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Mupirocin and vancomycin susceptibility in MRSA colonising anterior nares of patients scheduled for cardiac surgery

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Abstract

Background: Mupirocin has been recognised as the best and the most effective topical antimicrobial agent for decolonisation. With widespread use of mupirocin for decolonisation, increasing number of MRSA have developed resistance to mupirocin.
The society of thoracic surgeons recommends a glycopeptide (vancomycin) for cardiac surgical prophylaxis in patients known to be colonised with MRSA. Development of resistance to vancomycin among MRSA is a cause of concern.
Currently, there is very limited data regarding prevalence of mupirocin and vancomycin resistance in MRSA colonising the anterior nares of patients undergoing high risk surgeries.
Aims: To assess the prevalence of mupirocin and vancomycin resistance in MRSA colonising anterior nares of patients undergoing cardiac surgical procedures in our tertiary care hospital.
Material and Methods: Screening for MRSA was done by disc diffusion method using Cefoxitin disc. Screening for MuL and MuH was done by disc diffusion method using mupirocin disc of strength 5 µg and 200 µg respectively. Screening for detection of reduced susceptibility to vancomycin was done by Agar Dilution method. The MIC of mupirocin and vancomycin determined by Agar dilution method.
Results: Twenty two percent of MRSA isolates had MuL and eleven percent had MuH. One of the mupirocin sensitive MRSA, had a presumptively reduced susceptibility to vancomycin by BHI agar screen method.
Conclusion: Screening of patient populations for MRSA, MuH and VISA/VRSA colonisation, especially those undergoing high risk surgeries should be considered, to prevent self infection and nosocomial transmission of resistant strains.

Keywords: anterior nares, Colonisers, cardiac surgery, MRSA, mupirocin resistance, vancomycin resistance.

Introduction

Surgical site infection of the sternal wound and underlying mediastinum following cardiac surgical procedures is commonly caused by Staphylococcus aureus (S.aureus). Nasal colonisation with S. aureus has been recognized as a vital step in the pathogenesis of such infections. Patients colonised with Methicillin resistant Staphylococcus aureus (MRSA) are nearly ten times more prone to have a health care related MRSA infection when compared to non-colonised patients.[(1)] Apart from self-infection, colonised individuals act as potential reservoir for nosocomial transmission of the resistant strain.[(1,2)] Eradicating or suppressing MRSA colonisation has been used as a cost effective strategy for preventing infections and spread.[(1)] Mupirocin has been widely available for use as a topical antibiotic agent for many years and has been recognised as the best and the most effective topical antimicrobial agent for decolonisation.[(3)] With the pressure to prevent MRSA infections and widespread use of mupirocin for decolonisation, increasing number of MRSA have developed resistance to mupirocin.[(1)]

The emergence of mupirocin resistance among S. aureus has been clearly defined in many parts of the world: Spain 11.3%, USA 13.2%, Trinidad and Tobago 26.1%, India 6% and it appears to be increasing worldwide.[(4)]

Mupirocin susceptibility among S. aureus has been described under three categories which includes mupirocin sensitive, Low level mupirocin resistance (MuL) and high level mupirocin resistance (MuH). The MIC ≤4µg/ml, 8-256µg/ml and 512µg/ml represent mupirocin sensitive, MuL and MuH respectively.[(1)] MuH is associated with clinical failure and hence the presence of high level Mupirocin resistance excludes its clinical use. However MuL can be overcome by recommending higher than usual dosage.[(5)]

Apart from using mupirocin for the preoperative therapy to eliminate the nasal colonisation with S. aureus, the society of thoracic surgeons recommends a glycopeptide (vancomycin) for cardiac surgical prophylaxis in patients known to be colonised with MRSA. Development of resistance to vancomycin among MRSA is a cause of concern, as very few therapeutic options exist for treatment of such infections.[(6)]

Currently, there is very limited data regarding prevalence of mupirocin and vancomycin resistance in MRSA colonizing the anterior nares of patients undergoing high risk surgeries. This study was conducted to assess the prevalence of mupirocin and vancomycin resistance in MRSA isolated from anterior nares of patients undergoing cardiac surgical procedures in our tertiary care hospital.

Material and Methods

This study was conducted in the Department of Microbiology of our tertiary care hospital over a period of one and half years from June 2014 to December 2015, after acquiring approval from the institutional ethical committee (letter no. INST.EC/E.C/123/2013-14).

One hundred patients admitted to cardiac surgical unit were included in the study. Anterior nasal swabs were collected from these patients, using sterile cotton swabs and sent to Microbiology laboratory. The samples were inoculated on to Blood agar and MacConkey agar and incubated overnight at 37ºC. The isolates were identified by standard Microbiology procedures like colony morphology, Gram stain, Catalase test, and slide coagulase and tube coagulase test.[7]

Screening for MRSA was done by CLSI recommended disc diffusion method using Cefoxitin disc (30 µg). The Cefoxitin disc was placed on the lawn culture of the test organism on Mueller Hinton agar. The plates were incubated at 35ºC for 16-18 hours. The zone of inhibition around the disc was examined and the diameter of the zone measured using a ruler. The isolates having a zone size of ≥22 mm were interpreted as Methicillin sensitive and ≤ 21mm as Methicillin resistant.[8]

Screening for MuL and MuH was done by disc diffusion method using mupirocin disc of strength 5 µg and 200 µg respectively. The plates were incubated for 24 h at 37°C. The zone of inhibition was carefully examined with transmitted light. Isolates with a zone of inhibition of ≤ 14mm around the 5 µg were interpreted as MuL. Isolates with no zone around 5µg and 200 µg discs were interpreted as MuH.[9]

