

## Effect of Mupirocin Treatment in Eradication of *Staphylococcus aureus* Nasal Carriage among Intensive Care Unit Personnel

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**ABSTRACT**

**Background and Objective:** *Staphylococcus aureus* is the most common and important infectious agent. This bacterium can enter the bloodstream and cause some complications in the intensive care unit (ICU). This organism can frequently be found in the nose and transmitted by the carriers. This study aimed to determine the efficiency of eradicating *S. aureus* from the nose of ICU personnel in reducing the risk of *S. aureus* infections in the Panje Azar Hospital in Gorgan, Iran.

**Methods:** Sampling was done using sterile swabs collected from the anterior nasal passages. All samples containing Gram-positive cocci were sent to the laboratory of Faculty of Medicine for identification and evaluation of methicillin resistance. All *S. aureus* nasal carriers were treated with mupirocin ointment b.d for 5 days. The Samples were cultured again after five weeks to evaluate the eradication of *S. aureus* from the nose of subjects.

**Results:** Overall, seven ICU personnel (11.7%) were *S. aureus* carriers. Two isolates (3.3%) were found as methicillin resistant using both methods of disc diffusion and PCR. The frequency distribution of positive cases indicated a significant difference in terms of work experience ( $P = 0.012$ ).

**Conclusion:** The findings show that treatment of carriers with 2% mupirocin topical ointment eradicates *S. aureus* from the nose. No *S. aureus* isolates was found in reculture of nasal samples. Treatment of healthy carriers can significantly reduce the risk of infections caused by the bacterium in the ICU.

**Keywords:** ICU, Mupirocin, *Staphylococcus Aureus*.

## INTRODUCTION

*Staphylococcus* is a genus of gram-positive, catalase-positive, sporeless bacteria that often have no capsule and can grow in different environmental conditions. This organism is the second most common nosocomial pathogen. The bacterium has remained a public health concern and a challenge faced by physicians, due to its potential destructive power and increasing resistance against antibiotics. *Staphylococcus aureus* is able to cause a wide range of diseases: from very benign conditions such as folliculitis and furuncle to life-threatening disorders such as endocarditis, sepsis, staphylococcal toxic shock syndrome and staphylococcal scalded skin syndrome (1). The infections in hospitalized patients are categorized into two groups of community-acquired infections and nosocomial infections. In recent years, methicillin-resistant *S. aureus* (MRSA) infections have been considered as one of the most important nosocomial infections (2).

There are two different scenarios in dealing with MRSA strains, multidrug-resistant species in hospitals that are usually accompanied by some risk factors or predisposing factors (such as catheters, surgery, hospitalization and living in elderly care centers).

The community-acquired MRSA with less resistance and more power to cause severe skin disease and progressive pneumonia. These species produce more invasive diseases. *S. aureus* is one of the most common causes of endemic and epidemic nosocomial infections that can lead to significant morbidity and mortalities.

The number of nosocomial infections caused by *Staphylococcus* has significantly increased in recent years that may be due to using more invasive diagnostic and treatment procedures and lack of proper implementation of nosocomial infections control methods. The severity of complications of staphylococcal infections alone could explain the importance of investigating its control. *The S. aureus* is normally present in the anterior nares of the nose and approximately 25-30% of healthy individuals can be the carriers at any time. Some individuals such as physicians, nurses and hospital staff (50%, 70% and 90%, respectively) are more likely to

