Academic Sciences International Journal of Pharmacy and Pharmaceutical Sciences

ISSN- 0975-1491 Vol 4, Issue 4, 2012

Research Article

ANTIBIOTICS SURVEILLANCE: A SURVEY ON THE SUSCEPTIBILITY OF MICROORGANISMS TO ANTIBIOTICS IN RESPIRATORY TRACT INFECTIONS.

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Received: 21 Jun 2012, Revised and Accepted: 02 Aug 2012

ABSTRACT

Background: Resistance to antibiotics is clearly increasing in many Asian countries and is of particular concern in Streptococcus pneumoniae. The genetic relationship between penicillin-resistant S. pneumoniae strains from across Asia suggests that resistant clones have spread within and between countries. This study is done to evaluate the resistance patterns of microorganisms to antibiotics in respiratory tract infections by undertaking a surveillance study by using antibiogram reports.

Methods: The study was designed to determine the susceptibility of respiratory isolates of microorganisms to antibiotics. The bacterial strains were isolated from patients suffering from respiratory tract infections. This study had two phases. Phase-I: Retrospective study and Phase- II: Prospective Study. 147 subjects were included whose antibiogram reports available in the study.

Results: The analysis of microbial culture reports obtained from the patients' files showed that in the retrospective study among the various specimens sent for obtaining culture report, sputum specimens were most commonly employed in 49.09% of the cases whereas in the remaining cases bronchial wash (41.81%), pleural fluids (5.45%) and throat swab (3.63%) specimens were used. In the prospective study, bronchial wash was more commonly used in about 48.64% of cases while sputum specimen was used in 45.94% of the patients. Pleural fluids and throat swab were used in 2.7% of patients

Conclusions:. The sensitivity of Pencillins against all the isolates of organisms fell far above the acceptable levels indicating wide spread and inappropriate use of Penicillin in the community. Cephalosporins were found to be highly sensitive to gram negative species understandably. Monobactams showed absolute sensitivity towards Pseudomonas but were found to be resistant against Klebsiella.So it is the time to think, plan and formulate a strong antibiotic policy to address this present scenario.

Keywords: Susceptibility, Microorganisms, Antibiotics, Respiratory tract infections

INTRODUCTION

Resistance to antibiotics is clearly increasing in many Asian countries and is of particular concern in Streptococcus pneumonia[1]. The patterns of antibiotic resistance in Asia may be dependent on three factors: There is a high prevalence of certain resistant serotypes of S. pneumoniae in some areas, e.g. South Korea. The genetic relationship between penicillin-resistant S. pneumoniae strains from across Asia suggests that resistant clones have spread within and between countries. Genetic evidence also suggests that a non-susceptible clone related to isolates from Spain and South Africa has been disseminated in Asia[1, 2]. Relatively low rates of penicillin non-susceptibility in S. pneumoniae have been reported in India (4%), Bangladesh (13%) and Pakistan (20%). In contrast, 41% of isolates from SriLanka were reported to be penicillin intermediate [3].

Categorization of Resistance

• ***Prevalent***: Resistance to a particular antimicrobial agent in clinical use that occurs to a lesser or greater extent in part or all of a country and has an impact on patients and/or the provision of health care [4].

• ***Potential threat***: Resistance to a particular antimicrobial agent in clinical use that occurs elsewhere in the world and is having an impact on patients and/or the provision of health care, with the possibility of arising within, or spreading to, the country under consideration[4].

• ***Theoretical threat***: Not a prevalent problem nor a potential threat, but an organism having the theoretical risk of exhibiting resistance which would have a significant impact on the management of individual patients and/or public health[4].

• ***Unknown***: In many countries the prevalence of antimicrobial resistance is unknown particularly among pathogens causing infections in the community [4].

Mechanism of resistance

The leaf diagram summarizes the main mechanisms by which antimicrobial resistance proliferates within a population Figure:1[5]. [Resistance emerges when native microorganisms are exposed to antibiotics or when they acquire genetic resistance factors from neighboring organisms. Once resistant, microorganisms can spread through the population via human, environmental, or animal reservoirs[6]. The use of antibiotics should have created a catastrophic situation for microbial populations but the genetic flexibility allowed bacteria to survive and multiply under the antibiotic pressure [7]. Bacteria can resist antibiotics as a result of chromosomal mutation or by exchange of genetic materials, which carry resistance genes, through transformation, transduction or conjugation by plasmids.

