A double-blind, randomized, controlled trial of topical polysporin triple compound versus topical mupirocin for the eradication of colonization with methicillin-resistant *Staphylococcus aureus* in a complex continuing care population

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BACKGROUND: Intranasal mupirocin or Polysporin Triple (PT) ointment (polymyxin B, bacitracin, gramicidin), in combination with chlorhexidine body washes, have been used for eradicating methicillin-resistant *Staphylococcus aureus* (MRSA), but no comparative studies have been done.

METHODS: A double-blind, randomized, controlled clinical trial to compare the efficacy of mupirocin versus PT ointment in combination with chlorhexidine body washes in eradicating MRSA carriage was conducted. Asymptomatic MRSA carriers, medically stable and at least 18 years of age who were patients on medical wards, received twice daily application of either mupirocin or PT ointment to the anterior nares plus once daily 2% chlorhexidine body washes for seven days. Follow-up swabs from multiple sites using broth enrichment were conducted at 48 h, and one, two, four, eight and 12 weeks.

RESULTS: Of 103 patients eligible for analysis (54 mupirocin; 49 PT), no significant differences between the two groups with respect to baseline demographics, risk factors for MRSA or MRSA colonization sites were noted. At 48 h, 35 of 54 (65%) patients in the mupirocin group versus 15 of 49 (31%) in the PT group (P=0.001) were found to be MRSA negative at all sites. Significant differences were observed at one and two weeks but were not maintained at other intervals. In those with complete microbiological follow-up, MRSA eradication at all sites occurred in 12 of 39 (30.8%) mupirocin- and one of 36 (2.8%) PT-treated patients (P=0.001).

CONCLUSION: Both agents demonstrated poor efficacy and PT was significantly less efficacious than mupirocin at 12 weeks in eradicating MRSA from all sites.

Key Words: *Chlorhexidene; Eradication; MRSA; Mupirocin; Polysporin; Randomized clinical trial*

Un essai aléatoire et contrôlé à double insu du polysporin triple topique par rapport à la mupirocine topique pour éradiquer une colonisation de staphylocoque doré méthicillinorésistant dans une population de soins continus complexes

HISTORIQUE : La mupirocine intranasale ou l'onguent Polysporin Triple (PT) (polymyxine B, bacitracine, gramicidine), alliés à un nettoyant corporel à la chlorhexidine, sont utilisés pour éradiquer le staphylocoque doré méthicillinorésistant (SARM), mais il n'existe aucune donnée comparative sur le sujet.

MÉTHODOLOGIE : On a mené un essai clinique aléatoire et contrôlé à double insu pour comparer l'efficacité de la mupirocine par rapport à l'onguent PT en association avec des nettoyants corporels de chlorhexidine pour éradiquer le portage du SARM. Des porteurs asymptomatiques du SARM, dont l'état médical était stable, qui avait au moins 18 ans et qui étaient hospitalisés, se sont fait appliquer de la mupirocine ou de l'onguent PT dans les narines deux fois par jour, ainsi qu'un nettoyant corporel de chlorhexidine 2 % une fois par jour pendant sept jours. On a effectué des prélèvements de suivi en provenance de multiples foyers au moyen d'un bouillon enrichi au bout de 48 heures, une semaine, deux semaines, quatre semaines, huit semaines et 12 semaines.

RÉSULTATS : Chez les 103 patients admissibles à l'analyse (54 muporicine, 49 PT), on ne remarquait aucune différence significative entre les deux groupes pour ce qui est de la démographie de départ, des facteurs de risque de SARM ou de foyers de colonisation par le SARM. Au bout de 48 heures, 35 des 54 patients (65 %) du groupe traité à la muporicine par rapport à 15 des 49 patients (31 %) de ceux traités au PT (P=0,001) étaient négatifs au SARM à tous les foyers. On observait des différences significatives au bout de une semaine et deux semaines, mais elles n'étaient pas maintenues aux autres intervalles. Chez les patients qui avaient profité d'un suivi microbiologique complet, on a constaté l'éradication du SARM à tous les foyers chez 12 des 39 patients traités à la muporicine (30,8 %) et un des 36 patients traités au PT (2,8 %, P=0,001).

CONCLUSION : Les deux agents sont peu efficaces et le PT est considérablement moins efficace que la mupirocine pour éradiquer le SARM de tous les foyers au bout de 12 semaines.

