with methicillin-resistant *S. aureus* (MRSA) received vancomycin 1 gm. Antibiotic infusion was started within one hour of incision (two hours for vancomycin) and was re-dosed per accepted guidelines. Weight based dosing was employed at the discretion of the anesthesiologist. Standard pre-

operative surgical site skin preparation consisted of a 2% chlorhexidine gluconate/70% isopropyl alcohol solution. If needed, electrical clippers were used for hair removal at the surgical site and patients were actively warmed in the intraoperative and postoperative period.

Subjects were re-assessed within 1 to 3 days after surgery to record patient satisfaction and adverse events related to study treatment. If the pre-operative nasal culture grew *S. aureus*, a repeat nasal culture was ordered. The *S. aureus* isolates from those subjects who developed a *S. aureus* SSI were retrieved from the Clinical Microbiology laboratory for additional testing. Identification of MRSA was based on routine criteria, including the coagulase tube test and the automated Vitek 2 system [BioMérieux, Marci l'Etoile, France] and mupirocin susceptibility was performed by E-test. Isolates with a mupirocin MIC of ≥8μg/mL considered mupirocin-resistant [19, 21]. Further characterization by *spa* typing was performed if the pre-operative and post-operative *S. aureus* isolates from the same subject were available [22–24].

End points

The primary study end point was onset of a deep SSI within the 3 months after surgery caused by any pathogen or *S. aureus*. Potential SSI were identified by review of microbiology reports, hospital readmissions, if a report was received from another healthcare facility (as mandated by New York State Department of Health regulations) and during Infection Prevention and Control (IPC) rounds on inpatient units. Patient records were reviewed and the SSI classified using the Center for Disease Control and Prevention's National Healthcare Safety Network case definitions. IPC practitioners reviewing the records were blinded to study participation and receipt of study treatment; potential cases were discussed at a group meeting to ensure consistent application of the SSI case definition. Infections in subjects were retrieved from the IPC database maintained for routine SSI surveillance.

Statistical analysis

We expected no difference in SSI between treatment groups. Our baseline combined arthroplasty and spine fusion deep SSI rate was 1.5/100 procedures, with *S. aureus* as the infecting pathogen in 37% of cases. During the baseline period, all patients received a prescription for mupirocin ointment with instructions to apply to the nares twice a day for the five days prior to surgery and were provided 2% chlorhexidine wipes for use the evening prior and morning of surgery. We assumed a doubling of SSI rate in the povidone iodine group would be clinically relevant, and calculated a sample size of 3000 subjects would provide a power of 80% to detect a doubling of SSI rate to 3.0/100 procedures with an alpha level of 0.05 and a two sided Fisher's exact test. Analysis was conducted using SAS version 9.1, Cary, NC. Categorical variables were analyzed using Fisher's exact test.

The intent to treat group included those who were enrolled and met eligibility requirements for the study and the per protocol group included all eligible enrolled subjects who completed the assigned study regimen. Completion of the study regimen was defined as 2 applications of 6 chlorhexidine wipes to specific areas of skin from chin to toe, receiving

appropriate perioperative antimicrobial prophylaxis and receiving either 7 to 10 applications of mupirocin to the nares over the 5 days before surgery or 2 applications of povidone-iodine each nostril within 2 hours of surgical incision.

Study oversight

The study was approved by the institutional review board at our institution and informed consent was obtained from all study participants. The authors designed the study, and were solely responsible for the collection, analysis, interpretation and presentation of the data. 3M Corporation, the manufacturer of the nasal povidone-iodine solution, provided financial support but had no role in the study design, collection of the data or preparation of this manuscript.

Results

Subjects

During the 12 month enrollment period, 1,874 of the 1,903 patients assessed were enrolled and randomized; 177 of the enrolled patients did not receive the study intervention, the surgery for most of these individuals was cancelled or the actual surgical procedure performed was not eligible for inclusion in the study. The demographic and clinical characteristics and surgery types of the remaining 1,697 subjects in the intent to treat analysis are provided in Tables 1 and 2. The 1,539 subjects who completed the intervention are included in the per protocol analysis (Figure 1).