Objectives

The objective of the study is to survey the susceptibility of microorganisms to antibiotics in respiratory tract infections by using antibiogram reports.

MATERIALS AND METHODS

The study was conducted in Kovai Medical Center and Hospital, India from 2008 to 2010. It is 1500 bedded multi-specialty tertiary care hospital. The study constituted of two phases: Phase-I: A retrospective study. Phase-II: A prospective observational study. The inclusion Criteria: were, In-patients with signs and symptoms of respiratory tract infections, Patients with sputum, pleural fluid, bronchial wash or throat swab culture showed growth of microorganisms, Patients for whom antibiotic sensitivity testing was performed. Exclusion Criteria were, Out-patients, Patients receiving antibiotics without obtaining antibiogram report, Patients for whom antibiotic sensitivity testing was done on microorganisms isolated from specimens other than sputum, pleural fluid, bronchial wash and throat swab. Ethical approval is obtained from Kovai Medical Center and Hospital ethical committee.

Study Protocol

Resistance surveillance is well established as an essential cornerstone of any attempts to understand and control resistance[8-14]. An extensive literature survey was done on antimicrobial usage, antimicrobial resistance, challenges of antimicrobial resistance, strategies to minimize the spread of antimicrobial resistance, importance of antibiogram surveillance method. The literatures supporting the study were gathered from various journals like Australian prescriber, British medical journal, Journal of antimicrobial chemotherapy. The articles from the journals were obtained with the help of IDIS (Iowa Drug Information Systems), MEDLINE and from other internet sources. Information was also gathered from documents published by WHO (World health organization). A well-designed data entry form was used for collecting data for this study. Data collected included patient details, laboratory investigations, antibiotics prescribed and other drugs prescribed. For every subject in this study, name, inpatient number, date of admission, age, sex, ward of admission and length of stay in the hospital were recorded. Details of antibiotic therapy such as types of antibiotics, dose and route of administration, frequency of administration and duration of therapy and antibiogram report were recorded. The study was reviewed and approved by the authors' institutional review board.

Phases of Study

Phase-I: (Retrospective study):

In this phase, the details of discharged patients with respiratory tract infections having antibiogram were collected retrospectively from the microbiology laboratory and based on these details, the patients' records were obtained from the medical records department. Thereby, antibiogram reports and other patients' details were obtained. Only patients having antibiogram report were considered in this phase of study, since some of the patient's record did not have antibiogram report

Phase- II (Prospective Study):

In this phase, the details of in-patients for whom antibiotic susceptibility testing was done for respiratory tract infection were collected prospectively from the microbiology laboratory and patient's information were collected directly from the wards thereby antibiogram report and other patients' details were obtained.

Study duration for both the phases was 8 Months.

RESULTS

Even though there were a total of 1272 specimens of respiratory origin (sputum, bronchial wash and throat swab, pleural fluids) which were sent to the microbiology laboratory for culturing during our study duration, only the cultures of 238 patients were reported to have shown pathogenic growth. However, only the 147 subjects whose antibiogram reports available were included in the study. Out of these 147 patients, 110 were from Phase I (Retrospective cases), while the remaining 37 patients were from Phase II (Prospective cases). Evaluation of the demographic data of the subjects revealed that among the 110 patients included in the retrospective study, 74.54% (n=28) were males while 25.45% (n=28) were females. In the prospective study, out of the 37 patients 75.67% (n=28) were males and the remaining 24.32% (n=9) were females [Table: 1].

