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Evaluation of prevalence of low and high level mupirocin resistance in methicillin resistant Staphylococcus aureus isolates at a tertiary care hospital

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Original Article

Evaluation of prevalence of low and high level Mupirocin resistance in Methicillin Resistant Staphylococcus aureus isolates at a tertiary care hospital

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Abstract

Objective: To evaluate the trend of mupirocin resistance in MRSA, isolated at the Clinical Microbiology Laboratory of a tertiary care hospital.

Methods: A total of 200 MRSA strains recovered over a 2 year period from various body sites were tested using the 5 and 200µg discs of mupirocin to detect its resistance.

Results: High level and low level mupirocin resistance were detected in zero and 1 % of MRSA strains, respectively. Resistance to other non ß lactam antibiotics was also high. No MRSA strains were found to be resistant to vancomycin and tegicycline.

Conclusion: Mupirocin resistance was found to be very low among local clinical isolates of MRSA. Its judicious use to decolonize nasal carriers should be promoted among hospitalized patients to avoid further transmission and infections due to prevalent endemic MRSA strains in any health care setting. Concomitantly, regular surveillance and effective infection control initiatives are desirable to reduce the incidence of health care associated infections due to MRSA and also of mupirocin resistance.

Keywords: MRSA, Decolonization, Mupirocin, Resistance, Pakistan (JPMA 61:519; 2011).

Introduction

The role of methicillin resistant Staphylococcus aureus (MRSA) as being a major cause of nosocomial as well as community acquired infections is already known. It has been recognized that nasal colonization is a vital step in the pathogenesis of MRSA infections. In addition to self infection, colonized individuals are a potential MRSA reservoir for its spread. Hence, eradicating or suppressing MRSA colonization has remained a cost effective strategy for preventing infections and transmission.[1]

Mupirocin (pseuodmonic acid A) is a topical antimicrobial agent with excellent antistaphylococcal and antistreptococcal activity. It has already been recognized as the best and most effective topical antimicrobial agent for decolonization.[2-4] A nasal formulation is approved by the United States Food and Drug Administration for eradicating nasal carriage in adult patients as well as in health care personnel. Moreover topical application of mupirocin has also been proved to be effective in eradicating MRSA in cases of impetigo and burn wound infections, as per the recommendations by the IDSA Practice Guidelines for the Management of Skin and Soft-Tissue Infections.[5]

Studies describe two types of phenotypic resistance to mupirocin, low and high level, with MICs in the range of 8-256 µg/ml and ≥ 512µg/ml respectively. Detection and

differentiation of both types has important clinical implications. The presence of high-level mupirocin resistance (HLMR) excludes its clinical use, however low-level mupirocin resistance (LLMR) can be overcome by recommending higher than usual dosage.[6]

Resistance to mupirocin among clinical isolates of MRSA has already been reported worldwide.[7-9] Though mupirocin has been available as an over the counter drug in Pakistan, the extent of resistance in endemic MRSA isolates is still unknown. Therefore this study was planned to assess the level of mupirocin resistance through a cost effective and convenient method which can be easily adapted by any clinical microbiology laboratory.

Materials and Methods

This study was conducted in the Clinical Microbiology laboratory of the Aga Khan University Hospital, Pakistan. The hospital and its laboratory are accredited with the Joint commission of international accreditation (JCIA). The laboratory routinely participates in external quality control surveys with the College of American pathologists (CAP). This Clinical microbiology laboratory receives 400,000 specimens/year from both inpatients and outpatients from clinics and hospitals within the city as well as from all over the country via its laboratory collection points in 50 major cities and towns of Pakistan. Hence the laboratory data presented in this study represents strains prevalent across the country.

Collection of clinical isolates:

A total of 200 non duplicate clinical isolates of MRSA were randomly selected and studied between January 2008 and June 2009. These were isolated from abscess, tracheal aspirates, blood and urine. All specimens were processed in the central laboratory based in Karachi. Identification and sensitivity testing was done using standard microbiological procedure using Clinical laboratory Standards Institute (CLSI) guidelines.[10] Resistance to methicillin was determined using a 30µg cefoxitin disc (Oxoid Limited, UK), on Mueller-hinton agar according to current CLSI guideline. Staphylococcus aureus ATCC strain 33591 was used as the control.

Testing of susceptibility to mupirocin:

This was done by the disk diffusion method using 5µg and 200µg mupirocin discs (Oxoid Limited, UK) to determine low and high level resistance respectively. Criteria of zone diameter breakpoints for susceptible and resistant isolates were set at $\geq$ 14mm and $\leq$ 13mm respectively, as recommended by Finlay et al.[11] Antimicrobial resistance to 11 other antibiotics, amikacin (30µg), chloramphenicol (30µg), gentamicin (30µg), clindamycin (2µg), erthyromycin (15µg), fusidic acid (10), ofloxacin (5µg), trimethoprim-sulfametoxazole (25µg), tetracycline (30µg), vancomycin (30µg) and tegicycline (15µg) (Oxoid Limited, UK) was also determined by the disc diffusion method.

