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Original Article

Prevalence of Mupirocin Resistance in Patients Colonized with Staphylococcus Aureusin A Tertiary Care Rural Hospital

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Abstract
Introduction: *Nasal carriage of Staphylococcus aureus plays a key role in the epidemiology and pathogenesis of infection and is a major risk factor for the development of both community-acquired and nosocomial infections. A causal relationship between S. aureus nasal carriage and infection is supported by the fact that the nasal strain and the infecting strain share the same genotype. Nasal mupirocin, a nasal formulation is approved by the United States Food and Drug Administration for eradicating nasal carriage in patients as well as in health care personnel. The increasing prevalence of mupirocin resistance among Staphylococcus aureus & coagulase-negative Staphylococcus (CoNS) species could be an important threat to the future use of mupirocin against MRSA. Thus this study was carried out with the aimsto know the prevalence of mupirocin resistance in Patients colonized with Staphylococcus spp.*
Methodology: *A total of 229 hospitalised patients were randomly selected. S. aureus &CoNS isolates were tested for mupirocin resistance by the disk diffusion method using 5µg and 200µg mupirocin discs.*
Results: *Out of 229 hospitalised patients, MRSA was isolated in 21(9.17%) and MRCoNS in 27(11.79 %). 5(2.18%) isolates were Mupirocin resistance.*
Low-Level Mupirocin resistance (MuL) was seen in 1(0.44%) of MRSA and High-Level mupirocin resistance (MuH) was noted in 4(1.74%) isolates of MRCoNS
Conclusion: *The presence of mupirocin resistance in 1(0.44%) of MRSA and 4(1.74%) of MRCoNS is a cause of concern. Hence it is recommended that routine testing of MRSA for mupirocin resistance be conducted.*
Keyword- *Nasal carriage, MRSA, MRCoNS, Mupirocin resistance.*

Introduction

MRSA has become a major nosocomial pathogen in community hospitals, long term care facilities and tertiary care hospitals. MRSA colonization precedes infection and the major reservoir being the anterior nares.(1) Colonization may be either transient or persistent and may be at single or multiple body sites (2) Nasal colonization with S. aureushas been linked to surgical-site infection (3) bloodstream infection (4) and ventilator-associated

pneumonia.[5]In certain subgroups, such as; frequently hospitalized people, senile and immune compromised patients, colonization with S. aureus occurs more frequently. [6] Currently, the health problems associated with this microorganism have become more serious due to an increasing incidence of methicillin-resistant S. aureus.[7] Indiscriminate use of antibiotics, prolonged hospital stay, intravenous drug use, and carriage of MRSA in nose, axilla, and perineum are the important risk factors for the acquisition of MRSA infection.[8]

Nasal mupirocin (pseudomonic acid A) has an important role to play in the eradication of MRSA carriage.It acts by binding specifically to the bacterial isoleucyl- tRNA synthetase enzyme and inhibits its protein synthesis. With the increased use of mupirocin, both low and high level resistance has been reported during treatment with nasal mupirocin. [9] Mupirocin was first introduced in the UK in 1985 and was used to treat Staphylococcal and Streptococcal wound infections and to eradicate nasal carriage of Staphylococcus aureus including MRSA. [10] Within two years after its introduction, mupirocin resistance among MRSA isolates emerged in the UK [11]& since then in Ireland 2 %,[12] New Zealand 12.4% [13], the USA, 24% [14]

Although no performance standards or interpretive criteria have been published for mupirocin susceptibility testing, two mupirocin resistance phenotypes namely low level (MuL) and high level (MuH) mupirocin resistance are defined in Staphylococci.