Table 1: Number of patients in Phase I and Phase II

Gender	Retrospective Study (Phase I)		Prospective Study (Phase II)	
	Number of patients	Percentage	Number of patients	Percentage
Male	82	74.54%	28	75.67%
Female	28	25.45%	9	24.32%

Age group analysis of the patients showed that in the retrospective study, the most prominent age groups were '51 to 60 years' and '41 to 50 years' each comprising of 23.63% of patients (n=26), followed by '41-50 years' which constituted 17.27% (n=19) of the patients. In the prospective study, the most prominent age groups were 51-60 years which constituted 27.02% (n=10) followed by 61-70 years which constituted 23.63% (n=9). The most common cause for admission among the two phases of study seemed to be breathing difficulty which was present in 22.4% of the population. While 21.7% were admitted for reasons other than those associated with RTI, the remaining came with complaints of cough with fever (17%), cough with expectoration (11.5%), hemoptysis (11.5%), cough alone (9.5%) and COPD (6.1%). The increased number of reasons for admission other than those associated with RTI may be due to the prevalence of nosocomial infections. The duration of stay in hospital varied among the population. In the retrospective study most of the patients (37.27%) were admitted for 6-10 days while 25.45% stayed for 1-5 days. In prospective study, most of the patients (37.83%) had a hospital stay of 6-10 days while 27.02% were admitted for 1-5 days. Due to increased resistance shown by previously susceptible organisms, patients were at a risk, of longer hospital stays [15]. The monitoring of the antibiotic therapy in these patients was done. In retrospective phase, most of the patients received more than one antibiotic as part of the treatment. 34.54% patients were on two antibiotics while 25.45% were on three antibiotics. The number of patients receiving only one antibiotic was high (43.24%) in the prospective study while 32.43% were on three antibiotics. The increase of resistance is more evident in hospital settings where the antibiotic usage is maximum. [Table: 2]

Table 2: Number of antibiotics prescribed per patient

Number Of Antibiotics	Retrospective Study		Prospective Study	
	Number of patients	Percentage	Number of patients	Percentage
1	25	22.72%	16	43.24%
2	38	34.54%	12	32.43%
3	28	25.45%	6	16.21%
>3	19	17.27%	3	8.10%

The most commonly prescribed antibiotics during the period under study were Amoxycillin in combination with Clavulanate which accounted to 70 prescriptions, followed by Ofloxacin (39), Cefoperazone/Sulbactam (33), Moxifloxacin (30), Levofloxacin (29), Amikacin (28), Clindamycin (14), Piperacillin/Tazobactam (16), Ampicillin (11) and Azithromycin (11). These antibiotics were given most commonly for 6 to 10 days. The route of administration was parenteral in 29.9 % of the population, oral in 0.68% and a combination of both parenteral and oral in 11.56% of the population. These data reveal the extent of the usage of antibiotics, especially the increase in the use of parenteral antibiotics. The analysis of microbial culture reports obtained from the patients' files showed that in the retrospective study among the various specimens sent for obtaining culture report, sputum specimens were most commonly

employed in 49.09% of the cases whereas in the remaining cases bronchial wash (41.81%), pleural fluids (5.45%) and throat swab (3.63%) specimens were used. In the prospective study, bronchial wash was more commonly used in about 48.64% of cases while sputum specimen was used in 45.94% of the patients. Pleural fluids and throat swab were used in 2.7% of patients [Table: 3].

Table 3: Distribution of specimen with antibiogram report

Specimen Used	Retrospective Study		Prospective Study	
	No of patients	Percentage	No of patients	Percentage
Sputum	54	49.09%	17	45.94%
Bronchial Wash	46	41.81%	18	48.64%
Throat Swab	4	3.63%	1	2.7%
Pleural Fluid	6	5.45%	1	2.7%

The data of Gram's stain performed on the cultures obtained from the specimens revealed that gram negative organisms were highly prevalent in the retrospective phase of the study. In 94.54% of the cases, the organisms isolated were gram negative while gram positive organisms were found in only 5.45% of the cases. In the prospective the proportion varied a little with 75.67% cultures of gram negative organisms and 24.32% cultures of gram positive ones. Hence shows a significant increase in gram negative bacteria which are the most important cause of nosocomial infections. [Table: 4]

Table 4: Gram stain report

Gram Stain Report	Retrospective Study		Prospective Study	
	No of Patients	Percentage	No of Patients	Percentage
Gram Positive	6	5.45%	9	24.32%
Gram Negative	104	94.54%	28	75.67%

The culture reports also specified the microorganisms isolated from each specimen culture. This data indicated the prevalence of Klebsiella species and Pseudomonas species to be the highest in the retrospective study. Isolates of Klebsiella was found in 51.81% of specimens while Pseudomonas isolates were found in 42.72% specimens. There were also isolates of Staphylococcus (3.63%) and Streptococcus (1.8%). In the prospective study too, the isolates of Klebsiella and Pseudomonas species were more prevalent (48.64% and 27.02% respectively) as compared to the gram positive Staphylococci (16.21%) and Streptococci (8.1%) [Table: 5].