The collected data was analyzed and evaluated on the basis of averages and percentage values. The results were presented in the form of tables.

Results

Of the 200 strains of MRSA, 156 (78%) were isolated from pus or abscesses, 40 (20%) from tracheal aspirates, 3 (1.5%) from blood, and 1 (0.5%) from urine as shown in (Table). The overall frequency of low level and high level resistance to mupirocin was 1% and 0% respectively.

Table: Site of infection and frequency of resistance to mupirocin among 200 isolates of MRSA at the Aga Khan University Hospital.

Site of infection	No. of mupirocin-sensitive and resistant isolates			
	Number (%) of Isolates	Sensitivity to mupirocin (%)	LLR (5ug) (%)	HLR (20ug)
Blood	3 (1.5)	2 (66.6)	1 (33.3)	0
Pus/abscess	156 (78)	155 (99.3)	1 (0.64)	0
TA	40 (20)	40 (20)	0	0
Urine	1 (0.5)	1 (0.5)	0	0
Total	200	198 (99)	2 (1.0)	0

LLR= Low level mupirocin resistance
HLR= High level mupirocin resistance.

The 2 MRSA isolates that were found to be low level mupirocin resistant were also found resistant to other antibiotics compared to the mupirocin sensitive strains, with sensitivities limited to chloramphenicol and vancomycin.

The proportion of the MRSA strains resistant to other antibiotics was as follows: amikacin was 20%, chloramphenicol 9%, gentamicin 78.5%, clindamycin 72%, erthyromycin 84%, fusidic acid 15%, cefoxitin 100%, ofloxacin 83.5%, penicillin 100%, co trimoxazole 56%, tetracycline 72%, vancomycin 0% and tegicycline 0%.

Discussion

In this study high level mupirocin resistance was not found among clinical MRSA isolates and minimal number of isolates showed low level resistance. These findings are comparable to the resistance rates reported from neighbouring countries but are lower than the rates reported from other parts of the world.[7-9,12]

Since alternatives to mupirocin for eradicating MRSA carriage are limited, it is important to have the knowledge of prevalence of mupirocin resistance among MRSA as it will facilitate effective decolonization. Therefore it is essential for clinical laboratories not only to discriminate between susceptible and resistant strains but also to determine the level of resistance.

Keeping in view that the mupirocin resistant strains were also found to be multidrug resistant, it would be essential to eradicate these strains by decolonization rather than treatment with the limited and expensive therapeutic options available.

To the best of our knowledge this is the first report from Pakistan on mupirocin resistance in MRSA isolates. Detection of low frequency of mupirocin resistance in endemic isolates does not advocate its indiscriminate and widespread usage. Experience had shown that this leads to emergence of resistance. To keep the resistance in check, judicious usage will have to be implemented. This includes targeted prophylaxis rather than general prophylaxis; only in cases where isolate is sensitive to mupirocin. For this reason, nasal eradication should only be recommended in patients and health care workers under selective circumstances, such as in MRSA outbreaks. Other valid uses are in high risk patient population such as those with diabetes mellitus, peripheral vascular disease, indwelling tubes, decubitus ulcers or multi functional disabilities.

In this study we used disc diffusion method for detection of low and high level mupirocin resistance. The "gold standard" method for detection of mupirocin resistance is MIC determination by the agar dilution method. In developed countries, molecular techniques also have been utilized for the detection of the mupA gene. For a resource limited country, molecular methods add to the burden of growing costs of diagnosis and management. Additionally, agar dilution method proves to be expensive and laborious for routine application. This makes the disc diffusion susceptibility test a cheaper and simple alternative method for its routine use.

The sensitivity and specificity of this method has already been evaluated by Malaviolle et al previously.[13] They found that 5µg mupirocin disc has a sensitivity of 100% and a specificity of 98.1% whereas the 200µg mupirocin disk has a sensitivity of 100% and specificity of 92.3% to differentiate HLMR from LLMR. Malaviolle stated that the most accurate disk diffusion test results were obtained with the 20µg mupirocin disk test by using their proposed tentative interpretative breakpoints or with the concomitant use of 5µg mupirocin and 200µg mupirocin disks.[13] Hence the disc diffusion method could help in identifying low level mupirocin strains in a fast feasible way.

This literary proof and our study being the first report of mupirocin resistance from the county are the biggest strengths of our study. But the small sample size and lack of a confirmatory test do prove to be definite weaknesses. Studies with larger sample size will be required to explore the prevalence mupirocin prevalence further.

Hence, the assessment of prevalence of mupirocin resistance can be utilized as an important epidemiological tool in institutions before the introduction of mupirocin decolonization as a part of their infection control measures, as well as an indicator to monitor mupirocin's judicious usage.

In conclusion, only low level resistance was found in 1% of MRSA. It is recommended as a primary drug for nasal MRSA eradication.

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