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Methicillin-resistant *Staphylococcus aureus* (MRSA) is a major cause of nosocomial infections and poses formidable therapeutic problems in the medical realm (1-3). Nasal and extranasal carriage appears to play a significant role in the dissemination of MRSA within the hospital setting (4,5). Recommended efforts aimed at controlling the spread of 'hospital'-related strains of MRSA infection encompass active surveillance, barrier precautions, hand hygiene, antimicrobial stewardship and use of carriage elimination strategies (1,6-9). Topical intranasal mupirocin ointment in conjunction with antiseptic body washing is a commonly used for MRSA decolonization (10). However, many reports have documented that patients, especially long-term care and chronic medical patients, often become recolonized with the same or a new MRSA strain within a short time after an initial treatment (11-13). Moreover, frequent or continuous application of mupirocin for prolonged periods has promoted the emergence of mupirocin resistance (14-17).

Previous in vitro studies have suggested a synergistic action against *S aureus* for the combination of gramicidin and polymyxin B (18). Using broth microdilution techniques, this combination of agents demonstrated a fractional inhibitory concentration of 0.08 µg/mL and for bacitracin and gramicidin, the corresponding fractional inhibitory concentration was 0.05 µg/mL. All three of these agents are found in Polysporin Triple (PT; Pfizer Canada) ointment. A small case series of 11 MRSA-positive chronic care patients treated with PT demonstrated that nine of 11 patients were successfully decolonized using a seven-day course of PT applied to the nares twice daily in addition to the use of daily chlorhexidine bed baths (19). These promising in vitro and in vivo studies of the PT formulation, and the lack of any randomized clinical trial evaluating its efficacy for MRSA eradication, prompted us to design a double-blind, randomized, controlled trial to compare the efficacy of intranasal mupirocin or PT ointment, both used in combination with chlorhexidine body washes, in eliminating MRSA carriage in a complex continuing care population.

METHODS

Study design

The primary study objective was to compare the efficacy of mupirocin versus PT ointment in combination with 2% aqueous chlorhexidine body washes in eradicating overall MRSA carriage in complex continuing care patients. The secondary objective was the comparison of the efficacy of mupirocin and PT in eliminating nasal MRSA colonization. The study was conducted as a double-blind, randomized, controlled trial and was approved by the institutional review board of the University of Toronto (Toronto, Ontario). MRSA carriers were identified among complex continuing care patients at the Bridgepoint Hospital (formerly The Riverdale Hospital) and The Toronto General and Western Hospitals between 1999 and 2003. The treatment was allocated randomly according to a computer-generated randomization list kept by the hospital pharmacy. The study population represented medical patients who were on chronic care wards either awaiting placement or undergoing varying degrees of rehabilitation.

Study population

Patients were considered to be colonized with MRSA when a culture from at least one body site (nares, perirectal area, wounds or invasive devices exit sites) yielded MRSA. Asymptomatic MRSA carriers from one of the chronic care wards at the participating institutions, medically stable and at least 18 years of age were candidates for inclusion in the study. Patients were excluded from the study if any of the following criteria were present: evidence of active infection with MRSA; requirement for antibiotics as therapy for other conditions; administration of antibiotics in the previous week before enrolling in the study; burn wounds exceeding 5% of body surface area; pregnancy; poor survival expectation; known allergy to mupirocin or PT ointment; known colonization with a mupirocin-resistant strain of MRSA; or health care workers or other hospital personnel. Informed consent was obtained from all patients before enrollment in the study.

Demographic data and clinical characteristics of all patients were collected including age, sex, admission from acute care facilities, underlying medical conditions, independence (Katz Index of Independence in Activities of Daily Living) (20) and potential risk factors at time of first positive MRSA culture (open wound, decubitis ulcer, vascular access sites, nasogastric tube, feeding tube, ileostomy or colostomy, peritoneal dialysis catheter, abdominal drain, tracheostomy or the presence of an indwelling urinary catheter).