Table: 5 Distribution of microorganisms isolated

Microorganisms Isolated	Retrospective Study		Prospective Study	
	No of patients	Percentage	No of patients	Percentage
Klebsiella	57	51.81%	18	48.64%
Pseudomonas	47	42.72%	10	27.02%
Staphylococcus	4	3.63%	6	16.21%
Streptococcus	2	1.81%	3	8.10%

The therapy given to each individual was reviewed against the corresponding antibiogram report and the following observations were made. In the retrospective study, in 30 % of subjects the antibiotics given empirically were found to be sensitive to the microorganism according to the antibiogram. In 40.9% of the patients the antibiotics given empirically were changed according to the antibiogram report. In 25.45% of the patients, there were no changes made in the choice of antibiotics even after the antibiogram report was obtained. In the prospective phase, in most of the patients (43.24%), the empirical therapy held well with respect to the sensitivity of the microorganism against the antibiotics given. In 32.43% of the patients whose antibiogram reported lack of sensitivity, a change in the antibiotic therapy was made. In 24.32% of the patients the antibiogram reports did not translate into any changes in the choice of antibiotics given [Table: 6].

Table 6: Mode of treatment based on antibiogram report

Mode of treatment	Retrospective Study		Prospective Study	
	No of patients	Percentage	No of patients	Percentage
Patients Empirically Started On Sensitive Antibiotics	33	30%	16	43.24%
Antibiotics Changed According To Antibiogram	45	40.90%	12	32.43%
Antibiotics Not Changed According To Antibiogram	28	25.45%	9	24.32%

Antibiotic susceptibility testing was done on the isolates to determine the susceptibility of the isolate to an array of antibiotics which will determine the extent of resistance or sensitivity of the organism to each antibiotic.

