Original Research

CAN CLINDAMYCIN ALSO BE USED AS AN EFFECTIVE DRUG IN METHICILLIN RESISTANT STAPHYLOCOCCI AS AN ALTERNATIVE TO VANCOMYCIN

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Abstract

Introduction: Staphylococcus is one of the most common bacteria causing hospital-acquired infections, increasing cost of treatment and hospital stay. Antibiotic resistance in Staphylococcus has become a big problem among hospitalized patients. Vancomycin and Linezolid is the only therapeutic option in Methicillin resistant Staphylococcus infections but there are some adverse effects of these drugs. Therefore it is necessary to find out the most effective antibiotic other than vancomycin against methicillin resistant *Staphylococci.* **Aims and Objectives:** To evaluate the utility of commonly used drugs against *Staphylococcus* and also investigated the prevalence of erythromycin-induced clindamycin resistance along with antibiotic resistant pattern of *Staphylococcus*. **Material and Methods:** Total 450 non repeated *Staphylococcus* strains were isolated from different clinical samples and *S.aureus* identified by specific biochemical tests and Antibiotic susceptibility testing and D- zone test were carried out as per CLSI guidelines. **Result:** Among 450 Staphylococcus strains, 360 were *S.aureus* and 90 were coagulase negative Staphylococcus (CONS) in which 58.33% were MRSA 68.89% were MR-CONS. 99.04% MRSA and 100% MR-CONS were ciprofloxacin resistant and only 4% and 3.22% were Methicillin sensitive S.aureus and CONS respectively. Total 168 (46.67%) S. aureus and 47 (52.22%) CONS were clindamycin resistant out of which 92 (25.56 %) S. aureus and 3 (3.33 %) CONS were detected as inducible clindamycin Resistant. All inducible clindamycin resistant isolates were also resistant to cefoxitin (methicillin resistance) and ciprofloxacin and erythromycin. All staphylococcus were also sensitive to tigecycline, vancomycin and linezolid. All cefoxitin (methicillin) sensitive were sensitive to amikacin, gentamicin, tobramycin, netilmycin, tigecycline and vancomycin. **Conclusion:** Clindamycin and ciprofloxacin are highly resistance to Staphylococcus not suitable alternative drugs for the treatment of hospital acquired Staphylococcus infections because of high level resistance. Tigecycline, Amikacin and Netilmycin was found the most effective alternative drug for treatment

Key Words: Clindamycin, Methicillin Resistant Staphylococci, Vancomycin

Introduction

Staphylococcus is group of gram positive bacteria causing a number of diseases, ranging from mild skin infection to serious endocarditis.[1] It is the most common bacteria causing hospital-acquired infections, increasing cost of treatment and hospital stay. Antibiotic resistance in Staphylococcus has become a big problem among hospitalized patients. The increasing prevalence of methicillin resistance among *Staphylococci* has limited the use of penicillins and cephalosporins for the treatment. There is limited option for the treatment of methicillin resistant *Staphylococci* with vancomycin and linezolid, however their high cost, intra-venous drug administration and adverse drug reaction limit the use. [2]

Fluoroquinolone antibiotics could be an alternative to vancomycin for the treatment of methicillin resistant *Staphylococci* as this group of antibiotic has low cost and good oral absorption. Increasing number of Fluoroquinolone resistance among methicillin resistant *Staphylococcus* forced the investigators to look for antibiotics.[3,4]

Clindamycin could be an alternative to Vancomycin as it has good oral absorption and accumulation in abscesses. *Staphylococcus* can be resistant to Erythromycin through either *erm* or *msr*A gene. *Staphylococcus* having *erm* gene may possess inducible Clindamycin resistance. In disc diffusion antibiotic susceptibility testing inducible Clindamycin may appear susceptible to Clindamycin. Routine detection of inducible Clindamycin resistance in clinical isolates can decrease the cost of treatment and prevent the unnecessary use of antibiotics.[5]

Erythromycin resistant in Staphylococcus is due to either erm or msrA genes. Staphylococcus with erm-mediated erythromycin resistance may possess inducible clindamycin resistance but may show susceptiblity to clindamycin by disc diffusion method. Inducible clindamycin resistance can be detected by a simple D-zone test. If this test is come in routine laboratory test, clindamycin can be safely and effectively used in only truly clindamycin susceptible cases.[6]

Emergence of resistance among *Staphylococci* to various antibiotics has created problem to choose appropriate antibiotic for empirical treatment. Study on antibiotic resistance among methicillin resistant *Staphylococci* along with detection of inducible clindamycin has not been done in Kanpur. Therefore, the present study was undertaken to find out the most effective antibiotic other than vancomycin against methicillin resistant *Staphylococci*.