Interventions

Bactroban ointment (mupirocin; GlaxoSmithKline Inc, Canada) and Polysporin Triple ointment (polymyxin B sulfate 10,000 U/g, bacitracin 500 U/g and gramicidin 0.25 mg/g; Pfizer Canada – formerly Warner Lambert Canada) were distributed by the hospital pharmacy as 10 g aliquots in identical containers marked only with the patient's name. The ointments were similar in colour, odour and consistency. A small amount of ointment (approximately 1 cm) was applied with a cotton-tipped applicator to each of the anterior nares twice daily for seven consecutive days. Patients, investigators and all health care workers involved were blinded as to the nature of the ointment. In addition, all patients received 2% aqueous chlorhexidine body washes once daily for seven days. All ointment containers were collected after therapy for inspection by the pharmacist. Concomitant infection control measures for all patients consisted of contact isolation procedures and barrier precautions as per hospital infection control policy. All patients and their caregivers and family members received written and verbal instructions with respect to basic principles of infection control. The research coordinator assessed all study patients on days 2 and 4 of treatment to assess compliance and adverse events.

Microbiological evaluation

Follow-up swabs from the nares, perirectal area, wounds, exit sites or other sites as appropriate were conducted at 48 h, and one week, two weeks, four weeks, two months and three months after the end of treatment. Specimens were processed within 24 h to 48 h by the Microbiology Research Laboratory at The Toronto Medical Laboratories. Each swab was inoculated onto a Columbia blood agar plate with 5% sheep blood, a mannitol salt agar plate (MSAO) supplemented with oxacillin (4 µg/mL) and then placed in salt broth containing mannitol and 7.5% NaCl. All media were incubated at 35°C. Broth cultures were subcultured onto a colistin-nalidixic acid and MSAO plate at 24 h after incubation and both original and

subculture plates were inspected at 24 h and 48 h, respectively. Mannitol-fermenting colonies growing on MSAO plates were subcultured onto nonselective blood agar. Presumptive MRSA isolates from any media were identified by Gram stain, catalase test, *Staphaurex* rapid test and tube coagulase test positivity. Sensitivity to oxacillin was confirmed using a screen plate containing 6 µg/mL of oxacillin according to the Clinical and Laboratory Standards Institute (previously NCCLS) document for antimicrobial susceptibility testing.

Genotypic analysis and resistance testing

Genotypic analysis of strains was conducted at the Centre for Antimicrobial Resistance, Calgary, Alberta. Typing of MRSA strains was done with pulsed-field gel electrophoresis after DNA extraction and digestion with *Sma1* using a standardized protocol (21). The MRSA isolates were typed for SCC*mec* with a multiplex polymerase chain reaction (PCR) SCC*mec* typing assay that distinguished subtypes I, II, III, IVa, IVb, IVc, IVd and V (22). Isolates were then screened for mupirocin resistance using a screening 5 µg mupirocin disc and the E-Test (AB Biodisk, Sweden) with high-level resistance defined as a minimum inhibitory concentration of 256 µg/mL or greater (23). In addition, genotypic detection of methicillin and high-level mupirocin resistance was performed with a quadriplex PCR assay targeting the 16S ribosomal RNA (*Staphylococcus* genus specific), *nuc* (*S aureus* species specific), *mecA* (methicillin resistance) and *mupA* (mupirocin resistance) (24). Discrepancies between E-Test results and PCR assay were resolved with repeat testing.

Definition of efficacy

The results of bacteriological cultures for MRSA provided the basis for evaluating treatment efficacy at each time period. Successful eradication was defined as consistently negative cultures at all sites during the three-month postintervention period, whereas unsuccessful eradication was defined as a positive culture at any site at any time during follow-up.

Sample size and statistical analysis

The eradication rate with mupirocin had been shown to be about 60% in previous studies done in nursing home populations. (11) On the other hand, the eradication rate with PT was found to be 80% in a small case series (19). Based on these data, the study was designed to detect a difference of at least 20% in the overall MRSA eradication rate with a power of 80% (1–ß=0.80) and the α level set at 0.05. The target number of patients to be included in each study group and for whom complete evaluations were available was 91. Groups were compared using the χ^2 test and the Fisher exact test for categorical variables, and the *t* test for continuous variables. Two-sided $P<0.05$ were considered to be statistically significant. Statistical analysis was performed with EpiInfo 6.4 (Centers for Disease Control and Prevention, USA) and SPSS 9.0 (SPSS Inc, USA).