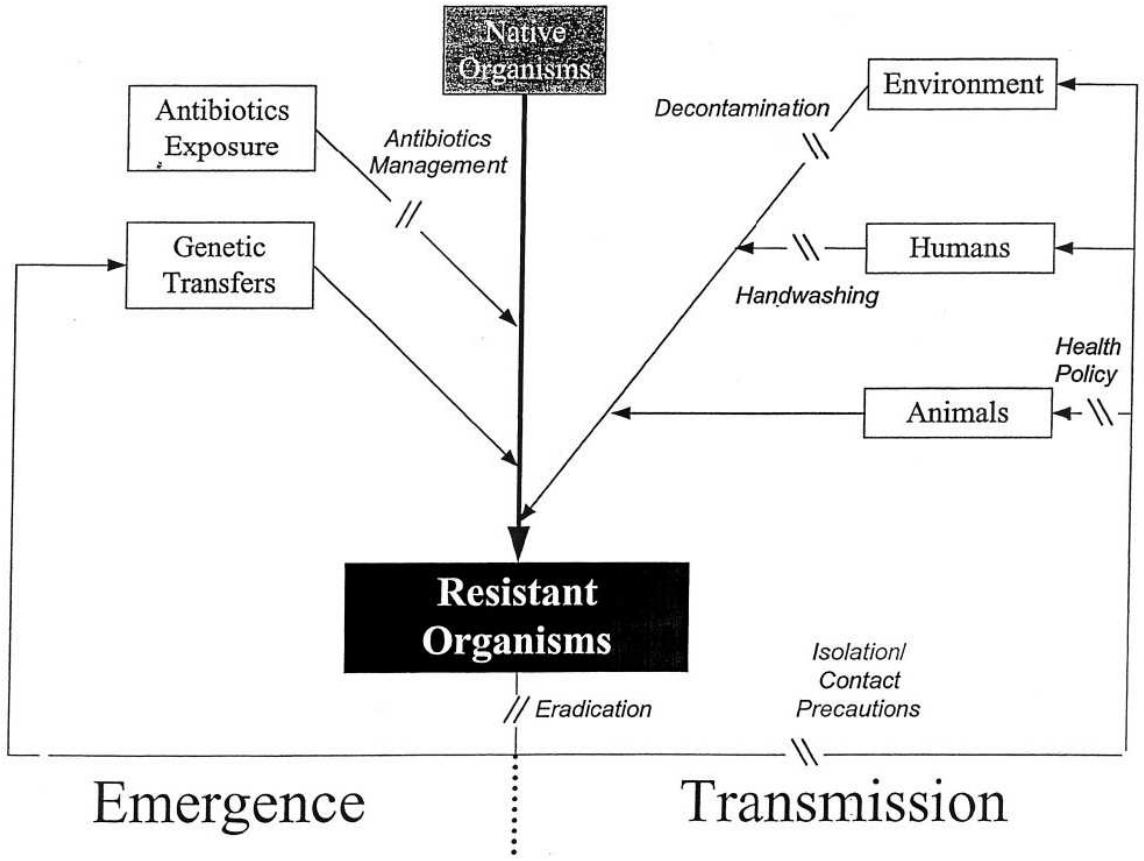

Fig. 1: Mechanisms leading to the proliferation of resistant microorganisms. Emergence of resistance is fueled mainly by antibiotics pressure and genetic transfers among organisms (*left side of diagram*). Transmission of resistant strains is facilitated by the existence of ecological reservoirs (*right side of diagram*). Measures aimed at interrupting the vicious circle leading to resistance are outlined in italic. [5]

DISCUSSION

The analysis of the antibiogram reports of the 147 patients resulted in the following interpretation. Gram negative organisms such as klebsiella and pseudomonas were found to be highly resistant against groups such as pencillins (69.4%, 74.7%) and miscellaneous (62.9 %, 72%). Gram positive organism such as staphylococcus was highly resistant against groups such as macrolids, monobactams (50%) and pencillins (48.6%) stretptococcus was found to be highly resistant against tetracyclines (83.3%). Pencillins are the group of drugs that are used mostly and were found to be highly resistant. This shows that there is a close link between development of antibiotic resistance and the use of antibiotics in the community [5]. A total of 75 isolates of klebsiella were isolated during the study period of these 100% were resistant to vancomycin, meropenem and cefpirome. 96.4 % were resistant to pencillin G and Clindmycin 95.9% was resistant to cloxacillin and 90.7% were resistant to Ampicillin / cloxacillin. Out of 57 isolates of pseudomonas 100% were resistant to Vanocomycin, cefpirome and cefepime, 97.9% were resistant to cefadrodil and cefaclor 97.5% were resistant to cefazolin, 97.4% were resistant to cloxacillin, 96% were resistant to Amoxicillin, 95.8% were resistant to Ampicillin 95.3% were resistant to pencillin G and 95.2% were resistant to cefuroxime. Of the 10 isolates of staphylococcus 80% were resistant to penicillinG and kanamycin 75% were resistant to Ampicillin 71.4%were resistant to cotrimoxozole 66.7% were resistant to piperacillin 62.5% were resistant to Nofloxacin and Erythromycin. Of the 5 isolates of streptococcus 100% were resistant to Tetracycline 66.5% were resistant to Doxycycline.50 % were resistant to Amoxicillin/Clavulanic acid, Piperacillin / Tazobactum, cefriaxone, and ciprofloxacin. Klebsiella and pseudomonas were found to be least resistant hence more sensitive against antibiotics such as imipenem, Cefoperazone/Sulbactum, Piperacillin/Tazobactum and amikacin respectively. Hence these drugs should be the mainstay in the treatment of infections caused by gram negative organisms. Staphylococcus and Streptococcus were least resistant hence more sensitive against antibiotics such as Ticarcillin/Clavulanic acid,Cefuroxime, Cefoperazone/Sulbactum and cefadroxil. Hence these drugs should be the mainstay in the treatment of infections caused by gram positive organisms. Cefoperazone/Sulbactum was found to be sensitive against all the four microorganisms included in the study.

