Changing Antimicrobial Resistance Pattern of Isolates from an ICU Over a 3 Year period

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Abstract

Objective: To study the changing patterns of antimicrobial resistance in gram negative bacilli esp. Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa species and Gram positive Staphylococcus aureus isolates from a 37 bedded ICU of a private hospital.

Methods: Antibiotic susceptibilities were determined by using disk diffusion and Vitek-2 system.

Results: A total of 13410 clinical samples were screened over a period of 3 years, among which 16.77 percent (2250 isolates) were culture positive. In recent years there has been an increased incidence of extended-spectrum β- lactamase (ESBL). The ESBL producing Escherichia coli and Klebsiella pneumoniae has shown an increase in resistance to the tune of 80-90% from 2011 to 2013. The prevalence of resistant strains of Acinetobacter species and Pseudomonas aeruginosa has shown an increase in Imipenem and Meropenem resistance at the rate of 75-80%.

Conclusion: Antibiotic resistance has shown an increase in gram negative pathogens and thereby has created a significant problem in choosing the right antibiotic for empirical usage. Rise in resistance has left little choice for the clinicians to select antibiotics. Klebsiella pneumoniae ESBL and Escherichia coli ESBL have become dominant organisms in the ICU. Piperacillin + Tazobactum, Imipenem and Amikacin have decreased sensitivity against Enterobacter. A number of old antibiotic compounds such as Polymyxins, Fosfomycin, and Aminoglycosides are re-emerging as valuable alternatives for the treatment of ESBL producing bacteria. Cases of MDR Escherichia coli and Klebsiella pneumoniae bacteria have increased in recent years and are now the most frequent cause of hospital acquired infections.

Introduction

Antibiotics are chemotherapeutic agents that inhibit or abolish the growth of microorganisms, which develop and disseminate resistance as a reaction to antimicrobials in accordance with the rule of physics, evolution and natural selection. In spite of considerable developments in antibiotics, anti-biotherapy, science, medicine and medical care, infectious disease and infectious complications related to resistant pathogens such as Staphylococci, Streptococcus pneumonia, Resistant Gram-negative bacilli as well as fungi and viruses, remain important for human morbidity and mortality.1 Antimicrobial resistance threatens the effective prevention and treatment of an ever increasing range of infection. As stated in the very recent last call for action to the medical community from the Infectious Disease Society of America (USA). We are in the midst of an emerging crisis of antibiotic resistance throughout the world. Resistance to antimicrobials is mediated by mechanisms like production of an enzyme, or alteration of antibiotic target site, or prevention of antibiotic access to the target site, or active efflux of antibiotics2,3 each of which pump out more than one drug. Infections caused by resistant microorganisms often fail to respond to standard treatments. This results in prolonged illness, higher health care expenses and a greater risk of death4.

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Material and Methods

All isolates were obtained from a range of clinical samples like urine, pus, blood, sputum, BAL, tracheal secretions from ICU. Patients were evaluated for sensitivity patterns by the Vitek-2 compact from BIOMERIEUX.6

The isolates were studied on the basis of site of infection, characteristics of patients, clinical signs and symptoms and antimicrobial sensitivity/resistance pattern.

Antimicrobial Susceptibility Testing

Organisms were tested for sensitivity by the Vitek-2 as per CLSI guidelines5 as seen in Table 1.

Results

Pursuant to the paper published in the earlier issue8 of JAPI which represented data for the year 2008 to 2009, the current data and results have been gathered by a year on year evaluation for the period January 2010 to December 2012. Multiple awareness programs for the clinicians about rational antibiotic therapy, giving them resistance/sensitivity patterns of the organisms prevailing in wards and ICU during the period 2010 to 2012, conducting seminars and distributing Antibiotic Stewardship guidelines has helped curb irrational antibiotic utilization. Awareness on type of patient and the right escalation and de-escalation has emphasized this approach.

Sending the doctors regular updates on a daily patient wise basis regarding sensitivity data and the appropriate antibiotic to be used has helped in reducing polypharmacy of antibiotics.