RESULTS

Patient population

Of 158 patients identified who were potentially eligible, 140 were randomly assigned to treatment but 37 patients did not receive the allocated intervention (seven died or were discharged before receiving the intervention, 11 required systemic antibiotics at initiation for other conditions, six inadvertently received other topical agents, five were found to harbour mupirocin-resistant MRSA or methicillin-sensitive *S aureus*, and eight were patient or physician withdrawals) and were withdrawn at baseline, leaving 103 patients eligible for analysis who received either mupirocin or PT ointment (Figure 1). There were no significant differences between the two groups with respect to age, sex, admission from acute care facilities, underlying medical conditions, independence in activities of daily living (Katz Index of Independence in Activities of Daily Living) and risk factors present at the time of first positive MRSA culture (Table 1).

MRSA colonization sites at baseline did not differ significantly between the two groups (Table 2). Only 11.7% (12 of 103) of all patients were colonized uniquely at the nares, whereas 58.3% (60 of 103) were colonized simultaneously at the nares and extranasal sites and 30.1% (31 of 103) were colonized at extranasal sites only. The most frequently

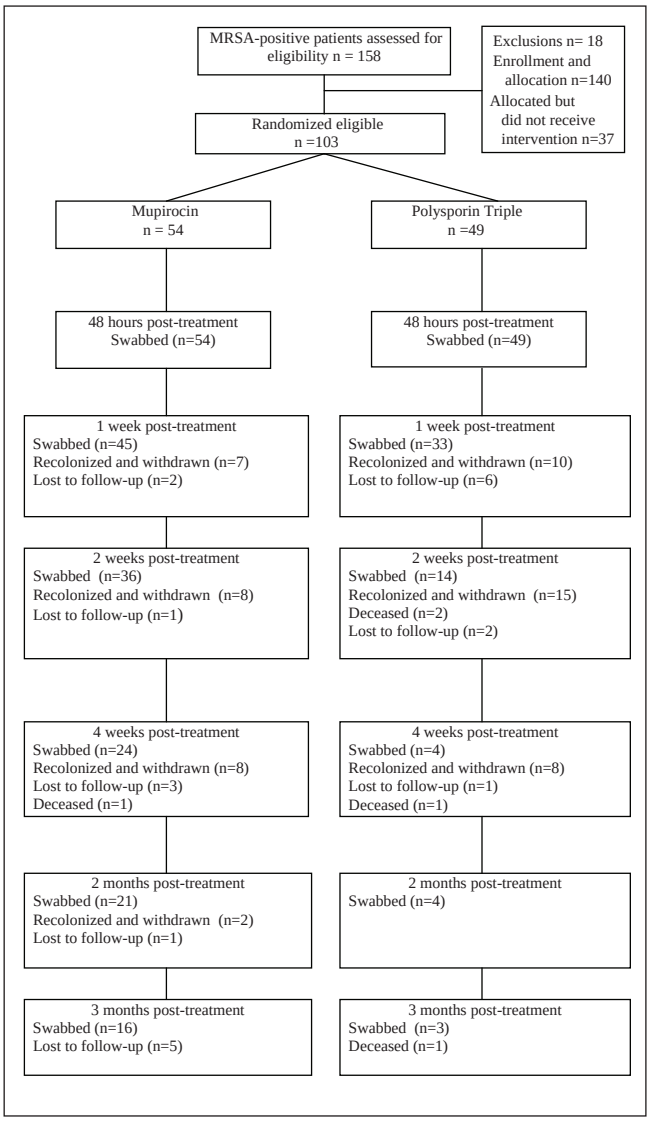

Figure 1) *Disposition of patients randomly assigned to mupirocin versus Polysporin Triple (Pfizer Canada). MRSA Methicillin-resistant* Staphylococcus aureus

