Reduced susceptibility to Vancomycin in methicillin resistant Staphylococcus aureus: a time for action

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ABSTRACT

Infections by Methicillin resistant Staphylococcus aureus (MRSA) is an often encountered therapeutic challenge. The problem is accentuated by the emergence of MRSA strains which are resistant to Vancomycin, the recommended agent for the treatment of MRSA infections. We therefore carried out this study to determine the MIC values of vancomycin for the MRSA isolated from different clinical specimens in Nepal Medical College. MICs were determined by agar dilution method. Out of the 82 MRSA isolates tested, 18 showed MIC of 2μg/ml and 29 isolates had MIC of 1μg/ml and 35 isolates had MIC of 0.5 μg/ml. Although none had a MIC in the intermediate or resistant zone, 18 (2.9%) had MIC in the upper limit of the sensitive zone which is a matter of concern and calls for prompt preventive actions.

Keywords: Methicillin Resistant Staphylococcus aureus, Vancomycin, Minimum Inhibitory Concentration

INTRODUCTION

Staphylococcus aureus is one of the important human pathogen. Infections by MRSA have a higher morbidity and mortality and are a treatment challenge. Vancomycin, a glycopeptide antimicrobial, is the first line treatment for infections caused by MRSA. Breakpoints have been developed by Clinical Laboratory Standards Institute (CLSI) to define vancomycin susceptibility for S. aureus. Until 2006, the Minimum Inhibitory Concentration (MIC) for vancomycin Intermediate Staphylococcus aureus (VISA) was defined as 8 to 16 μg/ml by the CLSI. However, when the vancomycin MIC was 4 to 8 μg/ml high rate of treatment failure occurred. As a result, in 2006, CLSI modified the breakpoint and currently vancomycin susceptibility is considered when the MIC is 2μg/ml. MRSA isolates with MIC 16 μg/ml are considered vancomycin resistant and with MIC of 4 to 8 μg/ml are intermediate. Even when the MIC value is at the limit of the susceptibility range there may be presence of heteroresistance which may result in clinical failure. High vancomycin MIC also correlates with resistance to several other classes of antimicrobial agents. This evolutionary trend may cause potential failure of treatment of S. aureus infections which necessitate further research and regulation of health policies.

MATERIALS AND METHODS

This study was carried out from September 2012 to April 2013. Eighty two clinical isolates of MRSA as confirmed by cefoxitin (30 μg) disc diffusion test were tested for the MIC for vancomycin by agar dilution method as recommended by the CLSI. The test organisms were inoculated in nutrient broth and incubated for 4 hours at 37 ºC. The turbidity was adjusted to 0.5 McFarland unit. It was then inoculated into Muller Hinton agar plates supplemented with 2% NaCl and containing different concentrations of vancomycin (0.25 μg/ml, 0.5 μg/ml, 1 μg/ml, 2 μg/ml, 4 μg/ml, 8 μg/ml, 16 μg/ml and 32 μg/ml). After overnight incubation at 37°C the MIC for each isolate was noted.

RESULTS

Among the 82 MRSA isolates tested, all had MIC for vancomycin within the susceptible range. However, MIC towards the upper limit of the susceptible range (2μg/ml) was found for 21.9% of the isolates (Table-1).

<table>
<thead>
<tr>
<th>MIC (μg/ml)</th>
<th>Number of isolates (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>0 (0)</td>
</tr>
<tr>
<td>0.5</td>
<td>35 (42.68)</td>
</tr>
<tr>
<td>1</td>
<td>29 (35.3)</td>
</tr>
<tr>
<td>2</td>
<td>18 (21.9)</td>
</tr>
</tbody>
</table>

According to the source of origin, inpatients accounted for higher number of MRSA and also higher number of strains with higher MIC of vancomycin (Table-2).

<table>
<thead>
<tr>
<th>MIC of vancomycin (μg/ml)</th>
<th>Inpatient</th>
<th>Outpatient</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.5</td>
<td>17</td>
<td>10</td>
</tr>
<tr>
<td>1</td>
<td>20</td>
<td>11</td>
</tr>
<tr>
<td>2</td>
<td>13</td>
<td>11</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>32</td>
</tr>
</tbody>
</table>
DISCUSSION
Vancomycin was introduced clinically in 1958 for the treatment of gram positive bacteria. Its use has increased dramatically due to the increase in the prevalence of methicillin resistance in both coagulase negative staphylococci and Staphylococcus aureus. The first report of decreased susceptibility to vancomycin in Staphylococcus aureus (VISA) came in 1997 from Japan. Since then reports from around the world are emerging. No vancomycin intermediate or resistant strains were found in the current study. Nevertheless, it is worrisome that 22% of the strains had the MIC in the higher limits of microbial susceptibility. Clinical failure due to hetero resistant strains are likely in infections caused by strains with elevated MIC. In a study 66 patients with vancomycin MICs of ≥1.5 mg/liter had a 2.4-fold increase in failure compared to patients with MICs of ≤1.0 mg/liter. Although some studies from abroad have reported the MIC for vancomycin for MRSA similar to our study (2μg/ml), others have found different prevalence of VISA and VRSA among their clinical isolates. Two strains of VISA and six strains of intermediate (VISA) were reported from Northern India. Song et al 11 reported 6.3% VISA among the MRSA and Thati et al 12 reported 1.9% VRSA among their clinical isolates. No VISA or VRSA have been reported as yet from Nepal. However, this study was prompted by the author’s experience in tertiary care hospital in Lalitpur, Nepal where 9.5% prevalence of VISA among the MRSA was recorded. The possible mechanism behind the vancomycin resistance in staphylococcal isolates could be the thickening of cell wall in resistant isolates. Recent exposure to vancomycin within one month of the current infection, prior recent hospitalization, surgery within last 6 months and those with blood stream infections prior to admission in intensive care unit may result in MRSA infection with higher vancomycin MIC.