be the carriers (3). Usually, these people can also contaminate those around them, which is one of the main causes of infection transmission to patients. It also significantly increases the risk of nosocomial staphylococcal infections in these patients (4). Unfortunately, one of the most important problems is the risk of transmission of MRSA infections, which will increase the chance of infection with resistant objects. The methicillin-resistance gene is also genetically stable and the dissemination of the resistance gene is probably due to antibiotic selection pressure (5). Another important problem in hospitals is the constant risk of hospital microbes' resistance to new antibiotics. One of these problems is the possibility of presence of vancomycin-intermediate *S. aureus* strains and more importantly vancomycin-resistant *S. aureus*. Such infections can question the work of the best medical specialists, cause economic loss by long-term occupation of the hospital beds, and corrupt the main objective of macroeconomic policy of health systems in the world (providing access to public health facilities available in the country). About 2-7% of hospitalized patients in the intensive care unit (ICU) become infected with nosocomial infections, leading to an average of 4-5 days of prolonged stay in hospital. The rate of these infections has increased by 36% over the past two decades (6). The incidence of nosocomial infections in Iran has been reported over 25% (7). It is necessary to study antibiotic resistance in *S. aureus* due to the increasing emergence of resistant strains. Awareness toward the layout of antibiotic resistance can be a useful guide for treatment and control of nosocomial infections. It is necessary to conduct these types of studies periodically and separately by hospital infection-control groups at each center. This study aimed to determine the frequency of *S. aureus* nasal carriers among staff of ICU in Panje Azar Hospital and then investigate the resistance pattern of *S. aureus* isolates, particularly MRSA. This study also investigated the effect of treating the carriers on the incidence of MRSA infections. The results of this study could pave the way for preventing the spread of MRSA infections in hospitals and can be extensible to the entire hospital if successful.

## MATERIAL AND METHODS

After explaining the objectives of the study and obtaining written consent, the anterior nasal swab samples were collected (two swabs from both nostrils) from ICU staff. The samples were immediately cultured on mannitol salt agar (MSA) to isolate *S. aureus*. The plates were transferred to microbiology laboratory of Golestan University of Medical Sciences in less than two hours, and then they incubated at 37 °C for 48-24 hours. The colonies suspicious of *S. aureus* were identified by isolating the colonies grown on MSA with changed colors (from pink to yellow) due to mannitol fermentation.

After purification and Gram staining, catalase test, slide and tube coagulase tests and DNase test were performed for definitive diagnosis. Catalase, coagulase and DNase positives were identified as *S. aureus* (8). Resistance to methicillin was assessed using 30 µg cefoxitin disks according to the CLSI 2013 guidelines (9).

For resistance against 30 µg cefoxitin, inhibition zone of  $\geq 23$ mm and inhibition zone of  $\leq 22$ mm were considered as susceptible and resistant, respectively.

In addition, methicillin-resistance in all *S. aureus* isolates was evaluated by the PCR method. The following specific primers were used according to the PCR temperature program presented in the table below.

mecA 1 (F)5' - AAAATCGATGGTAAAGGTTGGC - 3'  
mecA 2 (R)5' - AGTTCTGCAGTACCGGATTTGC - 3'

All personnel who were carrying *S. aureus* in their nose were treated with mupirocin ointment b.d for 5 days (10).

Mupirocin ointment (2%) contains 2 grams of the antibiotic per 100 grams. The sampling was performed again after five weeks to evaluate the presence of *S. aureus*. The study was recorded in the Iranian registry of clinical trials (Code: IRCT 2014102519666N1). We analyzed the data by SPSS version 16 using X<sup>2</sup> test and considering P-value of less than 0.05.

## RESULTS

Overall, 60 (45 females and 15 males with mean age of  $30.9 \pm 5.9$ ) participated in the study from the total of 65 personnel and physicians working in the ICU during April and May 2014.

After completing demographic checklist, the sampling was carried out using sterile swabs from the anterior nasal passage. In total, seven (11.7%) of them were the carriers of *S. aureus* and 88.3% were not. Frequency distribution of *S. aureus* nasal carriers among the ICU staff based on gender male (5%) in female (6/7%), the difference was not statistically significant gender and *Staphylococcus aureus* carriers ( $p=0.2$ ) (Table 2). Two isolates (3.3%) were identified as MRSA using both methods of disc diffusion and PCR. There was no statistically significant difference between the number of *S. aureus* nasal carriers in terms of gender and education level.