So this drug has to be the drug of choice in empirical therapy. Infections caused by antibiotic resistant organisms delays appropriate treatment because empiric therapies are found to be less effective this in turn leads to wide spread abuse of broad spectrum antibiotics. Against Ampicilin/Sulbactum the change in percentage of resistance in six months intervals were 33.33%, 27.27%, 33.33%, 42.85% and 58.82% respectively. Against Cefaclor the change in percentage of resistance were 60%, 66.66%, 72.72%, 85.71%, and 85.71% respectively. Against Cefuroxime the change in percentage of resistance in six months intervals were 52.9%, 42.8%, 75%, 88% and 85.71% respectively. Against Norfloxacin the change in percentage of resistance were 47.2%, 50%, 50%, 60% and 54.5% respectively. Against Tetracycline the change in percentage of resistance were 15.4%, 37.5%, 33.33%, 60% and 46.6% respectively. Against Ticarcillin/Clavulanic acid Pseudomonas showed an increase in trend of resistance. The changes in percentage of resistance were 16.6%, 37.5%, 0%, 57.1% and 60% respectively. These results prove that there is an increase in resistance of microorganism to antibiotics with time. Hence pathogenic microorganisms can now defy antibiotics to which they were previously susceptible. The limitation of this study is the sample size. Since the sample size is just enough to meet the significant result, in near future sample size will increased by expanding the sample collections by including more tertiary care hospitals in Coimbatore.

CONCLUSIONS

From the results of the study it was found that the sensitivity of Pencillins against all the isolates of organisms fell far above the acceptable levels indicating wide spread and inappropriate use of Pencillins in the community. Cephalosporins were found to be highly sensitive to gram negative species understandably. Monobactams showed absolute sensitivity towards Pseudomonas but were found to be resistant against Klebsiella. Hence Monobactams can be a preferred choice against infections caused by Pseudomonas. Flouroquinolones though being broad spectrum antibiotics were found to have an increased level of sensitivity towards gram negative organisms such as Klebsiella and Pseudomonas but had fairly good sensitivity towards gram positive organisms such as Staphylococcus and Streptococcus. Aminoglycosides were found to be considerably sensitive to all the gram positive and gram negative organisms observed in the study. Among the Aminoglycosides, Amikacin and Netilmicin showed least sensitivity against all the four organisms. Macrolide antibiotics against Streptococcus were found to be sensitive against the other microorganisms. Erythromycin was found to be the most sensitive macrolide antibiotic. Tetracyclines showed better sensitivity towards Staphylococcus than the rest of the organisms, against which they were resistant. Combinations of β-lactam antibiotics with β-lactamase inhibitors are now very commonly used in the treatment of infections. It is usual for the physicians to use these combinations as empirical therapy. It was seen that both Amoxycillin/clavulanic acid and Ampicillin/Sulbactum were found to be highly sensitive against all the four microorganisms observed in this study. This may be due to increased and injudicious use of these antibiotics. In the same group Cefoperazone/Sulbactum and Piperacillin/Tazobactum were found to have greater sensitivity against all the four microorganisms. Hence either of these two drugs could be a choice when considering empirical therapy. Patients who got admitted in the hospital with complaints other than that of respiratory tract infections were found to have acquired respiratory tract infections during their course of hospital stay. This may be due to the prevalence of nosocomial infections. Nosocomial acquisition of microorganisms resistant to antibiotics represents a threat not just to the patient's safety but also to the safety of the society as a whole. Decreasing the prevalence of resistant organisms requires active surveillance, adherence to vigorous isolation, environmental decontamination measures and effective antibiotic stewardship. The study emphasis that, antibiotic susceptibility testing should be carried out for all the patients who is in need of antibiotic therapy. Because of the immediate unavailability of antibiogram report it is better to obtain gram stain report before starting empirical therapy. Thereby it helps in choosing appropriate antibiotics having a narrow spectrum of activity. After obtaining the antibiogram report the sensitivity of the empirically started antibiotic should be checked against the same. Moreover the patient should be cautioned to follow the correct therapeutic regimen even after getting discharged from the hospital. This study conveys that the reason for antibiotic resistance is the inappropriate use of antibiotics due to lack of uniform policies and disregard to hospital infection control practices. Hence in the near future strong antibiotic policy and antibiotic prescribing guidelines have to be prepared and implemented in individual hospitals for respiratory tract infections. Otherwise, empirical therapies will be ineffective which will lead to widespread abuse of broad spectrum antibiotics which will ultimately result in further increase of resistance.

Conflict of interest

The authors have no conflicts of interest.

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