End points

In the intent-to-treat analysis, *S. aureus* deep SSI developed after 5 of 855 surgeries in the mupirocin group and 1 of 842 surgeries in the povidone iodine group (p=0.2). A deep SSI caused by any pathogen developed after 14 surgeries in the mupirocin group and 6 surgeries in the povidone iodine group (p=0.1). In the per protocol analysis, *S. aureus* deep SSI developed in 5 of 763 surgeries in the mupirocin group and 0 of 776 surgeries in the povidone iodine group (p=0.03). The overall deep SSI rate was 1.6/100 procedures in the mupirocin group and 0.7/100 procedures in the povidone-iodine group in the intent to treat analysis. The infecting pathogens are provided in Table 3. The *S. aureus* deep SSI rate was 0.6/100 procedures in the mupirocin group and 0.1/100 procedures in the povidone-iodine group in the intent to treat analysis. In the per protocol analysis, the *S. aureus* deep SSI was 0.7/100 procedures in the mupirocin group and there were no infections in the povidone-iodine group (Tables 4 and 5).

Adverse events and patient perception of study treatment

An adverse event resulted in study discontinuation in 10 of 855 (1.2%) subjects in the mupirocin group and 16 of 842 (1.9%) subjects in the povidone iodine group (P=0.24); most due to skin reactions to topical chlorhexidine (Figure 1). One patient in the povidone-iodine group discontinued the study after a vasovagal reaction during the application of the study medication. In the intent to treat analysis, those in the mupirocin group were more likely to report headache, rhinorrhea, congestion, sore throat or any treatment related symptom (Table 6). Patient perceptions of the study treatment were recorded for 555 mupirocin and

536 povidone iodine subjects. Although an equivalent proportion of subjects felt use of the study medication was very important to reduce risk of infection (57% of mupirocin and 60% of povidone iodine subjects), a significantly higher proportion of mupirocin subjects (213 of 555, 38%) reported application of the nasal treatment to be unpleasant compared to povidone iodine subjects (19 of 536, 3.6%), ($p<0.0001$).

Risk factors

Receipt of mupirocin and pre-operative *S. aureus* colonization were significant risk factors for *S. aureus* deep SSI by univariate analysis (Table 7). There was an insufficient number of outcomes to perform a meaningful multivariate analysis, therefore we stratified outcome by pre-operative *S. aureus* colonization status for more information. In the 274 *S. aureus* colonized subjects, *S. aureus* deep SSI occurred in 3 of 141 mupirocin subjects and none of 136 povidone iodine subjects ($p=0.08$). In the 1,252 subjects characterized as not *S. aureus* colonized by pre-operative nasal culture, 2 *S. aureus* deep SSI occurred in the 617 mupirocin subjects and none of the 637 povidone iodine subjects ($p=0.15$).

S. aureus antibiotic susceptibility testing and strain typing

Available *S. aureus* isolates from pre-operative nasal culture, post-operative nasal cultures and surgical site infections were tested for methicillin and mupirocin susceptibility. The proportion of subjects colonized with MRSA and methicillin-sensitive *S. aureus* (MSSA) before surgery was equivalent in both treatment groups (Table 8). The methicillin susceptibility of the *S. aureus* isolate obtained from a deep SSI matched the pre-operative nasal culture in 4 of the 6 *S. aureus* deep SSI in the intent to treat analysis. In the remaining 2 *S. aureus* deep SSI (both in the mupirocin group), the pre-operative nasal culture was no growth (data not shown). Mupirocin resistance was detected in 2 of 97 (2%) MSSA isolates and 1 of 16 (6%) of MRSA isolates; distribution of mupirocin MIC was similar in both treatment groups (Figures 2 and 3). In the intent to treat analysis, subjects with a pre-operative nasal culture yielding *S. aureus*, the proportion of post-operative nasal culture with no growth was 78 of 85 (92%) mupirocin subjects and 45 of 84 (54%) povidone-iodine subjects, ($p=0.03$). No deep *S. aureus* SSI occurred in patients colonized with mupirocin resistant *S. aureus*. The *S. aureus* strain isolated from pre-operative culture was different by *spa* typing from the post-operative strain in 2 of 33 (6%) subjects (Table 9).