The MIC of mupirocin for the isolates that showed MuL and MuH by disc diffusion method was determined by CLSI recommended Agar dilution method on Mueller Hinton Agar with a final concentration of 2- 1024 µg/ml of mupirocin.[8]

Screening for detection of reduced susceptibility to vancomycin was done by CLSI recommended Agar Dilution method. The test organism was inoculated into peptone water, so as to obtain turbidity equivalent to 0.5 McFarland standards. A spot inoculation with 10 µl of the inoculum, using a micropipette was made on BHI agar containing 6 µg/ml of vancomycin. The plates were then incubated at 37ºC for 24 hours and examined carefully with transmitted light for growth. Presence of a thin film or growth of single colony was taken as presumptive reduced susceptibility to vancomycin. Enterococcus faecalis ATCC 29212 and Enterococcus faecalis 51299 were used as controls.[8]

Determination of MIC of Vancomycin for the isolates which showed a presumptive reduced susceptibility on screening was done by CLSI recommended agar dilution method on Mueller Hinton Agar with a final concentration of 0.5 to 64 µg/ml of vancomycin.[8]

Result

A total of one hundred patients scheduled for coronary artery bypass grafting (CABG), valve replacements and septal defect closures were included in the study.

Out of the hundred patients screened, 51 (51%) patients were found to be colonised with Staphylococcus aureus. Methicillin resistance was found in 9 (9%) of the patients. Of the 9 MRSA, mupirocin resistance was found in 3 (33.33%) isolates on screening by disc diffusion method. Two (22.22%) of the three mupirocin resistant MRSA isolates had MuL and one isolate (11.11%) had MuH. The isolate that had MuH by disc diffusion was found to have a MIC of 1024µg/ml. The two isolates that had MuL were found to have a MIC of 32µg/ml and 128µg/ml. All of these three isolates were susceptible to vancomycin.

One of the mupirocin sensitive MRSA, had a presumptively reduced susceptibility to vancomycin by BHI agar screen method. On testing for MIC of vancomycin, the isolate was found to have a MIC of 8 µg/ml and was interpreted as Vancomycin Intermediate Staphylococcus aureus (VISA) as per CLSI guidelines.

Discussion

A short term preoperative therapy (5 days) with mupirocin is recommended for the elimination of Staphylococcal nasal colonisation in patients undergoing cardiac surgery.[6] It is also used for treating skin infections in general population. Mupirocin resistance was first reported from the UK in 1987. Since then, there has been an increase in mupirocin resistance among S.aureus worldwide.[10] The results of several studies show that the prevalence MuH in India among MRSA from clinical samples range from 0 to nearly 40%.[11-16]

There are very few studies which have been carried out to assess the mupirocin resistance among MRSA colonizing the anterior nares. In a study from Chicago, of the 591 MRSA isolates from the anterior nares of patients admitted to a tertiary care medical centre, 25 (3.4%) were resistant to mupirocin, of which 2.9% and 0.5% had MuL and MuH respectively.[17] Caierao et al. reported MuH among 4.84% of MRSA colonising the anterior nares of the patients admitted to Intensive care unit, while 13.33% of the isolates were found to have MuL.[18] In yet another study on mupirocin resistance among Staphylococcus aureus isolated from the anterior nares of health care providers, MuH was reported in two of the nine MRSA isolates accounting for 22.23%.[19]

In the present study 11.11% of MRSA are found to be have MuH. MuL was detected in 22.22% of MRSA in our study. MuL was more prevalent than MuH among MRSA and this is in conjunction with the previously published studies. However Jones JC et al. reported a higher prevalence (8.6%) of MuH than MuL (4.6%), in patients colonised with MRSA in a surgical intensive care unit.[20]

Co-existence of Methicillin resistance and MuH among the isolates raises concern, as mupirocin is used as a topical agent for decolonisation in patients harboring MRSA in their anterior nares. Presence of MuH among S.aureus has been associated with failure of decolonisation in patients on Mupirocin therapy, while isolates MuL can still be cleared with mupirocin therapy.(1)

A β-lactam antibiotic is recommended as an antibiotic of choice for standard cardiac surgical prophylaxis, in population not having a high incidence of MRSA. A combination of a β-lactam antibiotic with a single or two doses of a glycopeptides (vancomycin) may be used for prophylaxis in a setting of either high prevalence of MRSA in the institution, a presumed or known staphylococcal colonisation, patients susceptible to colonisation or a surgery for a patient having prosthetic valve. Development of resistance to vancomycin in Staphylococcus is an important issue to be considered while using vancomycin for routine prophylaxis.(6) Only few studies from India have reported VRSA/VISA from clinical isolates. Reports of Colonisation with VISA /VRSA are extremely rare. Banerjee T et al have reported colonisation of anterior nares with VISA among ICU patients. They found four strains of MRSA had vancomycin MIC in the range of 6-8µg/ml for vancomycin.(21) In the present study one MRSA strain had vancomycin MIC of 8µg/ml and was interpreted as VISA. Although VISA strains are rare causes of infection, they are as troublesome as VRSA when considering the treatment point of view.

Though all these studies, including our study have detected MuL, MuH and VISA among MRSA colonising the anterior nares, these are all isolated reports from different geographical areas with different study populations like health care workers, patients admitted to surgical ICU's, care givers for patients in the post-operative ward etc. Data on nasal colonisation with mupirocin resistant and vancomycin resistant MRSA in patients scheduled for high risk surgeries like cardiac surgery is very limited. Large scale studies on mupirocin resistance among MRSA colonisers and its clinical relevance is also lacking.

Conclusion

We conclude that screening of patient populations for MRSA, MuH and VISA/VRSA colonisation, especially those undergoing high risk surgeries like cardiothoracic surgeries should be considered in order to prevent self infection and nosocomial transmission of resistant strains.

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