VRSA are resistant to large number of currently used antimicrobial agents compromising the treatment options and increasing morbidity and mortality. In our study all the MRSA were multidrug resistant and among them a large number of isolates with MIC of vancomycin 2 μg/ml were resistant to higher number of drugs. The emergence of VRSA/VISA may be due to selection pressure. The huge scale development and subsequent spread of resistance to vancomycin is a fearsome threat to the already challenging therapy of MRSA. Strong organizational support and multiple strategies are required for the containment and prevention of MRSA and thus of VISA/VRSA. Infection control practices that have been documented to reduce the MRSA spread include: adherence to hand hygiene, contact precautions for patients with MRSA, active surveillance cultures, education, effective environmental cleaning and communication between healthcare workers and patients with MRSA.

Thus this study is an early alarm to all stakeholders to take adequate and timely measures to stop the emergence of VISA/VRSA. Strict infection control practices must be religiously followed. Regular education of the staff and monitoring of compliance are must. Since the 30mg vancomycin disc diffusion test often misclassifies the intermediately sensitive isolates as fully susceptible, microbiology laboratories must determine MICs for vancomycin and communicate the results to the treating doctors. "A stitch in time saves nine"- now is the time for appropriate action.

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Effectivity of Nd yag pi in treatment of acute primary angle closure glaucoma

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ABSTRACT
A Prospective hospital based study to note the efficacy of Nd Yag Peripheral Iridotomy (PI) in the treatment of acute primary angle closure glaucoma was carried out in Nepal Eye Hospital from Jan 2007 to Jan 2008. All the Patients (n=50) with acute primary angle closure glaucoma admitted to our hospital were selected for the study. Patients with secondary angle closure glaucoma were excluded. It is more common in age of 56-65 years (20%), in females (70%), and in tibetoburman ethnic group (56%). Mean duration of presentation to hospital was 5 days (22%) (Range 4-7 days). Grade 1 Angle closure was present in 74%. All 50 patients (100%) with AACG had undergone Yag PI. Out of 50 patients, 11 patients (22%) were surgically operated i.e. trabeculectomy. Among 11, 1 patient (9%) who had undergone trabeculectomy had presented with acute on chronic angle closure glaucoma. Majority of cases (66%) presented with visual acuity (VA) 1/60-PL at the time of presentation and the Intraocular pressure (IOP) in affected eye was 31-40 mmHg (42%). After performing Yag PI the mean visual acuity in the affected eye at the time of discharge was 6/60 (20%) and the IOP was 12 mmHg (40%). Prolonged duration of attack, elderly age, acute on chronic angle closure glaucoma, very high IOP at presentation, patients needing repeat Yag PI were found to have failure Yag PI. In this study 78% eyes had controlled IOP following Yag PI.

Keywords: Acute primary angle closure glaucoma, Nd Yag PI, IOP control.

INTRODUCTION
Glaucoma is one of the leading causes of irreversible blindness in the world. It affects approximately 65 million people around the world and an expected 7.5 million are blind due to this disease. It is the second most common cause of blindness worldwide.1 It is estimated that half the blindness from glaucoma in the world is caused by angle closure and it is one of the causes of bilateral blindness.2 Although it affects less than 10 percent of patients with glaucoma, acute narrow angle glaucoma is the most serious form of the disease. In the United States, fewer than 10% of glaucoma cases are due to angle-closure glaucoma. In Asia, angle-closure glaucoma is more common than open-angle glaucoma. In Acute angle closure glaucoma (AACG) the iris quickly covers the entire or almost the entire trabecular meshwork leading to sudden symptomatic elevation of intraocular pressure. AACG predominately affects females because of their shallower anterior chamber. As people age, the lens of the eye enlarges and pushes the iris forward, thus increasing the risk for angle-closure glaucoma. Acute angle-closure glaucoma is an emergency because optic nerve damage and vision loss can occur within hours of the onset of the problem. There is irreversible damage to optic nerve head and visual field loss in cases of glaucoma leading to irreversible blindness. So more emphasis has to be given for early diagnosis. Acute angle closure glaucoma is ocular emergency and receives distinction due to its acute presentation, need for immediate treatment. Rapid diagnosis, immediate intervention have profound effects on patient outcome and morbidity. In Nepalese population the effectivity of Yag PI has not been studied till yet. Therefore this study would provide baseline suggestion in the management of AACG. This study was to assess the demography, presenting signs and symptoms, IOP control, Improvement of visual acuity, effectivity of Yag PI and various causes of ineffectiveness of Yag PI.

MATERIALS AND METHODS
Fifty patients presenting to the glaucoma department of Nepal Eye hospital with uniocular AACG during a 24 month period were included in the study. With the verbal informed as well as written consent from the patients with AACG were included in the study. Patients with secondary angle closure glaucoma like phacomorphic glaucoma, malignant glaucoma were excluded. Initial examination included assessment of Snellen corrected visual acuity, intraocular pressure by Applanation tonometry, gonioscopy by Goldmann single mirror goniolens, Anterior segment was examined by Haag Striet 900 slit lamp and fundus examination by 90D lens.