Discussion

Healthcare systems and providers are challenged to improve patient safety and control cost by identifying important, modifiable SSI risk factors amenable to intervention. The use of nasal mupirocin to suppress *S. aureus* colonization and prevent subsequent invasive infection has proven effective in controlled studies, yet compliance in actual use may be problematic due to side effects and out of pocket patient expenses. Our study suggests pre-operative nasal povidone iodine with topical chlorhexidine is similar to pre-operative nasal mupirocin with topical chlorhexidine in preventing *S. aureus* deep SSI after arthroplasty and spine fusion surgery. Although target enrollment was not met, a statistically significant reduction in *S. aureus* deep SSI in the per protocol analysis was observed. Subjects in the povidone iodine group experienced lower rates of treatment related symptoms and were less

likely to report application of the treatment as unpleasant. Application of nasal povidone iodine by the patient care team just prior to surgery may ensure greater compliance.

Similar to other investigators, we identified pre-operative *S. aureus* colonization as a significant risk factor for subsequent *S. aureus* SSI [25–28]. In our study, all deep *S. aureus* SSI occurred in subjects with either a pre-operative nasal culture of no growth or a pre-operative nasal culture yielding *S. aureus* coupled with a post-operative culture of no growth. We feel this likely represents either incomplete suppression of *S. aureus* colonization at sites other than the nares or possibly an intra-operative or post-operative exposure from exogenous source. Mupirocin was more effective than povidone-iodine at clearing nasal *S. aureus* colonization. This result is not unexpected given the different mechanisms of the study treatments – the antibiotic mupirocin is intended to eradicate colonization in the nares, while the antiseptic povidone iodine only suppresses *S. aureus* for the duration of surgery. In two cases, the pre-operative and post-operative *S. aureus spa* type differed, and in one of these cases was associated with acquisition of mupirocin resistance in a patient who received povidone iodine. This finding may be due to colonization with heterogeneous *S. aureus* strains, postoperative re-colonization or acquisition of mupirocin resistance (in one case) due to a transient hypermutable state. Although mupirocin resistance was not associated with infection in our study, the number of resistant isolates was low and for several subjects with deep *S aureus* SSI, either the pre-operative culture was no growth or the isolate was unavailable for mupirocin susceptibility testing.

The use of mupirocin to decolonize the nares of patients prior to orthopedic surgery has been demonstrated as a cost effective intervention [29–32]. Brand nasal mupirocin is currently the only formulation available for application to the nasal mucosa and costs approximately $130/course, while nasal povidone iodine costs approximately $20/application – given the equal efficacy of both treatments in our study, povidone iodine provides more value, as defined as quality of outcomes divided by cost [33]. Implementing cost effective interventions to reduce SSI is even more critical as the payors move to reimburse healthcare providers base on episode of care, which requires hospitals and physicians to control costs and assume financial risk for outcomes [34].

Our study has several limitations. First, we failed to achieve our target enrollment due to an overestimation of number of potential subjects during study period. Regardless of under enrollment, the study effect was large enough that a statistical difference was noted in number of deep *S. aureus* SSI infections in the per protocol analysis. Second, the small sample size precluded a multivariate analysis. Although this is true, the randomization provided well balanced treatment groups with respect to clinical, demographic and surgical variables. Third, nasal culture alone was used as a screen for *S. aureus* colonization, which has a sensitivity of only 48% to 66%, and we did not quantify the amount of *S. aureus* in the nares [35, 36]. Although nasal culture alone may miss colonized subjects, we feel study outcome was unaffected as all subjects received treatment. We agree that certain colonized patients shed more *S. aureus* from the nares than other colonized patients, and this potential effect on *S. aureus* SSI warrants further study. Fourth, a portion of post-operative nasal cultures were not performed or *S. aureus* isolates did not undergo mupirocin susceptibility testing. We feel this did not introduce a bias or nullify our conclusions as the number of

missed cultures and isolates were equally balanced between groups. Finally, the study was performed at one institution and the results may not be applicable to other locations with different patient characteristics, or differing frequencies of *S. aureus* strain types or mupirocin resistance.

