

## Research and Reviews: Journal of Medical and Health Sciences

### Empirical Antibiotic Therapy and Emerging Drug Resistance

Chandrasekaran Venkatesh\*, Thiyagarajan Suganya, Dhandapani Gunasekaran, Palanisamy Soundararajan, and VN Mahalakshmi.

Department of Pediatrics, Mahatma Gandhi Medical College & Research Institute, Pillaiyarkuppam, Puducherry 607402, India.

#### Short Communication

Received: 24/01/2013

Revised: 04/02/2013

Accepted: 14/02/2013

#### \*For Correspondence

Department of Pediatrics, Mahatma Gandhi Medical College & Research Institute, Pillaiyarkuppam, Puducherry 607402, India.

Email: cvenkatesh@hotmail.com

**Keywords:** antibiotic, resistance, drug

#### ABSTRACT

Antibiotics in inappropriate doses and for inappropriate pathogens without microbiological evidence and drug susceptibility testing are a rampant practice in medicine of late. Two children with different infections with resistance to first line conventional antibiotics with emphasis on inappropriate hospitalization practices and empirical therapy as probable causes of drug resistance and ways of addressing this complex issue is discussed with relevant review of literature.

#### INTRODUCTION

Antibiotics in inappropriate doses and for inappropriate pathogens without microbiological evidence and drug susceptibility testing are a rampant practice in medicine of late. Two children with different infections with resistance to first line conventional antibiotics with emphasis on inappropriate hospitalization practices and empirical therapy as probable causes of drug resistance and ways of addressing this complex issue is discussed with relevant review of literature.

#### Case 1:

A two year old female child with partial exstrophy of bladder was brought to our hospital with history of dysuria and passing frank pus per urethra. She was treated elsewhere for her condition and was on clean intermittent catheterization and Co-trimoxazole prophylaxis. She also gives history of frequent episodes of dysuria with fever for which she received Amikacin injections from a nearby practitioner for varying duration through intramuscular route. There was no documentation of urinary tract infection either by significant bacteriuria or culture sensitivity. Her abdominal sonography examinations in the past revealed mild asymmetry in kidney size. Her nuclear scan results and renal functions were normal. A micturiting cystourethrography (MCUG) done outside did not reveal any reflux. Urinalysis after admission showed plenty of pus cells and white blood casts. Urine culture revealed heavy growth of *Klebsiella pneumoniae* which was resistant to Amikacin, Cephalosporins and extended spectrum Beta-lactam group of antibiotics. She was treated with a ten day course of Imipenem. Repeat urine culture became sterile and she was discharged on oral Cephalexin prophylaxis.

#### Case 2:

A Two and half year old male child with a diagnosis of right lower lobe pneumonia complicated by empyema was referred from another teaching institution with isolation of Methicillin Resistant *Staphylococcus aureus* (MRSA) in blood culture for further care (Resistance to Ampicillin, Cloxacillin, Gentamicin, Doxycycline, Ceftriaxone, Ciprofloxacin, Cotrimoxazole and Cefotaxime). In the past, the child had been hospitalized once for cold and treated as pneumonia with intravenous antibiotics at a private nursing home without a clear documentation of type of pneumonia and the reasons for admission. At admission the child was tachypneic with chest indrawing and decreased breath sounds in the right lower interscapular and infra axillary regions. The child was treated with oxygen,

intercostals tube drainage and intravenous Vancomycin at 40 mg/kg/day for two weeks (child had already received intravenous vancomycin for a week before the child was seen by us). Intercostal tube was removed by day 6 of hospital stay. Pleural fluid culture and repeat blood culture were sterile and child was discharged home.

## DISCUSSION

The emergence of resistance to antibiotics has been a major threat to successful disease control practices globally. Several thousands of people are affected due to it. The financial implications are also huge, affecting the functioning of health programs around the world. Preventing Human Immuno deficiency Virus (HIV) infection, Tuberculosis and Malaria deaths, the major killer diseases, have suffered setbacks due to emergence of drug resistance. Apart from these major killer diseases, drug resistance has affected the treatment of other invasive and noninvasive bacterial infections due to gram negative bacilli, *Staphylococcus aureus* and Enterococci. In India, the prevalence of MRSA has been found to vary between 8– 71 %, Extended spectrum Beta Lactamase (ESBL) producing gram negative bacteria between 19 –60%, Vancomycin resistant Enterococci between 23 – 63 %, Carbapenam resistant gram negative bacilli between 5.3 – 59%. The above organisms are responsible for most health care associated infections<sup>[1]</sup>. The discovery of the New Delhi Metalloproteinase 1 gene in organisms isolated from patients who received treatment in India<sup>[2]</sup> has created a major embarrassment to health care sector in India affecting the prospects of medical tourism. The world health organization has identified several key areas that contribute towards the development of drug resistance. These include among other things, poor drug quality, irrational drug prescription, lack of research and development in drugs and diagnostics and limited drugs and diagnostic arsenal to combat infections<sup>[3]</sup>.

The two cases presented above are diverse in that one child is an at risk child who is prone to develop recurrent infection and nosocomial sepsis and the other child had probably been colonized by a drug resistant organism during previous hospitalization. In at risk children like in those with chronic medical problems and those who undergo frequent procedures, a clear antibiotic policy should be followed that helps in preventing infection and at the same time prevents spread of hospital acquired organisms and drug resistance. Antibiotic rotation policy and having a higher threshold for starting antibiotics can be useful steps in that aspect. Avoiding hospitalization of children who are not sick and adhering to a narrow spectrum antibiotic appropriate to the disease process can also limit development of drug resistance. Empirical therapy till culture and drug susceptibility pattern are obtained has a role in serious bacterial infection, where the causative organism is fairly obvious either by a careful history or a detailed physical examination and typical clinical presentations. On the contrary, such therapy has become more of a substitute to a good clinical judgment and reasoning.

Periodic screening for multidrug resistant organisms should be carried out if feasible. Isolation or cohort nursing of such infected patients, use of decolonization treatment regimens, use of appropriate antibiotic prophylaxis during surgery or during invasive interventions can be useful. Similarly, use of an appropriate agent for empirical antibiotic therapy in case of unconfirmed/unknown infection can also be beneficial in preventing the spread of drug resistant microbes<sup>[4]</sup>. Effective monitoring and surveillance for drug resistance will require good laboratory back up and cost effective screening strategies with frequent interaction between clinical and lab personnel<sup>[5]</sup>. Several irrational drug combinations are of late flooding the Indian markets. These drug combinations have been approved by drug regulatory authorities in India without foreseeing the danger it can spell. The noteworthy drug combinations that are irrational include the newer betalactams and beta lactam inhibitor combinations, Ofloxacin and Ornidazole combination and Cefixime and Azithromycin combination<sup>[6]</sup>. Avoiding prescription of such new drugs on an empirical basis and having a good sense of clinical judgment with rational use of conventional antibiotics will go a long way in controlling the rot.

## CONCLUSION

Drug resistance is a growing threat to infection control practices Worldwide. Strong antibiotic policies that are enforced with an iron will and commitment from professional bodies and policy makers is the need of the hour in curbing this menace. Surveillance should be carried out for drug resistant organisms periodically and containment procedures should be instituted to prevent the problem from becoming totally unmanageable.

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