Decolonization of Methicillin Resistant *Staphylococcus areus* Nasal Carriage Among Health Care Workers

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Abstract: Methicillin-resistant *Staphylococcus aureus* (MRSA) has evolved as one of the most important causes of hospital infections worldwide. Screening for carriage of (MRSA) is fundamental to modern-day nosocomial infection control. Effective decolonization decreases the risk of subsequent staphylococcal infection and controls the spread of MRSA. The aim of this study was to identity the frequency of MRSA nasal carriage among health care workers in Assiut University Hospitals and to determine the efficacy of combined local mupirocin ointment and oral rifampin and trimethoprim /sulfamethoxazole for nasal MRSA decolonization for implementing various infection control policies to control the spread of MRSA in our Hospitals. Swabs were taken from the anterior nares of the 150 health care workers in different departments in Assiut University Hospitals, Egypt. Identification of *Staphylococcus aureus* was done by the conventional bacteriological methods. Methicillin resistance was detected by growth on oxacillin resistance screening agar base (ORSAB). For those who showed nasal carriage of MRSA, topical application of mupirocin & oral treatment with rifampin and trimethoprim/ sulfamethoxazole were administered for 5 days. Screening was carried out 48 hours, 1 month , 6 months and 9 months after the treatment cycle was completed. Out of 150 health care workers, 45.3% (68) were MRSA carriers. Post treatment screening showed a reduction in the number of carriers. After 48hs post treatment, they were 11.8%, followed by 1.5% after 1month. Recolonization occurred at 6 and 9 months post treatment (23.5% and 14.7% respectively) but were still less than before treatment. We conclude that we have a high percentage of MRSA nasal colonization among the studied health care workers. A single treatment cycle of combined local mupirocin, oral rifampin and trimethoprim/ sulfamethoxazole resulted in successful MRSA decolonization in the early post treatment period (within 1 month) with no documented adverse effects. However, nasal MRSA recolonization occurred again in the late post treatment period (≥6months). Screening and treatment should be made an essential protocol to decrease the number of carriers transmitting MRSA to the hospital settings.

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1. Introduction

Methicillin-resistant *Staphylococcus aureus* (MRSA) continues to be a global problem in infection control. For many years it has been a major cause for nosocomial infections in many countries **(Simor et al, 2002).** These strains show resistance to a wide range of antibiotics, thus limiting the treatment options to few agents, such as vancomycin and teicoplanin **(Peacock, 2005)**. It is therefore important to keep the prevalence of MRSA carriage and MRSA infections low **(Wertheim and Vos, 2005).**

All MRSA carriers are not the same; carriage may be transient, intermittent, or persistent for months to years **(Vandenbergh et al, 1999).** The anterior nares have been thought to be the most frequent site of MRSA carriage and should be targeted for surveillance screening in healthy health care workers (HCW) (**Buehlmann et al, 2008).** Nasal carriage of *S. aureus* is a known risk factor for subsequent infection. Transmission from health-care personnel to patients was evaluated in many studies, some of which reported a clear molecular and epidemiological evidence of MRSA transmission from health-care workers to patients (Richardson et al, 1990). Some studies have even described outbreaks of MRSA among patients associated with colonised health-care workers **(Dawson et al, 1997).** Other studies considered transmission likely (Albrich and Harbarth, 2008).

Decolonization may be defined as treatment to eradicate *S. aureus* or MRSA carriage. There is a controversy regarding the effectiveness of MRSA decolonization, and it is not recommended in some studies **(Buehlmann et al, 2008).** In other studies, the potential benefits of decolonization were ensured and include decreased risk of subsequent staphylococcal infection and prevention of staphylococcal transmission to reduce endemic rates of infection or manage outbreaks **(Andrew et al, 2009).**

Eradication therapy varied between studies. Several topical and systemic antimicrobial agents have been used for MRSA decolonization, with limited success rates **(Simor et al, 2007)**. A variety of agents, both topical and systemic, have been used

for decolonization. Although. mupirocin (Bactroban Nasal, GlaxoSmithKline) has been most commonly used **(Andrew et al, 2009)** yet resistance to the use of mupirocin alone has been reported **(Wertheim and Vos, 2005).** Chlorhexidine baths have been used in combination with intranasal mupirocin in uncontrolled trials and during outbreaks**(Sandri et al, 2006).** The use of combination therapy has been effective in treating MRSA in the nares and at other sites. Such combinations included the use of oral antibiotics plus rifampin which ensures excellent penetration into secretions and tissues **(Bradley, 2005).** However, development of resistance of *S. aureus* to rifampin after treatment with a regimen containing rifampin ranged from 0-40% **(Falagas et al, 2007).** The wide-scale use of systemic antibiotics has been associated with the development of drug resistance and the loss of valuable therapeutic agents for subsequent treatment of infection. Eradication of MRSA is not guaranteed or permanent. Thus "decolonization" rather than "eradication" may be a more appropriate term. The effect of any eradication or decolonization strategy seems to last 90 days at most, although more prolonged follow- up has been infrequent **(Loeb et al, 2003)**. We carried out this study to identity the frequency of MRSA nasal carriage among health care workers in Assiut University Hospitals and to determine the efficacy of combined local mupirocin ointment and oral rifampin and trimethoprim /sulfamethoxazole for nasal MRSA decolonization for implementing various infection control policies to control the spread of MRSA in our Hospitals.