In conclusion, the use of nasal povidone iodine may be considered as an alternative to mupirocin and a component of a multifaceted approach to reduce SSI.

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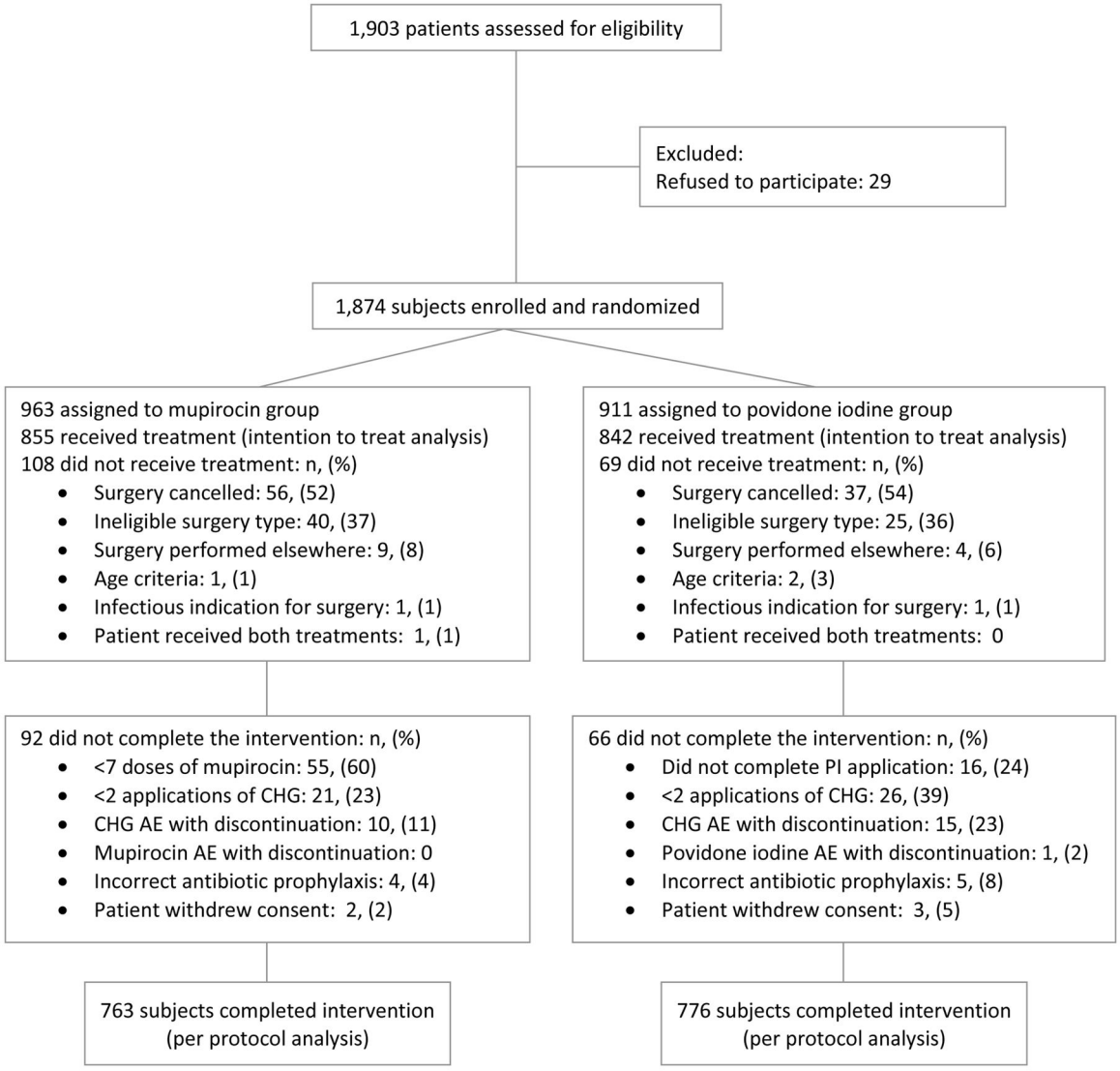