Low-level resistance (MICs, 8 to 256 µg/ml) is usually associated with point mutations in the chromosomally encoded *ileS*gene whereas high-level resistance (MICs, ≥512 µg/ml) is generally due to a plasmid-mediated gene, *mupA*(also referred to as *ileS2)*, which encodes an additional modified isoleucyl-tRNAsynthetase[15] and is typically located on mobile genetic elements, which likely facilitates the dissemination of this resistance mechanism. The mupAgene is typically plasmid mediated and some of these plasmids are conjugative**.** MupB is a new high level mupirocin resistance mechanism in Staphylococcus aureus. [16]

Detection and differentiation of both types has important clinical implications. The presence of high-level mupirocin resistance (MuH) excludes its clinical use, however low-level mupirocin resistance (MuL) can be overcome by recommending higher than usual dosage.

A recent randomized trial of mupirocin use for MRSA decolonization reported a high rate (24%) of mupirocin resistance at study enrollment, emphasizing the need to test for mupirocin resistance prior to implementing routine mupirocin use. [17]

Several studies have reported the prevalence of mupirocin resistance among the clinical isolates and the health care worker but the true extent of Mupirocin Resistance in Patients Colonized with Staphylococcus aureusin our country is unknown and there are very few studies carried out on this issue. Thus, this study was carried out with the

Aims

To know the prevalence of mupirocin resistance in patients colonized with S. aureus and Coagulase-negative Staphylococcus spp. (CoNS).

Materials and methods

A Prospective cross-sectional study was carried out from the period of December 2013 to April 2014. Approval was obtained from the Ethical Committee for carrying out the study. Informed consent was obtained from the patients or their relatives. Patients who were admitted for more than 48 hours admission in the hospital were included. A total of 229 patients were randomly selected. The age, sex, duration of stay in the hospital and other relevant information were obtained in a proforma. The nasal swabs were collected from patient with informed Consent from Orthopaedics, ICU, medicine, pediatric, Surgery and Gynecology.

Nasal swabs from both nostrils were collected by rotating a sterile cotton swab pre-wetted with sterile saline five times on the vestibule of both anterior nares. The swabs were immediately

placed in test tubes for further processing in the laboratory.

Nasal swabs from both nostrils were streaked on blood agar (BA) for 24 h at 37°C. Identification of Staphylococcus aureus was done by standard biochemical techniques. [18] All the confirmed Staphylococcus isolates were subsequently tested for methicillin resistance using cefoxitin disc (30µg).The Isolates were considered methicillin-resistant if the zone of inhibition was 21mm or less. [18]

The isolates of Staphylococcus were then tested for mupirocin resistance by the concomitant use of 5µg and 200µg mupirocin discs to determine low and high level resistance respectively. [19]

Criteria of zone diameter breakpoints for susceptible and resistant isolates set at > 14mm and < 13mm respectively.[19] 3 different phenotypes are:

Mupirocin Susceptible: A zone diameter of greater than or equal to 14 mm for both 5 and 200µg discs (Figure A)

Low-level resistance (MuL): Isolates that showed zone diameters less than 14 mm in the 5µg disc but more than or equal to 14 mm in the 200µg disc. (Figure B)

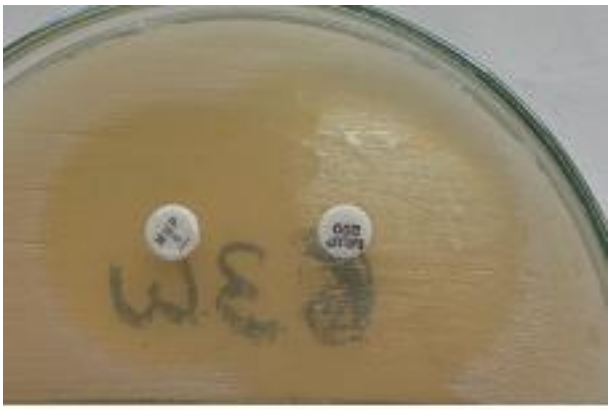
High-level resistance (MuH): Isolates with zone diameters less than 14 mm for both 5µg and 200µg (Figure C)

(Antibiotic Discs were procured from Mast group, UK). Statistical analysis was done by using (Microsoft Excel) standard normal test (z test). A p value of <0.05 was taken as statistically significant.

