

# Effect of mupirocin and intensified hygienic practices in the decolonization of MRSA in nasal carriers - A comparative study

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## Abstract

**Background:** Mupirocin is an effective topical antibiotic for the elimination of MRSA in carriers. Widespread usage in clinical practice and over the counter availability has led to the development of resistance to this drug. The presence of Mupirocin resistance in *Staphylococcus aureus* is also a cause of concern. **Materials And Methods:** MRSA Positive isolates were tested for in vitro susceptibility for Mupirocin by using 5 µg and 200µg Mupirocin discs. Those who were sensitive to Mupirocin were advised to apply 2% Mupirocin intranasally twice a day for 7 days and those individuals who were resistant to Mupirocin were advised to Intensify their routine hygienic practices. **Results:** Mupirocin was sensitive in 23(44.2%) among 52 MRSA Inpatients, 12(37.5%) among 32 MRSA HCWs and 9 (60%) among 15 MRSA Community subjects. Mupirocin was resistant in 29 (55.7%) among 52 MRSA Inpatients, 20(62.5%) among 32 MRSA HCWs and 6 (40%) among the 15 MRSA Community subjects. Among those who followed 2% Mupirocin application, 8(18.1%) were culture negative for *Staphylococcus aureus* nasal carriage in all the four follow up swabs. Among those who followed Intensified Hygienic Practices, 14 (25.4%) were culture negative for *Staphylococcus aureus* nasal carriage in all the four follow up swabs. **Conclusion:** Decolonization with modified hygienic practices like regular hand washing, nasal washing gave good results than using Mupirocin ointment.

**Key Words:** Methicillin Resistant *Staphylococcus aureus*; Colonization; Mupirocin; Intensified Hygienic Practices; Decolonization

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## INTRODUCTION

Multidrug resistant strains of *S aureus* have been reported with increasing frequency worldwide, most commonly Methicillin resistant *Staphylococcus aureus* (MRSA) infections account for 40-60% of all nosocomial infections

in many centers across the world.<sup>1</sup> Explosion of number of MRSA infections were reported in populations without prior healthcare contact. This increase has been associated with the recognition of new MRSA strains, often called community acquired MRSA (CA- MRSA) strains.<sup>1</sup> MRSA is a serious threat to hospitalized patients globally and also public as community acquired infections.<sup>2</sup> Nasal colonization with *S. aureus* plays pivotal role in the increasing prevalence of MRSA infections worldwide.<sup>3</sup> Colonized patients were considered as a chief source of *S. aureus* in hospital; approximately 10% to 40% of people on admission have nasal carriage of *S. aureus*.<sup>4</sup> Colonization of MRSA allows people in the community to unknowingly harbor and spread this life threatening bacteria. Colonization with MRSA has been identified as an important factor for the development of infections in both community and hospital settings.<sup>5</sup> Colonization sites

of MRSA include anterior nares, throat, web spaces, rectum, axilla, and groin. Colonization is well described with up to 30% of the population thought to be carriers and associated with higher risk of infection in the hospital setting.<sup>5</sup> Treatment of infections caused by Staphylococcus aureus has become more problematic since the occurrence of Methicillin resistance. Vancomycin has been regarded as the first-line drug for treatment of MRSA. Unfortunately, there has been an increase in the number of resistant cases with both Vancomycin-Intermediate and Vancomycin-Resistant S. aureus (VISA and VRSA). This has triggered off alarms in the medical community as S. aureus causes life-threatening infections in hospitalized patients and the community. MRSA strains are resistant to all  $\beta$  lactam antibiotics thereby significantly limiting the treatment options. Mupirocin is an effective topical antibiotic for the elimination of MRSA in carriers. Widespread usage in clinical practice and over the counter availability has led to the development of resistance to this drug. The presence of Mupirocin resistance in Staphylococcus aureus is also a cause of concern. Ancient health traditions from around the world advocate regular, routine hygienic cleansing of the body including body cavities since time immemorial. The traditional medical knowledge of Ayurveda suggests the nasal discharge to be one of daily excretas of the human body and has to be removed by cleansing.

Hence, there is a need to screen the Hospital and the Community population for nasal colonization of MRSA and evaluation of the strategies available for decolonization to prevent serious infections and their implications.

### OBJECTIVES

- To study the effect of topical 2% Mupirocin in MRSA nasal colonizers who are sensitive to Mupirocin by in vitro testing.
- To study the effect of intensified hygienic practices in MRSA nasal colonizers who are resistant to Mupirocin by in vitro testing.

