

Mupirocin resistant staphylococcus aureus nasal colonization among healthcare workers

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Mupirocin (pseudomonic acid A or bactroban) derived from *Pseudomonas fluorescens* has been available as a topical antibiotic for many years. Mupirocin specifically binds to bacterial isoleucyl-tRNA synthetase (IRS) and inhibits protein synthesis.^[1] It has been approved for use in ointment formulations that are used for the topical treatment of impetigo, and secondary wound infections caused by *Staphylococcus aureus*. In addition, it is used in a nasal formulation which is used for elimination of methicillin -resistant *S. aureus* (MRSA) from nasal colonization in adult patients and health care personnel and has been used to control outbreaks.^[2] The first report of emergence of resistance to this drug was reported in 1987, 2 years after its introduction.^[3] Since then, increasing mupirocin resistance has been reported widely in various countries, mainly because of the widespread use of mupirocin, among the community, hospital settings^[2] and as breakthrough infections as well.

Resistance of MRSA to mupirocin is categorized into two types: Low-level or intermediate resistance (MupL or MupI), with minimum inhibitory concentration (MICs) of 8–256 µg/ml, and high-level resistance (MupH), with MICs ≥512 µg/ml. A plasmid-mediated MupA gene coding a novel IRS appears to be associated with high-level resistance, while low-level resistance is associated with chromosomal point mutations associated with changes in the native IRS. High-level mupirocin resistance has been associated with failure to clear the organism from patients on mupirocin therapy.^[2] Another novel gene, MupB is also responsible for high-level of mupirocin resistance.^[4] Insertion sequences have been identified flanking the MupA gene in plasmids, which

might facilitate movement of the MupA gene between bacterial isolates. In addition, these plasmids typically carry resistance determinants to other antimicrobial agents, including macrolides, gentamicin, tetracycline, and trimethoprim which mean that mupirocin use could select for increased drug resistance in Staphylococci.^[2]

Resistance to mupirocin can be routinely detected in clinical laboratories by disc diffusion using 5 µg and 200 µg discs which can differentiate between MupL and MupH. With the 5 µg disc, isolates with low-level or high-level resistance will show no zone around the disk, whereas the zone for susceptible isolates is 14 mm. Isolates showing resistance in the 5 µg disc but with zone diameters >14 mm in the 200 µg disc are considered to be MupL strains, whereas those with zone diameters <14 mm for both 5 and 200 µg are reported as MupH strains.^[5] In addition E test can be used to know the MIC to mupirocin and polymerase chain reaction can be used to detect MupA and MupB genes.

Majority of studies evaluating mupirocin resistance from India have been done among clinical isolates of staphylococci. High-level and low-level mupirocin resistance was detected in 10 (5%) and 2 (1%) *S. aureus* strains, respectively by Gadepalli *et al.*^[6] Pulsed-field gel electrophoresis analysis of the high-level mupirocin-resistant MRSA isolates suggested clonal



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dissemination. Oommen *et al.* found that rates of MuH were found to be 2% in MRSA and 28% in methicillin-resistant coagulase-negative *Staphylococcus* spp. (MRCoNS).^[7] Another study from Chennai showed emergence of hospital-acquired MRSA with both mupirocin and inducible clindamycin resistance among MRSA ST239 isolates.^[8] Jayakumar *et al.*^[9] isolated only 5 (3.3%) In contrast higher resistance to mupirocin, that is, 18.3% was detected in MRSA by Chaturvedi *et al.*, of which 53.3% and 46.7% isolates were MuH and MuL, respectively.^[10]

Though mupirocin use in India is currently not a big problem, its use is likely to increase and could lead to an increase in resistance. Clinicians may increase the use of mupirocin to eradicate MRSA colonization in individual patients with recurrent furunculosis. Another factor that may lead to an increasing mupirocin use is a growing interest in the preoperative eradication of the *S. aureus* colonization as a strategy for preventing postsurgical infections in hospitals. Mupirocin is also increasingly been used to eradicate *S. aureus* colonization in both patients and health care personnel in response to outbreaks of staphylococcal infection and also to eradicate or suppress *S. aureus* carriage among dialysis patients as a strategy for preventing infection in the health care settings.

An increasing number of reports of MupH could mean the potential loss of one of the major treatment methods for controlling MRSA, therefore mupirocin must be used cautiously and correctly. Routine hospital screening of patients and healthcare workers for MRSA colonization may increase mupirocin use and in turn mupirocin resistance. Monitoring for mupirocin resistance whenever mupirocin is to be routinely used, could limit the emergence of resistance. However, not much literature documenting the level of resistance in nasal colonization among healthcare workers is available from India. Kaur *et al.*^[11], in this issue have evaluated mupirocin resistance in nasal carriage of *S. aureus* among

healthcare workers of a tertiary care rural hospital and reported resistance rates of 1.43% and 3.57% in MRSA and MRCoNS, respectively. Hence, a strategy of concomitant screening for MRSA and mupirocin resistance should be put in place for better outcomes. In addition, MupH strains may be treated with other alternatives like chlorhexidine, neomycin and newer agents like reptapumulin.

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How to cite this article: Watal C, Oberoi JK. Mupirocin resistant staphylococcus aureus nasal colonization among healthcare workers. *Indian J Crit Care Med* 2014;18:709-10.

Source of Support: Nil, **Conflict of Interest:** None declared.