Results

Out of 229 patients,Staphylococcus aureus was isolated in 63(27.51%) out of which 21(9.17%) were MRSA.(Table No 1)The male patient 14 (11.66%) were more colonized when compared to female patients 7 (6.42%) but there is no statistical significance.

5(2.18%) isolates of 229 patients were Mupirocin resistance. Low-Level Mupirocin resistance was seen in 1(0.44%) isolates of MRSA and 4(1.74%) isolates of MRCoNS showed High-Level mupirocin resistance.



Mupirocin Susceptible

Low level mupirocin resistance

High level mupirocin resistance

Table No 1: Culture results of 229 nasal swabs of hospitalized patients

Isolates		No & %
Coagulase Positive Staphylococcus n=63	MRSA	21(9.17%)
	MSSA	42 (18.34%)
Coagulase Negative Staphylococcus n= 91	MRCoNS	27(11.79 %)
	MSCoNS	64(27. 95%)
Other organism*		53(23.14%)
Sterile culture		22(9.60%)
Total		229

(*Other organism- diptheroids, Candida, Mucor, Aspergillus and Gram negative bacilli)

The above table depicts MRSA of 9.17% and MRCoNS of 11.79 %

Discussion

Nasal carriage of Staphylococcus aureus plays a key role in the epidemiology and pathogenesis of infection and is a major risk factor for the development of both community-acquired and nosocomial infections. [20] A causal relationship between S. aureus nasal carriage and infection is supported by the fact that the nasal strain and the infecting strain share the same genotype. [21]

Mupirocin derived from Pseudomonas fluorescens is a topical antibiotic that has been extensively used for treating MRSA associated skin and soft-tissue infections, decreasing certain types of surgical site infections and eliminating nasal colonization of MRSA among patients and medical staff [14, 22, 1]. Prolonged, widespread or uncontrolled use and multiple courses of mupirocin are all associated with the development of mupirocin resistance [13]

In our study out of 229 patients, MRSA was isolated in 21(9.17%) and MRCoNS in 27(11.79 %). Mupirocinresistances were found in 5(2.18%) isolates of 229 patients. Low-Level Mupirocin resistance was seen in 1(0.44%) isolates of MRSA and High-Level mupirocin resistance in 4(1.74%) isolates of MRCoNS.

Prolonged or repeated topical application of mupirocin may lead to the development of a reservoir of high-level resistance determinants in CoNS which may then be transferred toS. aureus in patients on mupirocin therapy. This pattern of acquisition of plasmids bearing resistance genes either from other S. aureus strains or from coagulase-negative Staphylococcus species, a phenomenon that has been documented in vitro and in vivo.[23, 24]

The prevalence of Mupirocin resistances in our study was 2.18%. Similar were the findings of Tara babu et al, who noted twenty (3.4%) isolates were resistant to mupirocin; 17(2.9%) isolates had low-level mupirocin resistance and 3(0.5%) had high-level mupirocin resistance.[25]

Jeffrey et al observed 13.6% had a nasal swab culture result positive for MRSA. The rate of mupirocin resistance in their study population was 13.2%. (4.6% with low level mupirocin resistance and 8.6% with high level mupirocin resistance)[26]

Genotypic method such as PCR is used as the final confirmatory test for detection of mupirocin resistance but the due to limitation of funds this was not done. Another limitation of our study is the lack of data regarding outpatient use of mupirocin.

Conclusion

The prevalence of 2.18%mupirocin resistance in patients colonized with Staphylococcus spp. in the absence of widespread routine use of mupirocin is a cause of concern. Since there are not many effective alternatives for mupirocin resistant strains.

Mupirocin-resistance MRSA has also been associated with an increase in in-hospital mortality, compared to the level associated with mupirocin-susceptible MRSA.[27] Hence it is recommended that monitoring the prevalence of mupirocin resistance to be carried out to guide therapeutic and prophylactic use of mupirocin.

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