TABLE 1
Baseline demographic and clinical characteristics of study population

Characteristic	Mupirocin (n=54)	Polysporin Triple (n=49)	P
Age, years (mean ± SD)	72±13	71±14	0.5
Sex, n (%)			
Male	22 (40.7)	25 (51)	0.3
Female	32 (59.3)	24 (49)	
Admitted from acute care facilities, n (%)	45 (83.3)	44 (89.8)	0.34
Underlying conditions, n (%)			
Cardiovascular disease	40 (74.1)	32 (65.3)	0.33
Respiratory disease	6 (11.1)	5 (10.2)	0.88
Neurological disease	14 (25.9)	15 (30.6)	0.6
Renal disease	9 (16.7)	11 (22.4)	0.5
Metabolic disease	24 (44.4)	23 (46.9)	0.8
Dermatological disease	3 (5.6)	2 (4.1)	0.73
Malignant disease	5 (9.3)	2 (4.1)	0.3
Katz ADL index*, n (%)			
A	19 (35.2)	15 (30.6)	0.41
B	9 (16.7)	7 (14.3)	
E	1 (1.9)	0 (0)	
F	6 (11.1)	2 (4.1)	
G	19 (35.2)	24 (49)	
O	0 (0)	1 (2)	
Patients with risk factors present at time of first positive MRSA culture, n (%)			
Total	35 (64.8)	39 (79.6)	0.1
Open wound	10 (18.5)	11 (22.4)	0.62
Decubitus ulcer	10 (18.5)	9 (18.4)	0.98
Intravenous/other vascular access	2 (3.7)	6 (12.2)	0.15
Nasogastric tube/gastrostomy or jejunal tube	12 (22.2)	13 (26.5)	0.61
Ileostomy/colostomy	1 (1.9)	1 (2)	1
Peritoneal dialysis catheter/abdominal drain	1 (1.9)	4 (8.2)	0.19
Endotracheal tube/tracheostomy tube	2 (3.7)	4 (8.2)	0.42
Foley catheter	14 (25.9)	10 (20.4)	0.51

**Katz index of independence in activities of daily living (ADL) (20): A Independant in all 6 functions; B Independent in all but one of the 6 functions; C Dependent in bathing and one other function; D Dependent in bathing, dressing and one other function; E Dependent in bathing, dressing, going to the toilet and one other function; F Dependent in bathing, dressing, going to the toilet, transferring and one other function; G Dependent in all 6 functions; O Dependent in at least 2 functions but not classified as C, D, E or F. MRSA Methicillin-resistant* Staphylococcus aureus

TABLE 2
Methicillin-resistant *Staphylococcus aureus* (MRSA) colonization sites of patients randomized to receive mupirocin or Polysporin Triple*

	Patients with MRSA colonization, n (%)		
Group	Nares only	Extranasal sites only	Both nares and extranasal sites
Mupirocin (n=54)	7 (13)	15 (27.8)	32 (59.3)
Polysporin Triple (n=49)	5 (10.2)	16 (32.7)	28 (57.1)
Total (n=103)	12 (11.7)	31 (30.1)	60 (58.3)

**Pfizer Canada*

encountered extranasal sites of colonization in both groups were the perirectal sites, open wounds or decubitis ulcers with 68%, 16.5% and 7.8% of these sites, respectively, found to be positive with no significant differences between the two groups. Feeding tube and chronic vascular access sites made up the remainder of the positive sites.

TABLE 3
Treatment results for methicillin-resistant *Staphylococcus aureus* (MRSA)-negative cultures at all sites during the follow-up period

	MRSA-negative cultures at all sites/Screened patients within group, n/n (%)		
Follow-up	Mupirocin group	PT group	
48 h	n=54	n=49	
	35/54 (64.8)	15/49 (30.6)	RR 2.12; 95% CI 1.33 to 3.37; P=0.001
1 week	n=45	n=33	
	29/45 (64.4)	8/33 (24.2)	RR 2.66; 95% CI 1.40 to 5.05; P<0.0001
2 weeks	n=36	n=14	
	25/36 (69.4)	5/14 (35.7)	RR 1.94; 95% CI 0.93 to 4.06; P=0.03
4 weeks	n=24	n=4	
	20/24 (83.3)	3/4 (75)	RR 1.11; 95% CI 0.61 to 2.01; P=1
2 months	n=21	n=4	
	17/21 (81)	2/4 (50)	RR 1.62; 95% CI 0.60 to 4.41; P=0.23
3 months	n=16	n=3	
	12/16 (75)	1/3 (33.3)	RR 2.25; 95% CI 0.44 to 11.43; P=0.22

PT Polysporin Triple, Pfizer Canada

Efficacy and safety

The results of the study with respect to each time period are presented in Table 3. Within 48 h postintervention, 35 of 54 patients (65%) in the mupirocin group were found to have MRSA-negative cultures at all sites as compared with only 15 of 49 (31%) in the PT group (RR=2.12; 95% CI 1.33 to 3.37; P=0.001). Similar differences, which were statistically significant, were observed at post-treatment time points of one and two weeks but were not maintained at four weeks, two months and three months post-treatment. No significant differences in the eradication rates of MRSA were present at the three-month evaluation between the mupirocin or PT groups.