### MATERIALS AND METHODS

**Study design:** A cross sectional study.

#### Source of data

- Inpatients of MIMS teaching hospital, Mandya irrespective of any departments.
- Subjects from the Community of field practice area (Kyatamgere) adopted by Department of Community Medicine, MIMS, Mandya.
- Health Care Workers including Doctors, nurses, students and non-teaching staff of Mandya Institute of Medical Sciences.

**Study setting:** Department of Microbiology, MIMS, Mandya

**Study period:** April-2015 to March-2016

**Sample Size:** 900 (300 from Inpatients, 300 from Community, 300 from Health care workers)

#### Inclusion criteria:

##### For community:

- Subjects of age above 18years, both the sexes and all economic groups.
- No previous hospitalization in the past 1 year.
- No exposure to antibiotics in a month prior to the study.

##### For Inpatients:

- Subjects of age above 18 years, both the sexes and all economic groups.
- Patients with >48 hours of hospital admission.

##### For Health Care Workers

- HCWs irrespective of any Departments

#### Exclusion criteria

##### For community

- Subjects below the age of 18.
- Hospitalization in the past 1 year.
- Exposure to antibiotics in a month prior to the study.

##### For Inpatients

- Subjects below the age of 18.
- Patients admitted to the hospital who have a length of stay <48 hours.
- Those who had Sino nasal symptoms like Rhinitis, Headache, Cough, Post nasal discharge.

##### For HCW

- Those who had Sino nasal symptoms like Rhinitis, Headache, Cough, Post nasal discharge.

#### Method of collection of data

A total of 900 subjects (300 from the community, 300 inpatients and 300 health care workers) were screened for MRSA after obtaining informed written consent from the subjects. Nasal swabs were obtained by using sterile cotton swabs by rolling the swab inside of each nostril with application of an equal pressure.<sup>6</sup> The collected samples were inoculated onto Nutrient agar, Blood agar and Mannitol salt agar and incubated at 37°C for 24-48 hours. Golden yellow colonies in nutrient agar, Beta hemolytic colonies in Blood agar and yellow colonies in Mannitol salt agar were processed further. Golden yellow colonies from Nutrient agar were subjected to Catalase test, Gram's staining and Coagulase test (Slide and tube) with

respective controls.<sup>7</sup> MRSA Positive isolates were tested for in vitro susceptibility for Mupirocin by using 5 µg for and 200µg Mupirocin discs, Fusidic acid (10µg) and Cotrimoxazole (25µg) (HI-Media). Zone diameters were interpreted as per CLSI guidelines.<sup>8</sup> Those isolates whose zone of diameter ≥14 mm for both 5 µg and 200 µg Mupirocin discs were considered as Mupirocin sensitive isolates and the respective subjects were taken as Mupirocin sensitive for intervention with 2% Mupirocin ointment intranasally for 7 days twice daily. Those isolates whose zone of diameter < 14 mm for 5µg and ≥14mm for 200 µg Mupirocin disc were considered low level resistance. Those isolates whose zone of diameter <14mm for both 5µg and 200 µg were considered high level Mupirocin resistance. Both Low level and High level Mupirocin resistance were considered as Mupirocin resistant isolates<sup>9</sup> and the respective subjects were taken as Mupirocin resistant for intervention with intensified hygienic practices. They were advised intensification of routine general hygienic measures such as taking baths every day, washing hands, feet, face and with special reference to nasal cavity and oral cavity, i.e. cleansing of nose by using a simple modification of traditional nasal irrigation, viz: Jalaneti, by Hand technique.<sup>10,11</sup> Accordingly, they were asked to pour some previously boiled and cooled water into their cupped palm. Then they were asked to gently sniff the water up the nose followed by blowing of the nose lightly. Also the subjects were

advised to gently wipe the inner sides of the nasal cavities with their little fingers. They were advised to repeat the procedure for a few times every day as per their convenience. After 7 days of intervention, follow up swabs were taken from both the groups (Group who were advised Intranasal Mupirocin application and Group who were advised Intensified hygienic practices) at weekly intervals for the duration of 1 month. Thus four follow up swabs were taken from each individual of each group. All the above mentioned follow up swabs were inoculated onto NA, MSA and BA, samples with no growth on the primary isolation media were considered as Negative for Staphylococcus and thus MRSA colonization. The Staphylococcal isolates grown were tested for Catalase, Coagulase, Gram's staining, Methicillin resistance by disc diffusion method (Cefoxitin30 µg).