2. Material and Methods

This is a prospective cohort study with a follow- up period of 9 months. A total of one hundred and fifty health care workers from different departments and units of Assiut University Hospitals were enrolled in the study after taking their concents. The HCW recruited in the study were from the operative room of the Ophthalmology department (n=4), the Trauma Intensive Care Unit (n=61) and the Neonatal Intensive Care Unit (n= 85).

Nasal Swabs

A swab from both anterior nares was obtained from each health care worker according to **Abed El-Jalil et al (2008)** for MRSA detection . Colonization was defined as MRSA identified from the nares of these persons in the absence of MRSA infection **(Como-Sabetti et al, 2006).**

Culture , Identification and Screening for MRSA

Nasal swabs were immediately plated on mannitol-salt agar and incubated at 35ºC for 72 hrs. Mannitol fermenting colonies were examined by Gram stain and tested for catalase production and coagulase test. Isolates which showed positive growth on mannitol salt agar were subcultured on oxacillin resistance screening agar base (ORSAB, Oxoid Limited , Basingstoke, England) to detect oxacillin resistant strains **(Simor et al, 2002).**

Treatment of colonized health care workers

Colonized health care workers were treated with local mupirocin twice per day for 5 days as recommended by the manufacturer (Turixin®, GlaxoSmithKline, Munich, Germany). In addition they received oral rifampin, 600 mg and oral TMP/ SMX, 160 mg/ 800 mg given twice a day for five days **(Ellison et al, 1984).**

Post treatment screening

Post treatment screening was done according to the German recommendation on MRSA patients issued by the Robert-Koch Institut **(Anonym, 1999).** A minimum wash-out period of 48 h was required between the last treatment and the first set of screening swabs. Successful decolonization was considered to have been achieved if results were negative for 3 consecutive sets of cultures (24 h between each). Follow up screening was repeated after 1month, 6 months and 9 months after the treatment cycle was finished. Health care workers in the Ophthalmology Operative Room (n=4) refused to continue screening after 1 month post treatment.

3. Results

A total of one hundred and fifty health care workers were screened for MRSA nasal carriage. Sixty eight (45.3%) were found to be colonized as shown in table (1).

Table 1: Frequency of MRSA nasal carriage among health care workers in different departments.

Number of screened healthcare workers in different units	Number (%) of MRSA nasal carriers
• Operative room of Ophthalmology dept. (n=4)	4 (100)
• Trauma Intensive Care Unit (n=61)	49 (80.3)
• Neonatal Intensive Care Unit (n=85)	15 (17.6)
Total (150)	68 (45.3)

MRSA: Methicillin Resistant *Staphylococcus aureus*

The frequency of detection of nasal MRSA colonization in HCW in different departments is presented in table (2). Screening was done 48hs , 1 month, 6 months, and 9 months post treatment. Health care workers from the Operative room of the

Ophthalmology department didn't continue screening after 1 month post treatment.

Table 2: Frequency of MRSA nasal carriers after combined treatment in different departments .

Departments	No. (%) of HCW with MRSA nasal colonization				
	Before treatment	24 hs post treatment	1 month post treatment	6 months post treatment	9 months post treatment
Operative room of ophthalmology dept.	4	1 (25)	0 (0)	-	-
Trauma Intensive Care Unit	49	6 (12.2)	1 (2)	13 (26.5)	6 (12.2)
Neonatal Intensive Care Unit	15	1 (6.7)	0 (0)	3 (20)	4 (26.7)
Total	68	8 (11.8)	1 (1.5)	16 (23.5)	10 (14.7)

HCW: Health care workers.
MRSA: Methicillin Resistant *Staphylococcus aureus*

4. Discussion

Screening for carriage of methicillin resistant staphylococcus aureus (MRSA) is fundamental to modern-day nosocomial infection control, both for epidemiologic investigation and day-to-day decision on barrier isolation **(Safdar et al, 2003).**

Although many body sites such as hands, rectum, perineum, axillae, vagina, pharynx, gastrointestinal tract, and intact or inflamed skin are frequently colonised for varying time periods, the main reservoir of MRSA is the anterior nares. Among nasal *S. aureus* carriers, approximately one-half also carry the organism on their skin **(Wertheim et al, 2005).**