In this study we investigated the prevalence of erythromycin-induced clindamycin resistance along with antibiotic resistant pattern of Staphylococcus isolated from clinical samples.

Aims and Objectives

This study aimed to evaluate the utility of commonly used drugs against Staphylococcus.

Materials and Methods

Specimen

A total of 450 Staphylococcus strains were obtained from pus, blood, CSF, sputum and urine sample from different clinical departments of Rama Medical College and Hospital between July 2014 and January 2015.

Specimen processing

All samples except blood were inoculated in Thioglycolate media, incubated for 4-6 hrs and subculture on Blood agar and MacConkey's agar.

Identification of organism The obtained organisms were identified by observing colony character, by microscopy using gram stain and by using specific biochemical tests (catalase test and slide coagulase test, tube coagulase and mannitol fermentation test).[7]

Antibiotic sensitivity test

Antibiotic susceptibility test and D- zone test were carried out as per CLSI guidelines. The D-zone test was performed by double disk diffusion method, placing erythromycin (15 µg) and clindamycin (2 µg) disks 15 mm apart on the same plate **[Fig.1]**. Staphylococcus aureus American Type Culture Collection (ATCC) BAA-977 (having inducible ermA gene; inducible clindamycin resistance) and S. aureus ATCC BAA-976 (having inducible msrA gene; efflux erythromycin resistance) were used as quality control strain. For antibiotic susceptibility test 0.5 MacFarland bacterial suspension was prepared and performed by Kirby- Bauer disk diffusion method on Mueller-Hinton agar. Methicillin resistance detection was done in Staphylococcus by cefoxitin (30µg) disk diffusion method. All staphylococcus were tested for penicillin, oxacillin, cefoxitin, ciprofloxacin, tetracycline doxycycline, tigecycline, amikacin, gentamicin, tobramycin, netilmycin, erythromycin resistance.[6,7]

Result

A total of 450 Staphylococcus strains were isolated from various clinical samples among which 360 were identified as Staphylococcus aureus in which 210 (58.33%) were MRSA and 90 as Coagulase Negative Staphylococcus (CONS) in which 62 (68.89%) were Methicillin resistant CONS(MR-CONS).**[Fig 2- Fig 3]** Out of 210 MRSA isolates, ciprofloxacin resistance was seen in 208 (99.04%) isolates. All 62 (100 %) methicillin resistant CONS were also resistant to ciprofloxacin. Resistance to ciprofloxacin was seen in only 6 (4.00 %) Methicillin sensitive Staphylococcus aureus(MSSA) and 2 (3.22%) Methicillin sensitive Coagulase Negative Staphylococcus(MS-CONS).**[Fig 4]** Total 168 (46.67%) S. aureus and 47 (52.22%) CONS were resistant to clindamycin out of which 92 (25.56 %) S. aureus and 3 (3.33 %) CONS were detected as inducible clindamycin Resistant. All inducible clindamycin resistant isolates were also resistant to cefoxitin (methicillin resistance), ciprofloxacin and erythromycin. All staphylococcus were sensitive to tigecycline, vancomycin and linezolid. Resistance to aminoglycoside was seen in only cefoxitin (methicillin) resistant staphylococcus Out of 210 MRSA, 17 (8.50%) were resistant to amikacin, 19 (9.04%) were resistant to

netilmycin, 23 (10.95%) were resistant to gentamicin and 28 (13.33%) were resistant to tobramycin. All cefoxitin (methicillin) sensitive were sensitive to amikacin, gentamicin, tobramycin, netilmycin, tigecycline and vancomycin.**[Fig 5-Fig 6]**