Figure 1.
Flow Diagram of Study Participants

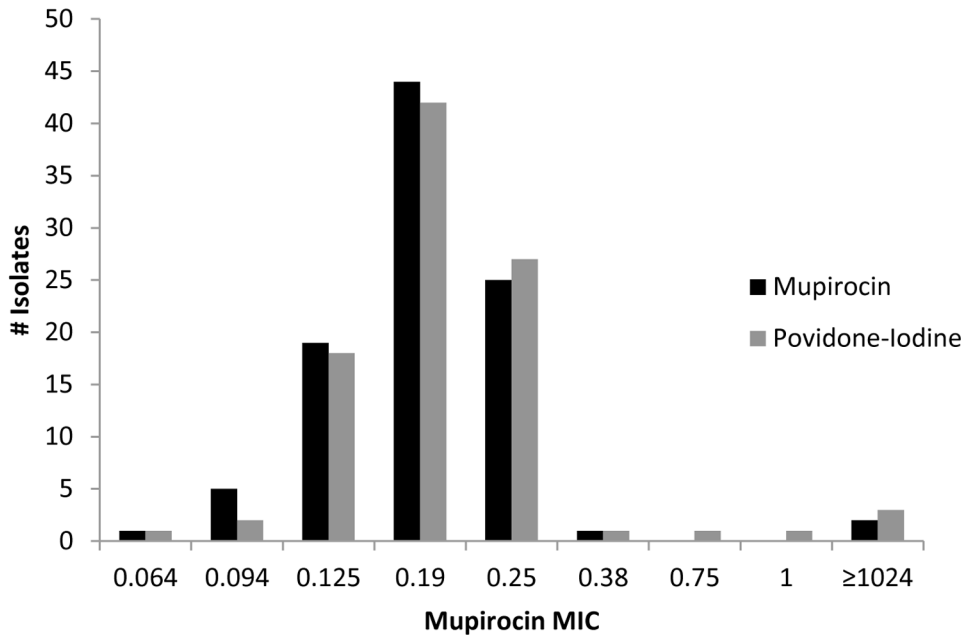

Figure 2.
Mupirocin Minimum Inhibitory Concentration of Pre-operative MSSA Isolates by Study Drug, Intent to Treat Analysis

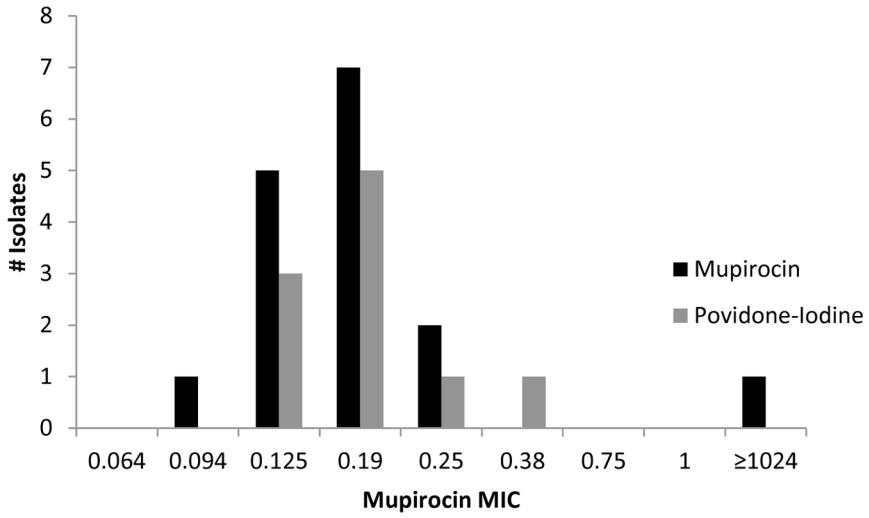

Figure 3.