Eradicating MRSA nasal carriage from epidemiologically-implicated health care workers (HCWs) has been used on a number of occasions to control MRSA outbreak **(Ben Ayed et al, 2010).**

As routine decolonization is not a policy in our hospitals, we reported a very high rate of nasal carriage (45.3%). Our results were much higher than those of the study at Ain Shams University hospital, Egypt, which reported the rate of nasal MRSA carriage to be 20% **(Abdel Rahman et al, 2010).** In another study at Nazami Hospital in Iran, the prevalence of nasal carriage of MRSA in HCWs was only 5.3% (**Askarian et al, 2009).** The mean nasal MRSA carriage in health-care workers in many studies was 4.1% **(Bertin et al, 2006; Seybold et al, 2006).** In an Italian hospital MRSA carriage was reported in only 1.5% among HCW **(Orsi et al, 2008).** In countries such as The Netherlands that routinely decolonize MRSA carriers, very low prevalences of MRSA carriage are reported due to the routine decolonization which has been underestimated in the past as a strategy to control the spread of MRSA **(Buehlmann et al, 2008).**

It is well known that staphylococcal dispersal from asymptomatic personnel of MRSA to patients, is mainly dependent on whether the person is a nasal carrier **(Hare and Thomas, 1956).** It is therefore recommended that screening of health-care workers should not be restricted to outbreak settings because there is a trend for higher colonisation rates in settings with endemic MRSA **(Albrich and Harbarth, 2008).** Such settings with endemic MRSA as in our hospitals. These settings have lower awareness of the threat of the bacteria **(Harbarth et al, 2008).** Compliance with hand hygiene and contact precautions among health-care workers were repeatedly shown to be poor in hospitals with endemic MRSA **(WHO, 2005)**

Evidence indicating an association between nasal *S. aureus* carriage and subsequent *S. aureus* infection has led to the development of decolonization programs aimed at decreasing the *S. aureus* infection rate **(Wertheim et al, 2005).** Studies of pooled data in systematic reviews or meta-analyses, strongly support the efficacy of decolonization in patients at high risk of infection **(Bode et al, 2010).**

Mupirocin has no structural similarities with existing systemic antibiotics that might lead to the development of cross-resistance, and in its topical form, it has minimal toxicity **(Bradley et al, 2005).** It has become the topical agent of choice for the elimination of MRSA carriage. However, the increased use of this antibiotic has been followed by reports of MRSA out break with both low and high-level mupirocin resistance **(Simor et al, 2007).** It was reported that single-cycle of mupirocin decolonization, even when effective, was followed by recolonization in many studies **(Harbarth et al, 2008; Robicsek et al, 2009).** So, additional cycles may be needed to prolong the effect, but the use of multiple cycles may increase the risk of MRSA resistance to mupirocin **(Simor et al, 2007).**

In the present study we evaluated the efficiency of a combination therapy consisting of local mupirocin, oral rifampin (600 mg) and oral TMP/ SMX (160 mg/ 800 mg) all given twice a day for five days **(Ellison et al, 1984).** The effectiveness of TMP-SMX as a treatment for MRSA infections was proved by **Grim et al (2005).** It is reported that *S. aureus* can be internalized by human cells and can survive intracellularly **(Garzoni et al, 2007).** So,

some systemic antibiotics, especially rifampin and cotrimoxazole, may achieve better tissue and intracellular levels, leading to higher MRSA eradication rates **(Yamaoka , 2007).**

The effect of the decolonization strategy used in this study was evaluated after 48hs, 1 month , 6 months and 9 months post treatment. Nasal MRSA colonization rates among HCW decreased after 48 hs post treatment (to 25% in the operative room of the Ophthalmogy dept, 12.2% in the Trauma Intensive Care Unit and 6.7% in the Neonatal Intensive Care Unit). Maximum decolonization was achieved after 1 month post treatment when the majority became free while only 2% of the HCW remained nasal carriers in the Trauma Intensive care Unit. However, recolonization was detected again at 6 months post treatment ranging from 20% to 25.5% in the neonatal and Trauma Intensive Care Units respectively. Our findings are consistent with **Loeb et al (2003),** who reported that the effect of any eradication or decolonization strategy seems to last 90 days at most.