The number of patients who were swabbed progressively declined due to recolonization with seven and 10 patients at one week, eight and 15 patients at two weeks, eight and eight patients at four weeks, two and no patients at two months and four and two patients at three months in the mupirocin and PT groups, respectively, found to be MRSA positive (Figure 1 and Table 3) in at least one site. There were no significant differences in the number of patients lost to follow-up or deceased between the two groups (15 mupirocin and 13 PT). Overall in the population not lost to follow-up or deceased where no microbiological evaluation was possible, consistently negative cultures for MRSA at all sites during the three-month postintervention period were found in only 17.3% (13 of 75) of those

TABLE 4
Treatment results for methicillin-resistant *Staphylococcus aureus* (MRSA)-negative cultures at nares during follow-up period

	MRSA negative cultures at nares/Screened patients within group, n/n (%)		
Follow-up	Mupirocin group	PT group	
48 h	n=39	n=33	
	30/39 (76.9%)	14/33 (42.4)	RR 1.86; 95% CI 1.21 to 2.86; P=0.002
1 week	n=33	n=19	
	27/33 (81.8)	6/19 (31.6)	RR 2.59; 95% CI 1.31 to 5.12; P<0.0001
2 weeks	n=25	n=11	
	21/25 (84)	3/11 (27.3)	RR 3.08; 95% CI 1.16 to 8.21; P=0.002
4 weeks	n=15	n=3	
	14/15 (93.3)	1/3 (33.3)	RR 2.8; 95% CI 0.56 to 13.95; P=0.056
2 months	n=12	n=1*	
	11/12 (91.7)	1/1 (100)	RR 0.92; 95% CI 0.77 to 1.09; P=1
3 months	n=8	n=2*	
	8/8 (100)	0/2 (0)	P=0.022

**1 patient not swabbed at two-month follow-up. PT Polysporin Triple, Pfizer Canada*

TABLE 5
Treatment results for methicillin-resistant *Staphylococcus aureus* (MRSA)-negative cultures in patients with only extranasal colonization sites

	MRSA-negative cultures at extranasal sites/Screened patients within group, n/n (%)		
Follow-up	Mupirocin group	PT group	
48 h	n=15	n=16	
	9/15 (60)	6/16 (37.5)	RR 1.60; 95% CI 0.75 to 3.41; P=0.21
1 week	n=12	n=12	
	8/12 (66.7)	2/12 (16.7)	RR 4; 95% CI 1.06 to 15.08; P=0.013
2 weeks	n=12	n=6	
	7/12 (58.3)	2/6 (33.3)	RR 1.75; 95% CI 0.51 to 5.98; P=0.62
4 weeks	n=9	n=3	
	6/9 (66.7)	2/3 (66.7)	RR 1; 95% CI 0.40 to 2.52; P=1
2 months	n=9	n=3	
	6/9 (66.7)	1/3 (33.3)	RR 2; 95% CI 0.38 to 10.58; P=0.52
3 months	n=8	n=3	
	4/8 (50)	2/3 (66.7)	RR 0.75; 95% CI 0.26 to 2.16; P=1

PT Polysporin Triple, Pfizer Canada

who received a decolonization intervention, including 12 of 39 (30.8%) mupirocin and one of 36 (2.8%) PT-treated patients (P=0.001). Using a best-case worst-case scenario analysis (25) to account for patients lost to follow-up or deceased, the overall MRSA eradication rate could have been as high as 50.0% and 28.6% and as low as 22.2% and 2.0% in the mupirocin and PT groups, respectively.

Among those MRSA positive at the nares (nares-only positive and nares plus extranares sites positive), at 48 h post-treatment (Table 4), 30 of 39 (76.9%) patients were found to be MRSA negative in the mupirocin group compared with 14 (42.4%) of 33 in the PT group, P=0.002 (RR=1.86; 95% CI 1.21 to 2.86). However, the results were not significantly different at four weeks and two months of follow-up. Overall, by the end of follow-up at three months, 21.1% (eight of 39) patients in the mupirocin group remained MRSA negative at the nares versus no (zero of 33) patients in the PT group (P=0.005). Analysis of the subgroup of patients who were colonized only in the nares (seven patients in the mupirocin group and five in the PT group) with negative extranares sites, no significant differences in the eradication rates were demonstrated at each point of the follow-up. In addition, when patients with only extranasal colonization were analyzed, no significant differences were observed in the decolonization rate between the two groups at any point during follow-up (Table 5).