Table 1-Thermocycler temperature protocol

Duration	Temperature (°C)	Condition Stage
30 seconds	95	Denaturation
30 seconds	55	Annealing
60 seconds	72	Extension
5 minutes	72	Final extension

Table 2- Frequency distribution of *S. aureus* nasal carriers among the ICU staff of panje Azar Hospital based on gender and education level

P-value	Number of carriers in each group (%)	Number of subjects (%)	Number Education level and Gender
0.08	(%30) 3	(%16/7)10	Diploma or less
	(%8) 4	(%83/3)50	Bachelor's degree
0.2	(%6/7) 4	45	Female
	(%5) 3	15	Males

Figure 3- Frequency distribution of *S. aureus* nasal carriers among the ICU staff of panje Azar Hospital based on work experience

P-value	Number of carriers in each group (%)	Number of subjects (%)	Number Work experience
0.012	(%3.7) 1	(%45)27	<5
	(%14.3)	(%38)23	6-10
	(%66.7) 4	(%10)6	11-15
	(%25) 1	(%6.7)4	>15

This is due to the difference in the selective method of determining methicillin resistance. Thus, in the studies that they used disk diffusion, the frequency of MRSA was expected to be higher than the actual value (3). Hence, PCR or using 30-mcg cefoxitin is considered a more suitable method of determining exact cases of MRSA. In this study, resistance to methicillin was evaluated using 30 micrograms cefoxitin disks according to the 2013 CLSI guidelines, and PCR method was used to find the *mecA* gene.

The *S. aureus* carriers had  $11.1 \pm 4.4$  years work experience, while those without *S. aureus* had  $6.4 \pm 4.6$  years work experience. The highest frequency (66.7%) was observed in the carriers with 11 to 15 years of work experience and the lowest frequency (3.7%) in the ones with less than 5 years. The frequency distribution of positive cases indicates a significant difference in terms of work experience ( $P = 0/012$ ) (Table 2). Methicillin-resistance evaluation of the seven *S. aureus* isolates using the disk diffusion test showed that two samples (MRSA) were resistant to cefoxitin (30 micrograms). Meanwhile, PCR results showed that both MRSA isolates found in the phenotypic method had the *mecA* gene. The results of re-cultivation of samples from *S. aureus* nasal carriers after 5 weeks showed that none of these individuals was positive and the use of Mupirocin helped them to eradicate the bacterium.

## DISCUSSION

The disk diffusion test was used to investigate the frequency of MRSA isolates. Of the seven *S. aureus* isolates, two MRSA samples were resistant to cefoxitin (30 micrograms) and the frequency of MRSA in

the study population was 3.3%. The prevalence of MRSA in healthcare workers of health centers in the other parts of Iran has been reported differently ranging from 0 in Karmostaji study in 2005 to 30% in Ghasemian study in 2002 (2). The results showed that the use of mupirocin ointment and the emphasis on hand washing could significantly reduce the number of *S. aureus*. Sarmadian et al. study in 2004 at Valiasr Hospital showed that intranasal application of mupirocin for five days in 19 *S. aureus* carriers could eradicate the bacterium in 17 (89.5%) and no recurrence was observed in 87% of them after five weeks (4).

In the present study, mupirocin treatment was effective in all seven carriers, with no recurrence observed in the fifth week. Kalmeijer et al. study in 2002 showed the efficacy of 83.5% for treatment of *S. aureus* nasal carriers referred to the hospital for surgery. It was found that the risk of infection in deep tissues of the surgical site in Mupirocin-treated patients was five times less than the control group (11). In a large scale study, 91% successful eradication of *S. aureus* carriers with Mupirocin has been reported (12). Different results have been reported on the effectiveness of eradicating carriers in prevention of surgical, orthopedic and cardiac surgery wound infections, while Gernaat and Kluytmans studies clearly demonstrated that treatment with Mupirocin could significantly decrease postoperative infections (13, 14).

The results of the present study confirms the findings of the two mentioned studies, and well demonstrates the strong effect of treating carriers on preventing infections in the ICU. This indicates the importance of this drug combination in controlling *S. aureus* infections, especially MRSA infections.

## CONCLUSION

In this study, the low number of carriers in the ICU wards is considered a positive point that can have an important role in the control of nosocomial infections in Gorgan, since ICUs are one of the main sources of nosocomial infections dissemination.

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## CONFLICT OF INTEREST

All contributing authors declare no conflicts of interest.

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