Many investigations stated that follow-up lasted at least 4 weeks after completion of therapy, suggesting that success of decolonisation might be overestimated in some studies **(Blok et al, 2003).** We emphasize on that as we found an excellent success of decolonization after 1 month (98.5% , 67/68), but recolonization was detected at 6 and 9 months post treatment (23.5% and 14.7% respectively). Recolonization may be acquired from the hospital environment or from colonized extranasal sites or from subclinical infections **(Simor et al, 2007).**

In the current study, the efficacy of MRSA decolonization was on the basis of a single decolonization course. We reported a very high percentage of decolonization by this regimen which was much higher than that reported by other studies after a single decolonization course which achieved success in only 46.7% of patients **(Buehlmann et al, 2008, Simor et al 2007).**

In accordance with Roccaforte et al (1988) who used rifampin, TMP/SMX and Bacitracin local ointment, we found the regimen used in this study for decolonization to be safe and effective on short term follow up. However, relapse limits its value. In addition, **Richard et al, (1984)** evaluated a regimen consisting of rifampin and TMP/SMX only. They reported that this regimen decreased the number of MRSA-colonized patients, but not permanently as recolonization occurred again more than 6 months after treatment.

In settings of high endemicity or frequent outbreaks, decolonization therapy aims to reduce MRSA prevalence (rather than achieve MRSA eradication) and obtain outbreak termination. Therefore, shorter follow-up periods may be preferred because they likely reflect the true effect of decolonisation therapy rather than the chances of reinfection. By contrast, when MRSA prevalence is low and outbreaks are rare, the goal of decolonisation therapy is to prevent MRSA from becoming endemic and to ensure that health-care workers remain free of MRSA after decolonisation. In these settings extended follow-up may be indicated **(Albrich and Harbarth, 2008).**

By referral to many studies, the duration of therapy did not affect treatment success and decolonisation occurred in 90% of health-care workers treated for 5 days, 82% for 7 days, 93% for 10 days, and 85% for 14 days (Blok et al, 2003).

Many regimens were reported with various degrees of success. A recent systematic review of 23 randomized, placebo-controlled trials was performed to assess the efficacy of decolonization in an overall population (healthy volunteers, health care workers, and patients) comprising both MRSA and MSSA carriers **(Ammerlaan et al, 2009)**. The intervention consisted of topical decolonization alone or in combination with systemic treatment. Decolonization eliminated nasal carriage in 90% of the study participants overall. However, efficacy was lowest in the studies that assessed topical decolonization alone in patients admitted with MRSA carriage **(Harbarth et al, 1999).** Higher success rates have been achieved with topical decolonization accompanied with, or followed by, systemic decolonization **(Simor et al, 2007).**

In a multicenter, randomized, controlled trial, decolonization consisted of nasal mupirocin ointment, chlorhexidine soap, and a 7-day course of rifampin and doxycycline **(Simor et al, 2007).** The success rate was 47% after 1 decolonization cycle and 76% after 2 cycles. In places like Pakistan where mupirocin is not routinely available, oral fluoroquinolones, like oral levofloxacin in combination with topical gentamycin ointment can be used for decolonization of staphylococcal carriage **(Akhtar , 2010)**. Other regimens include, a 7-day regimen of nasal mupirocin, chlorhexidine body wash, and oral rifampicin and doxycycline that resulted in successful MRSA eradication at 3 months' post-treatment in 74% (64 / 87) of patients regardless of the presence of extranasal MRSA colonization **(Simor et al, 2007).** In the study of **Buehlmann** et al (2008), a combination consisting of mupirocin nasal ointment, chlorhexidine mouth rinse and full body wash with chlorhexidine soap for 5 days in addition to vancomycin, cotrimoxazole, rifampin and fusidic acid were used for eradication of MRSA carriage after a mean ($\pm$ SD) of 2.1 $\pm$ 1.8 decolonization cycles. This study reported a success rate of 87%.

Measures used to control the spread of MRSA include screening, decolonization of carriers, patient isolation in a single room, hand decontamination, and protective clothing **(Siegel et al, 2007).**

Work restrictions for health-care workers with MRSA varied in different studies, colonised or infected personnel were allowed to work without restrictions other than education as the condition in our hospitals and emphasis on hand hygiene and standard precautions . Other institutions instructed the health-care workers to work only in dedicated MRSA areas or where MRSA was present. In other studies, colonised or infected health-care workers were temporarily removed from patient care for varying durations until documentation of negative follow-up cultures was obtained **(Bertin et al, 2006).** In settings with endemic MRSA or limited resources as in our hospitals, priority should be given to HCW in high-risk units such as ICUs, burn units, or surgical wards **(Patel and Madan , 2000).**

We conclude that we have a high percentage of MRSA nasal colonization among the studied health care workers. A single treatment cycle of combined local mupirocin, oral rifampin and trimethoprim/ sulfamethoxazole resulted in successful MRSA decolonization in the early post treatment period (within 1 month) with no documented adverse effects. However, nasal MRSA recolonization occurred again in the late post treatment period (≥6months). Screening and treatment should be made an essential protocol to decrease the number of carriers transmitting MRSA to the hospital settings.

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