Mupirocin Minimum Inhibitory Concentration of Pre-operative MRSA Isolates by Study Drug, Intent to Treat Analysis

Table 1

Demographic Characteristics of Subjects in the Intention-to-Treat Analysis

Characteristic	Mupirocin (n=855)		Povidone-iodine (n=842)	
Age (years)				
Median	62.4		61.8	
Range	19.2–93.2		19.1–92.4	
Female sex–no. (%)	523	(61)	499	(59)
Race–no. (%)				
White	677	(79)	670	(80)
Black	138	(16)	145	(17)
Asian	23	(2.7)	21	(2.5)
Native Hawaiian/Pacific Islander	0		1	(0.1)
American Indian/Alaska native	2	(0.2)	0	
Other	20	(1.9)	6	(0.7)
Ethnic group–no. (%)				
Hispanic	97	(11)	88	(10)
Non-Hispanic	746	(87)	749	(89)

Table 2

Clinical and Surgical Characteristics of Subjects in the Intention-to-Treat Analysis

Characteristic	Mupirocin (n=855)		Povidone-iodine (n=842)	
BMI (kg/m^2)				
Median	29.5		29.5	
Range	14.9–58.9		12.0–57.3	
Current smoking – no. (%)	104	(12)	114	(13)
Medical comorbidities – no. (%)				
Diabetes mellitus	110	(13)	104	(12)
Rheumatoid arthritis	36	(4.2)	36	(4.3)
Pre-op *S. aureus* colonization - no. (%)				
MSSA	137	(16)	130	(15)
MRSA	25	(2.9)	21	(2.5)
Any S. aureus	162	(19)	151	(18)
Pre-op serum albumin (g/dL)				
Median	4.2		4.2	
Range	2.9–6.9		2.8–5.2	
ASA score–no. (%)				
1	35	(4.5)	39	(5.0)
2	486	(62)	524	(68)
3	254	(32)	206	(27)*
4	9	(1.1)	4	(0.5)
Receipt of blood products–no. (%)	179	(21)	158	(19)
Post-op glucose ≥ 180 mg/dL - no. (%)	40	(4.7)	46	(5.5)
Procedure type – no. (%)				
Spine fusion	148	(17)	145	(17)
Spine fusion, revision	12	(1.4)	10	(1.2)
Arthroplasty surgery				
Knee	299	(35)	297	(35)
Knee, revision	24	(2.8)	24	(2.8)

Characteristic	**Mupirocin (n=855)**		**Povidone-iodine (n=842)**	
Hip	298	(35)	293	(35)
Hip, revision	35	(4.1)	29	(3.4)
Shoulder	33	(3.9)	42	(5.0)
Shoulder, revision	7	(0.8)	1	(0.1)
Median operative time (minutes)				
Spine fusion	202		205	
Spine fusion, revision	256		299	
Arthroplasty surgery, unilateral				
Knee	93		87	
Knee, revision	137		128	
Hip	94		93	
Hip, revision	138		123	
Shoulder	106		109	
Shoulder, revision	122		119	
Bilateral arthroplasty – no. (%)	49	(6.2)	73	(9.3)*

*p<0.05 by chi-square

Table 3

Deep SSI Pathogens, Intent to Treat Analysis

	Mupirocin		Povidone-Iodine	
	n	(%)	n	(%)
Methicillin-sensitive *S. aureus*	4	(24)		
Methicillin-resistant *S. aureus*	1	(6)	1	(17)
Coagulase-negative Staphylococci	4	(24)	1	(17)
S. agalactiae			1	(17)
E. faecalis	1	(6)	1	(17)
P. acnes	2	(12)		
E. coli	1	(6	1	(17)
P. mirabilis	2	(12)		
P. aeruginosa			1	(17)
B. fragilis	2	(12)		
Total	17	100	6	100

Table 4

Any Deep Surgical Site Infection, by Analysis and Treatment

	# Subjects	# Deep SSI	p-value
Intent to treat			
Mupirocin	855	14	0.1
Povidone iodine	842	6	
Per protocol			
Mupirocin	763	13	0.06
Povidone iodine	776	5	

Table 5

S. aureus Deep Surgical Site Infection, by Analysis and Treatment

	# Subjects	# *S. aureus* Deep SSI	p-value
Intent to treat			
Mupirocin	855	5	0.2
Povidone iodine	842	1	
Per protocol			
Mupirocin	763	5	0.03
Povidone iodine	776	0	