Antibiotics with low Minimum Inhibitory Concentration (MIC) showing sensitivity (S); intermediate sensitivity (I) or resistance (R) have been shown to the treating doctors thereby guiding them to use a more rational selection of the antibiotics. The MIC though not used for therapeutic dose calculations has been very useful for a better targeted antibiotic approach. Sensitivity patterns have shown drastic difference in the ICU and ward levels. Isolates showed an increase in the last 3 yrs. (Figures 1 and 2) This is a further 3 year observation on the spectrum of organisms dominating the hospital and the attempt to rationalize the use of antibiotics to prevent the further upgradation of resistance of these pathogens to the antimicrobials used. For betterment and upgradation in the detection of sensitivity pattern the conventional disc diffusion method was enhanced to an automated system of Vitek-2 compact (BIOMERIEUX).6 The automated system improved the results by giving the MIC of each antibiotic and more accurate sensitivity/resistance inferences could be used for a definitive antibiotic usage. However, the last 3 years (from 2010) showed a dramatic rise in the Extended Spectrum Beta Lactamases (ESBLs) and Metallo Beta Lactamases (MBLs) in Gram Negative Bacteria (GNB). Spelt disaster for use of third generation Cephalosporins and Aztreonam.7 True to reported observations such organisms were frequently found co-resistant to Fluoroquinolones like Levofloxacain and Aminoglycosides.

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Escherichia coli and Klebsiella pneumoniae (Figures 4 and 5) have
shown an increase in ESBL up to 80% in indoor patients, ESBL in community patients has been to the tune of 65-70%. Multi drug resistant Acinetobacter species and Pseudomonas aeruginosa (Figure 3) have shown an increase in imipenem and meropenem (carbapenem) resistance to the tune of 75-80%. In spite of increase in isolates of Staphylococcus Aureus over a period of time, sensitivity of staph aureus to Teicoplanin and Vancomycin has remained unchanged but resistance to Linezolid has increased by 30% (Figure 6). However due to the strict infection control techniques and good hand hygiene practices, infections due to Acinetobacter species have reduced.

Based on the clinical scenario and standard guidelines it was found that barely 1% to 2% i.e. About 41 samples from the total of 2081 isolates were found to be colonizing isolates.

Collection of samples of blood and urine following strict aseptic techniques, samples mostly from critically ill ICU patients and microbial susceptibility tests with colony counts for respiratory samples like tracheal aspirates, protected brush specimens, BAL samples.

Urine cultures often grow organisms as the catheter is a common site for colonization. Hence, in these subsets of patients, it is necessary to differentiate colonization from infection to ascertain the need for treatment. All patients with a colony count of >10^3 were considered as having significant bacteriuria and were treated with antibiotics. But treatment of asymptomatic bacteriuria in the catheterized patient was not recommended unless pus cells showed in repeat culture.

Similarly in case of burns or chronic wounds, the local examination of the wound and the surrounding tissue provides valuable information for the clinician to decide whether the organism isolated is a colonizer or the true pathogen.

Demarcation of the isolates as contaminant, commensal or true pathogen was left to the discretion of the clinician based on correlation with the characteristics presented by the patient in that condition.

**Discussion**

The proportion of bacteria with resistance to antibiotics has risen between 2010-2013. The emergence of resistance to most classes of antibiotics, has led to reconsideration of polymyxins as a valuable therapeutic option. Parenteral use of Colistin was abandoned in most countries because of reports of serious nephrotoxicity and neurotoxicity. It remains the last resort amongst antibiotics for multidrug resistant infections due to Pseudomonas aeruginosa and Klebsiella pneumoniae.

**Future Issues**

Fostering innovation and research and development of new vaccines, diagnostics, infection treatment option and other tools.
Continued need to define a new molecule. Minimize irrational antibiotic usage. Simultaneous administration of more than one agent Eg. an inhibitor of multidrug efflux pump lowers MICs’ of various drugs.

Also molecules like Colistin, Tigecycline, Aminoglycosides need to be given in combination therapy with other antibiotics due to their limitations, which remains a difficult task and requires added clinical trials to determine the right dosages and right combinations.

Conclusions

Bring all stake holders together to agree on and work towards a co-ordinated response.

Strengthening NAMS.

Actively encouraging innovation, research and development.

Last but not the least enhancing and following best infection control practices in clinics and hospitals.

Abbreviations


References