**Statistical analysis:** Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version software. Categorical data was represented in the form of Frequencies and proportions. **Chi-square test or Fischer's exact test** (for 2x2 tables only) was used as test of significance for qualitative data.

**P value** (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.

**Statistical software:** MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.

## RESULTS

Out of 300 Inpatients, 52 (17.3%) were MRSA carriers. Out of 300 HCWs, 32 (10.7%) were MRSA carriers. Out of 300 samples from the community, 15 (5%) were MRSA carriers. Overall MRSA carriage was 99 (11%). However, this observation was not statistically significant.

**Table 1:** Prevalence of MRSA in the three study groups

Study Groups	MRSA n(%)
Inpatients (n=300)	52 (17.3%)
HCW (n=300)	32 (10.7%)
Community (n= 300)	15 (5%)
<b>Total (n=900)</b>	<b>99 (11%)</b>

Chi square value for 2 d.f is 3.80 and with the P- Value is 0.149.

**Table 2:** Mupirocin Susceptibility of MRSA isolates in the three study groups

Study Group	Mupirocin Susceptibility			Total
	Sensitive (%)	Resistant (%)		
		MuL	MuH	
Inpatients	23(44.2)	12 (23.1)	17(32.7)	52
HCW	12 (37.5)	8 (25)	12 (37.5)	32
Community	09 (60.0)	2 (13.3)	4 (26.6)	15
<b>Total</b>	<b>44 (44.4)</b>	<b>22 (22.2)</b>	<b>33 (33.3)</b>	<b>99</b>

Out of 52 culture positive MRSA from Inpatients, 23(44.5%) were sensitive to Mupirocin and 29(55.8%) were resistant to Mupirocin. Among 29 isolates which were resistant to Mupirocin, 12 (23.07%) showed low level resistance and 17 (32.6%) showed high level resistance. Out of 32 culture positive MRSA from Health care workers, 12(37.5%) were sensitive to Mupirocin and 20 (62.5%) were resistant to Mupirocin. Among 20 isolates which were resistant to Mupirocin, 8(25%) showed low level resistance and 12(37.5%) showed high level resistance. Out of 15 culture positive MRSA from the Community 9 (60%) isolates were sensitive to Mupirocin and 6 (40%) were resistant to Mupirocin. Among 6 isolates which were resistant to Mupirocin, 2 (13.3%) showed low level resistance and 4(26.6%) showed high level resistance.

### Inpatients

In the first follow up, out of 23 Inpatients who followed intranasal application of 2% Mupirocin, 8 were culture positive for *Staphylococcus aureus*. 15 yielded no growth of *Staphylococcus aureus*. Of 8 *Staphylococcus aureus* isolated, 3(13%) were MRSA and 5 (21.7%) were MSSA. In the second follow up, 12 swabs were culture positive for *Staphylococcus aureus* which included 8 subjects who were previously positive and 4 subjects who were negative in FW1. 11 swabs yielded no growth of *Staphylococcus aureus*. Of the 12 *S. aureus* isolated, 2(8.7%) were MRSA and 10(43.5%) were MSSA. In third follow up, 14 swabs were culture positive for *S. aureus* which included 11 subjects who were previously culture positive and 3 who were negative in FW2. Of 14 *S. aureus* isolated, 2 (8.7%) were MRSA, 12 (52.2%) were MSSA and 2 yielded no growth of *Staphylococcus aureus*. 4 subjects who were positive and 3 subjects who were negative for *S. aureus* carriage in FW2 were not available for the third follow up. In the fourth follow up, 15 were culture positive for *S. aureus* which included 14 subjects who were positive in FW3 and 1 drop out inpatient who was culture positive in FW2. Of 15 *S. aureus* isolates, 1 (4.3%) was MRSA and 14(60.8%) were MSSA. 3 yielded no growth of *Staphylococcus aureus*, of which one dropped out subject in FW3. Five subjects were not available for the fourth follow up. In the first follow up, out of 29 Inpatients who followed Intensified hygienic practices, 5 were culture positive in the first follow up for *S. aureus* and 24 yielded no growth of *Staphylococcus aureus*. Of the 5 *S. aureus* isolated, 1(3.4%) was MRSA and 4(13.8%) were MSSA. In second follow up, 8 swabs were culture positive for *S. aureus* of which 5 were culture positive and 3 were culture negative in the FW1. Of the 8 *S. aureus* isolated, 1 (3.4%) was MRSA and 7 (24.1%) were MSSA. 21 yielded no growth of *Staphylococcus aureus*. In the third follow up, 13 were culture positive for *S. aureus* and all were MSSA

and included 6 subjects who were culture positive and 7 subjects who were culture negative in FW2. Twelve yielded no growth of *Staphylococcus aureus*. Four subjects who were culture negative in FW2 were not available for the FW3. In the fourth follow up, 13 were culture positive for *S. aureus* and all of them were MSSA. Nine yielded no growth of *Staphylococcus aureus*. Seven subjects were not available for FW4.