Table 6

Treatment related symptoms, Intent to Treat Analysis

	Mupirocin (n=855)		Povidone-iodine (n=842)		
	Number (%)		Number (%)		P value
Study treatment					
Headache	15	(1.8)	2	(0.2)	0.002
Rhinorrhea	47	(5.5)	1	(0.1)	<0.0001
Nasal irritation	13	(1.5)	8	(1.0)	0.38
Congestion	15	(1.8)	3	(0.4)	0.007
Cough	6	(0.7)	3	(0.4)	0.5
Pharyngeal pain	10	(1.2)	0	0	0.002
Any	76	(8.9)	15	(1.8)	<0.0001
CHG wipe					
Pruritis	7	(0.8)	12	(1.4)	0.26
Rash	4	(0.5)	3	(0.4)	1.0
Any	10	(1.2)	13	(1.5)	0.54

Table 7

Univariate Analysis of Risk Factors for deep *S. aureus* Surgical Site Infection

Risk	RR (95% CI)	P value
Mupirocin	1.01 (1.001–1.012)	0.04
Female sex	1.00 (0.17–6.03)	0.99
Current smoking	1.76 (0.19–15.6)	0.61
Pre-op culture = S. aureus	6.79 (1.1–41.2)	0.02
Diabetes	1.60 (0.19–14.9)	0.65
Post-op glucose ≥ 180mg/dL (day 1,2)	1.60 (0.09–29.9)	0.6
Rheumatoid arthritis	5.60 (0.6–50)	0.08
Immunosuppressive medication	5.10 (0.29–89.9)	0.77
ASA score ≥3	1.69 (0.28–10.1)	0.55
Receipt of blood products	0.98 (0.11–8.8)	0.99
BMI ≥ 30 kg/mm2	0.28 (0.03–2.5)	0.22
Pre-op albumin ≥ 3.5 g/dL	0.33 (0.02–5.8)	0.7
Bilateral arthroplasty surgery	0.94 (0.05–16.8)	0.52
Revision surgery	2.70 (0.31–24.1)	0.35

Table 8

Methicillin Sensitivity of Pre-operative Nasal Culture *S. aureus* Isolates by Study Drug, Intent to Treat Analysis

	Mupirocin		Povidone-Iodine	
	n	(%)	n	(%)
MSSA	135	(16)	130	(15)
MRSA	24	(3)	21	(3)
Culture no growth	692	(81)	683	(81)
Sample not obtained	4	(0)	8	(1)
Total	855		842	

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Table 9

Mupirocin Sensitivity of Pre-operative Nasal, Post-operative Nasal and Deep Surgical Site Infection *S. aureus* Isolates by Study Treatment, Per Protocol Analysis

			Mupirocin		Povidone-iodine	
Pre-operative	**Post-operative**	**Deep SSI**	**n**	**(%)**	**n**	**(%)**
Sensitive	Sensitive	no SSI	6*	(4)	34^	(25)
Sensitive	Resistant	no SSI	0	(0)	1#	(1)
Sensitive	Isolate not tested	no SSI	0	(0)	4	(3)
Sensitive	Culture no growth	no SSI	74	(53)	43	(32)
Sensitive	Sample not obtained	no SSI	24	(17)	19	(14)
Resistant	Isolate not tested	no SSI	1	(1)	0	(0)
Resistant	Culture no growth	no SSI	1	(1)	2	(1)
Resistant	Sample not obtained	no SSI	1	(1)	1	(1)
Isolate not tested		no SSI	28	(20)	31	(23)
Culture no growth	Sample not obtained	Sensitive	2	(1)	0	(0)
Sensitive	Culture no growth	Isolate not tested	1	(1)	0	(0)
Isolate not tested	Culture no growth	Sensitive	2	(1)	0	(0)

*Analysis of the 6 pre-post pairs by *spa* typing revealed 5 pairs were identical and one pair was unable to be typed

^Analysis of the 34 pre-post pairs by *spa* typing revealed 26 pairs were identical, one pair was different and 7 pairs were unable to be typed

#Analysis of the pre-post pair revealed different *spa* types