Fig 1: D-ZONE TEST

FIG 2: DISTRIBUTION OF STAPHYLOCOCCUS

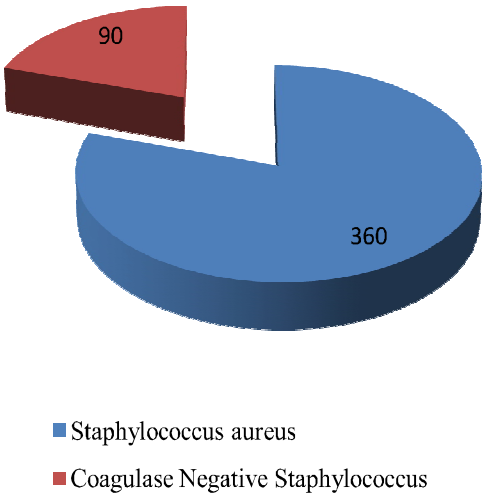


FIG 3: METHICILLIN RESISTANCE

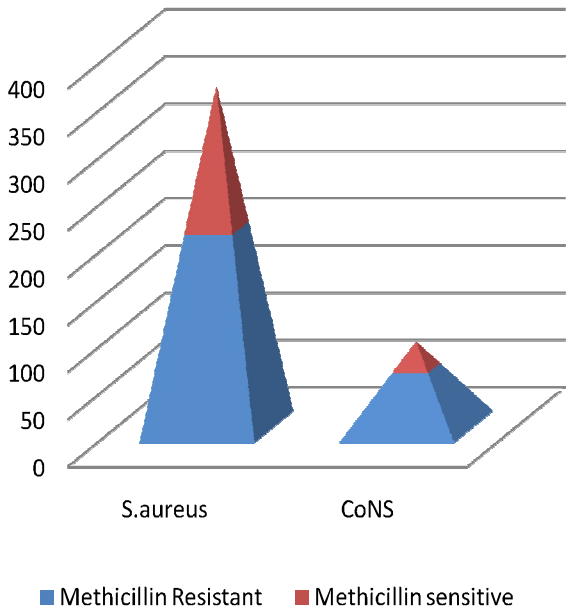


FIG 4: CIPROFLOXACIN RESISTANCE

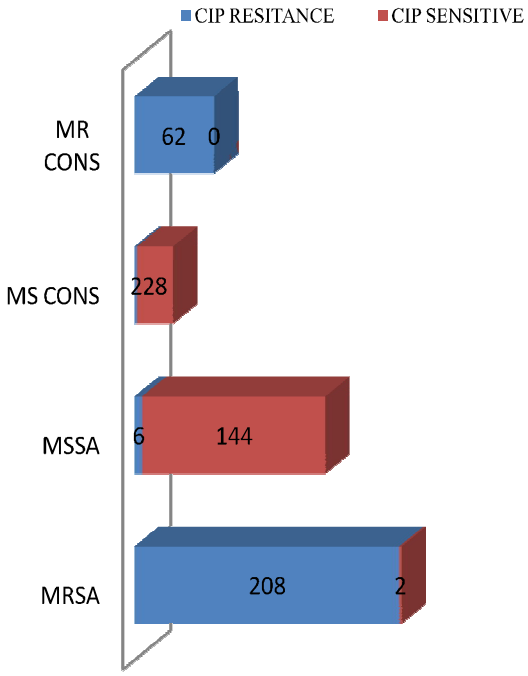


FIG 5: ANTIBIOTIC RESISTANT PATTERN OF S. AUREUS

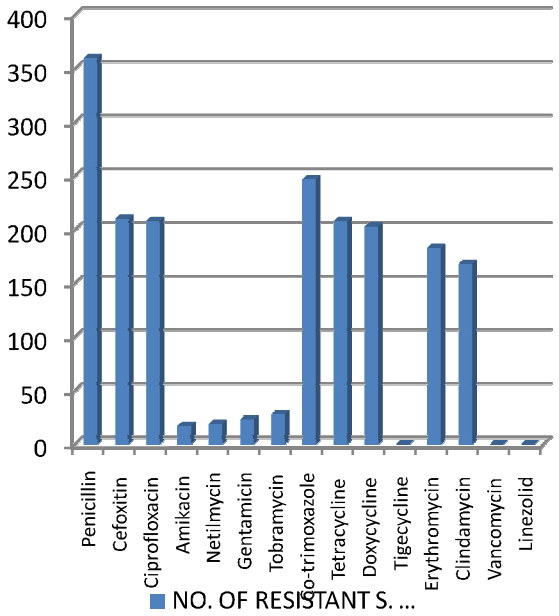
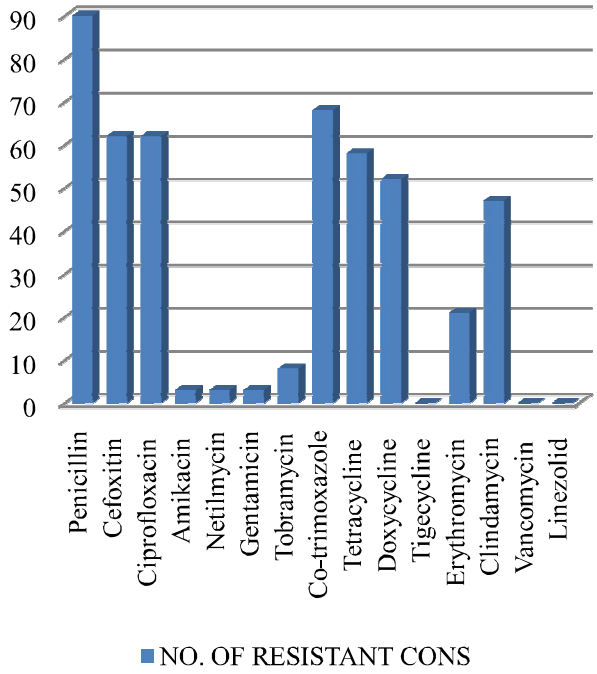