### HCWs

In the first follow up, out of 12 HCWs who followed Mupirocin application, 3 were culture positive for *S. aureus* nasal carriage. Of the 3 *S. aureus* isolated, 1(8.3%) was MRSA and 2(16.7%) were MSSA. 9 yielded no growth of *Staphylococcus aureus*. In the second follow up, 7 were culture positive for *S. aureus*, which included 3 subjects who were previously culture positive and 4 who were culture negative in FW1. Of the 7 isolates, 1(8.3%) was MRSA and 6 (50%) were MSSA. 5 yielded no growth of *Staphylococcus aureus*. In the third follow up, 6 were culture positive for *S. aureus* and all were MSSA. 6 yielded no growth of *Staphylococcus aureus*. In the fourth follow up, 6 were culture positive for *S. aureus*. Of the 6 isolates, 2 (16.7%) were MRSA and 4 (33.3%) were MSSA. 6 yielded no growth of *Staphylococcus aureus*. In the first follow up, out of 20 HCWs who followed Intensified hygienic practices, 4 were culture positive for *S. aureus* and all were MSSA. 16 yielded no growth of *Staphylococcus aureus*. In second follow up, 11 were culture positive for *S. aureus* which included 4 subjects who were culture positive in FW1. 9 yielded no growth of *Staphylococcus aureus*. Of the 11 isolates, 2(10%) were MRSA and 9 (45%) were MSSA. In the third follow up, 9 were culture positive for *S. aureus* and all were MSSA. 11 yielded no growth of *Staphylococcus aureus*. In fourth follow up, 9 were culture positive for *S. aureus* and all were MSSA. 11 yielded no growth of *Staphylococcus aureus*.

### Community

In the first follow up, out of 9 subjects from the Community, 2 were culture positive for *S. aureus* and both 2 (22.2%) were MSSA. 7 yielded no growth of *Staphylococcus aureus*. In second follow up, 5 were culture positive for *S. aureus* and all were MSSA. Of these 5 culture positives, 2 subjects were culture positive and 3 subjects were negative in FW1. 4 yielded no growth of *Staphylococcus aureus*. In third follow up, 3 were culture positive for *S. aureus* and all were MSSA. 1 yielded no growth of *Staphylococcus aureus*. 3 subjects who were culture negative for carriage and 2 subjects who were positive for carriage in FW2 were not available for FW3. In fourth follow up, 4 were culture positive for *S. aureus* and all of them were MSSA. 2 yielded no growth of *Staphylococcus aureus*. Out of the 4 MSSA carriers, 2 subjects were dropouts in FW3. Of the two subjects with

no growths, 1 had yielded MSSA in FW3. Three subjects were not available for FW4. In the first follow up who followed intensified hygienic practices, out of 6 Subjects from the Community, were culture positive for *Staphylococcus aureus*. In the second follow up, 2 were culture positive for *S. aureus* and all were MSSA. 4 yielded no growth of *Staphylococcus aureus*. In the third follow up, 2 were culture positive for *S. aureus*, and both were MSSA. 1 yielded no growth of *Staphylococcus aureus*. 3 subjects were not available for follow up. Of the 3 dropout subjects, 1 was culture positive and 2 were culture negative in FW2. In fourth follow up, none of them yielded growth of *S. aureus*. 4 subjects were not available for follow up. Of these 4 subjects, 2 were culture positive and 1 was culture negative for *Staphylococcus aureus* carriage in FW3 and the other person was a dropout subject in FW3. Among those who followed 2% Mupirocin application, 8(18.1%) were culture negative for *Staphylococcus aureus* nasal carriage in all the four follow up swabs. Among those who followed Intensified Hygienic Practices, 14 (25.4%) were culture negative for *Staphylococcus aureus* nasal carriage in all the four follow up swabs.