Study patient assessments on days 2 and 4 of treatment did not reveal any adverse events or drug reactions that were suspected of being related to either the PT, mupirocin or the chlorhexidine body washes.

Genotypic analysis and resistance testing

On testing of the first MRSA isolate from each patient, high-level mupirocin resistance was detected in five (9.3%) of the mupirocin and five (10.2 %) of the PT groups, respectively. A total of 62 (60.2%) isolates were available for full genotypic testing and all were CMRSA-1 (USA 600), SCC*mec* type II, which was representative of MRSA strains seen in the region during the time of the study (26). No isolates were identified that had the community-associated MRSA profile of USA 300 or USA 400. There were no differences in the pulsotypes or SCC*mec* types between the mupirocin or PT groups.

DISCUSSION

This is the first double-blind, randomized, controlled clinical trial undertaken to evaluate the efficacy of intranasal mupirocin in comparison with PT in hospitalized chronic complex medical patients colonized with MRSA. The study demonstrated that intranasal PT ointment applied twice daily in conjunction with 2% chlorhexidine body washes exhibited significantly lower overall MRSA eradication rates than mupirocin but the results were not significant after four weeks. Overall, at three months, 12 of 39 (30.8%) mupirocin- and one of 36 (2.8%) PT-treated patients met the criteria for MRSA eradication and the difference was significantly lower for those in the PT treatment group. The finding of a negative MRSA nares culture in the PT group was significantly higher up to two weeks post-intervention compared with mupirocin and variable but not significantly different at later intervals. Overall, at three months, the nares clearance rate was significantly higher in the mupirocin versus the PT group, 21.1 % (eight of 39) versus zero of 33, respectively (P=0.005).

Although previous findings suggested that PT might be used as an effective alternative to mupirocin for decolonization of

MRSA (18,19), our results revealed unexpected findings from what was hypothesized, emphasizing the importance of a randomized trial and the limitations and bias of a small uncontrolled cohort study with short follow-up, which influenced the design of the study. Overall, both agents demonstrated poor efficacy with only 17.3% (13 of 75) of those who received a decolonization intervention found to have consistently negative cultures for MRSA at all sites during the three-month postintervention period.

Previous uncontrolled and observational studies have reported rates of elimination of MRSA using intranasal mupirocin of 60% to 90% in the nares but the follow-up periods have been short and multiple site cultures were not done (11,27). We did not apply the ointments to extranares MRSA-colonized sites given the use of the chlorhexidine body washes and the concerns with mupirocin resistance. Whether the combination of nasal and extranasal PT ointment could lead to improved outcomes requires further study, especially with the recent finding of the efficacy of PT ointment when applied as a prophylactic agent in hemodialysis patients (28).

The eradication of MRSA observed in our study at three months was comparable to that described in other randomized trials in which multiple site cultures and broth enrichment were performed to maximize the sensitivity of detecting MRSA. We are aware of only two other double-blind, randomized, controlled trials that examined eradication of MRSA colonization in chronic medical patients with similar designs and rigourous microbiological methods (12,29). Harbarth et al (12) studied MRSA decolonization in chronic hospitalized patients with interventions of either intranasal mupirocin or placebo plus daily chlorhexidine body washes, and MRSA eradication was reported in only 25% and 18% of patients, respectively, at four weeks. Wendt et al (29) studied nursing home and hospitalized patients with significant comorbidities in a trial comparing intranasal mupirocin plus 2% chlorhexidine mouth rinse for five days plus either 4% chlohexidene or placebo daily body washes and found an overall rate of eradication of MRSA at day 30 of 8% for the chlorhexidine group and 13% for the placebo group.

Our results are not generalizable to all patient settings. Our patients were complex medical patients with multiple comorbidities, with a high frequency of either open wounds or decubitus ulcers (approximately 40%), indwelling catheters, feeding tubes, or tracheostomy tubes (50%), and both nares plus extranares sites of colonization (approximately 60%), all of which would make eradication of MRSA difficult (30,31). In addition, the use of multiple site cultures and broth enrichment would be expected to be more sensitive than other methods to detect MRSA (29,32). Whether the use of concomitant systemic agents would have led to improved results is unknown (33). In summary, although neither agent demonstrated clinically meaningful efficacy, the use of PT for MRSA eradication in the regimen as outlined in our study cannot be recommended. Further studies of a rigorous design are required to determine which, if any, regimens are optimal and in which patient populations.

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