FIG 6: NO. OF RESISTANT CONS



Discussion

During the last four decade, the epidemiology of Staphylococcus has been altered by the emergence of methicillin resistance. Methicillin resistant Staphylococcal infection has been increasing worldwide; however, there are CONSiderable differences from time to time and place to place studies.[5] In this study, 58.33% of the total isolates of the *S. aureus* and 68.2% CONS were found methicillin resistant. Previous studies have shown significantly less prevalence of methicillin resistant Staphylococcus reported from various parts of the India ranging from 30-44%.[1,8,9] The present study showed an alarmingly high percentage of methicillin resistance infection in this hospital. Such a high prevalence of MRSA may be due to several factors. The indiscriminate use of antibiotics, sub-therapeutic dosage, improper monitoring in the administration of various antibiotics, patient's compliance, and unethical treatment before visiting the hospital might have been contributing factors.[1,8]

Comparison of antibiotic resistance pattern among methicillin-resistant and methicillin-sensitive *Staphylococcus* isolates showed that resistance to ciprofloxacin as well as to other antibiotics tested was significantly higher in methicillin-resistant isolates than in methicillin-sensitive isolates. Resistance of methicillin-resistant Staphylococcus to cotrimoxazole (97%), and erythromycin (61.7%) was more than aminoglycosides. High resistance to these drugs has also been reported in other studies.[10,11] Erythromycin induced clindamycin resistance was

observed in 23%, which is more than other studies, reported from different part of India. Inducible clindamycin resistance was observed significantly more in methicillin-resistant Staphylococcus isolates.[12,13]

The increased number of multiple antibiotic-resistant in methicillin resistant Staphylococcus have gained much attention over the years.[10] Fluoroquinolone compounds such as ciprofloxacin, first synthesized in the 1980s, were found to have extended antimicrobial spectra that included gram-positive bacteria, and were hoped to be useful in eradicating methicillin resistant Staphylococcus.[4] However, since these compounds became available for clinical use, resistance among methicillin resistant Staphylococcus has been reported from different parts of the world.

In this study, significantly higher percentage (92.5%) of MRSA isolates showed resistance to ciprofloxacin. Similar results of over 90% resistance have been reported in some studies reported from India. [12] Neeta D Gade et al. reported that maximum resistance (92.5 %) to ciprofloxacin was observed in MRSA.[1] Resistance to ciprofloxacin had steadily increased from 39% in 1992 to 68% in 1996 reported by Mehata AP *et al.*[14] In such conditions ciprofloxacin may not be useful drug for empirical treatment of nosocomial infection.

In the present study, 80.4% MRSA showed resistance to ciprofloxacin. This different patterns and levels of resistance may arise following exposure to different fluroquinolones, and different strains may produce different types of resistance.[15]

Methicillin and ciprofloxacin resistant Staphylococcus are also resistance to other antibiotics, like aminoglycosides.[16,17] In such situations clindamycin may be better option, as it is available in both intravenous and oral formulations and drug distributes well into the tissue except central nervous system.[18] Clindamycin is also cost effective than some of the other antibiotics.[19]

In the present study, tigecycline, vancomycin and linezolid were found to be useful drugs in treating methicillin resistant Staphylococcal infections. None of the MRSA isolates showed resistance to tigecycline, vancomycin as well as to linezolid.

In the present study, 3.7% methicillin resistant Staphylococcus isolates were resistant to Amikacin, 2.3% resistant to gentamicin, 2.4% resistant to netilmycin and 3.5% resistant to tobramycin. Many studies reported different range of resistance to aminogycosides ranging from 41-54%.[20]

Typing of MRSA strains is necessary for thorough epidemiological investigations of sources and modes of spread of these strains in hospitals and to design appropriate control measures.[21]

Conclusion

We concluded that Clindamycin and Fluroquinolone (ciprofloxacin) are not suitable alternative drugs for the treatment of hospital acquired Staphylococcus infections because of high level resistance.

Tigecycline was found as the most effective alternative drug followed by amikacin and netilmycin.

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