## DISCUSSION

Eradication of MRSA carriage is a crucial clinical challenge as it was demonstrated to reduce the risk of infection in MRSA colonized patients and prevent MRSA cross transmission to patients who were non-colonized. The efficacy of MRSA decolonization treatment remains controversial. However, the success rate reported in prospective studies ranged from as low as 25% to as high as 95% depending on treatment used and the inclusion criteria. In our study, after Mupirocin susceptibility by disk diffusion testing, we divided the subjects into 2 groups. Those who were sensitive to Mupirocin were grouped as Mupirocin application group and thus advised intranasal application of 2% Mupirocin and those who were resistant to Mupirocin were grouped as Intensified hygienic group and thus advised intensification of Hygienic practices. Follow up swabs were taken from both the groups at weekly intervals for 4 weeks. These swabs were processed and the *Staphylococcus aureus* colonies, if any were subjected for susceptibility testing with cefoxitin (30µg). Among those who followed 2% Mupirocin application, 8(18.1%) were culture negative for *Staphylococcus aureus* nasal carriage in all the four follow up swabs. Among those who followed Intensified Hygienic Practices, 14 (25.4%) were culture negative for *Staphylococcus aureus* nasal carriage in all the four follow up swabs. Thus, a reduced rate of *Staphylococcus aureus* nasal carriage was observed in the group who followed Intensified Hygienic Practices compared to the group who followed 2% Mupirocin application. A number of placebo controlled trials

evaluating nasal mupirocin for eradication of *S. aureus* carriage have been conducted among health care workers, inpatients and the Community. In a study conducted by Doebbling *et al.*<sup>12</sup> among HCWs, they reviewed data from follow up studies. On the basis of intent to treat analysis, they found that the application of Mupirocin twice a day for 5 days led to a significantly lower rate of positive nasal carriage rates of *Staphylococcus aureus* at 48-72 hrs 22(13%) of 170 Mupirocin recipients vs 157(93%) of 169 placebo recipients. The lower rate of carriage persisted at four week follow up 18% vs 88%. Fernandez *et al.*<sup>13</sup> conducted a similar study that reported by Doebbling *et al.*,<sup>12</sup> among 68 HCWs randomized to receive either Mupirocin or Placebo, culture positivity rates of *Staphylococcus aureus* were 13% and 91% immediately after treatment and 67% and 94% at 6 months after treatment respectively. Bommer *et al.*<sup>14</sup> conducted patient blinded trial comparing Mupirocin (3 times per day for 10 days) with placebo among 54 patients undergoing long term hemodialysis. They performed nasal cultures for *S. aureus* at days 3, 8, 10, 21, 42, 70 and 140 days after commencement of treatment and they found significantly lower rates of positivity of *Staphylococcus aureus* among Mupirocin recipients than among Placebo recipients on day 10 {8(24% of 33 patients vs 19 (90%) of 21 patients respectively} In a study conducted by Ellis *et al.*<sup>15</sup> in the community (healthy soldiers), eradication rate at the end of the follow up (56 days) was 88% with Mupirocin application and 65% with placebo treatment. However, we reported lower rates of eradication among Mupirocin application group when compared to intensified hygiene practicing group. This finding in our study suggests that simple hygienic measures are effective in preventing long term colonization of staphylococcus and thereby MRSA in the Hospital and Community. Colonization with *Staphylococcus* in the nose from exogenous sources, which appears to be the primary mother focus, can be correlated with the British Medical Journal 1895 which quotes that the nose is one of the dirtiest organs in the human body.<sup>16</sup> Ancient health traditions from around the world advocate regular, routine hygienic cleansing of the body since time immemorial. The traditional medical knowledge of Ayurveda suggests the nasal discharge to be one of 'Kha malas', the 12 daily excreta of the human body and has to be removed by cleansing. The cupped hand technique using boiled and cooled water, in our study is also a simple modification of the nowadays popular nasal irrigation technique of 'Jal Neti' used for various Sino nasal complications.<sup>11,17</sup>

## CONCLUSION

Decolonization with modified hygienic practices like regular hand washing, nasal washing gave good results

than using 2% Mupirocin ointment. Regular cleansing of the nostrils appears to not allow the stagnation of secretions, thereby preventing colonization and hence transmission of *Staphylococcus aureus*. Nasal washing in particular and maintaining body hygiene in general is a simple and inexpensive method that reduces MRSA colonization, relieves a variety of nasal conditions and also helps in minimizing antibiotic resistance.

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