

IRRATIONAL USE OF ANTIBIOTICS IN CHILDREN LEADS TO ANTIMICROBIAL (DRUG) RESISTANCE; A CASE REPORT

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Abstract

Antimicrobial resistance is an emerging, critical human health issue. The World Health Organization (WHO) has declared antibiotic resistance as a top health issue worldwide. Extensive use of Antibiotics against the microbial disease is one the foremost cause of antimicrobial resistance in pediatrics and adults. The case study has been designed to report an irrational use of antibiotic among 10 year old child who has been visited to the same physician in local hospital of Sargodha, Pakistan from last 3 years. During their first visit to the physician, he was diagnosed with acute upper respiratory track infection (URTI) and was treated with tablet Claritek (clarithromycin) 250 mg TDS (Three times in a day) along with tablet Paracetamol (acetaminophen) BID (twice a day). Child recovers initially from the infection but develop the symptom of fever, cough, sore throat and runny nose again. He visited the hospital and doctor writes the same prescription, with increase dose of antibiotic which result in developing antimicrobial (drug) resistance in that particular child. The doctor didn't care and keep on increasing the dose without considering their adverse side effect specifically on children's. The purpose of this report is to highlight the flaws of Medical practitioners, Community Pharmacist, Dispensing Pharmacist and other health care workers that didn't interact with each other to ensure the correct diagnoses, prescription as well as safe dispensing of medicine to the patient.

Key Words: Irrational therapy, Misuse of Antibiotics, Drug Resistance, Role of Pharmacist

Introduction

Irrational use of medicines is a global problem. It has been estimated that less than half of all medicines are prescribed, dispensed or sold inappropriately [1, 2] and that less than half of all patients take their medicines as prescribed or dispensed [3]. Irrational use of medicines can harm patients in terms of poor patient outcome, unnecessary adverse reactions and wastage of resources, often out- of pocket payments by patients. Irrational use of antibiotics is particularly serious because it is contributing to antimicrobial resistance that is increasing rapidly worldwide and is causing significant morbidity and mortality [4, 5]. Data show that in low-and middle-income countries less than 40% patients in the public sector and less than 30% in the private sector are treated in compliance with clinical guidelines, and that the situation has not improved significantly over the last 20 years [2].

Antibiotic resistance is defined as the resistance of microorganism to anti microbial agent and that happens when bacteria changes to protect itself from antibiotics. The inappropriate antibacterial treatment and the overuse of antibiotics have contributed to the emergence of antibiotic resistance. Antibiotic resistance is a serious and growing phenomenon in contemporary medicine and has emerged as one of the pre-eminent public health concerns of the 21st century, in particular as it pertains to pathogenic organisms (the term is especially relevant to organisms that cause disease in humans). A World Health Organization report released April 30, 2014 states, "this serious threat is no longer a prediction for the future, and it is happening right now in every region of the world and has the potential to affect anyone, of any age, in any country. Antibiotic resistance—when bacteria change so antibiotics no longer work in people who need them to treat infections—is now a major threat to public health [6].

Worldwide, infants and children represent a higher proportion of the population. 28% of the world's population is accounted by children younger than 15 year of age. Across the globe this category has higher than average risk of developing disease. The use of antibiotic has a routine practice for the treatment of pediatric illness [7, 8]. Thus children and infants are subjected to innumerable discrepancies in antibiotic medications.

Rational use of medicines requires the patients to take medications that are appropriate to their

clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community [9]. As stated by a famous humanitarian, A little simplification would be the first step toward rational living.

Although the "irrational prescription" is not a new global topic and has been a reason for concern for many years, still many countries including Pakistan are not paying enough attention to this old but ongoing problem across the world. We were therefore, prompted to initiate this novel and unique pilot study to investigate the incident of irrational use of antibiotic in our tertiary and to attract the attention of concern authorities.

Case Report

A 10 year old boy was brought to the local hospital of Sargodha, Pakistan. He was presented with the severe symptoms of cough, cold, sneezing, running nose and intermittent fever from the period of last three days. There were no symptoms associated with the lower respiratory track infection (LRTI) i.e. bronchitis, asthma or COPD. Other chief complaints by the patient include vomiting, diarrhea, and nausea. Cough is along with sputum that is clear mostly but some time sputum purulent.

His primary treatment includes injection Gravinate (Dimenhydrinate) 50mg/mL x IM, injection Klaricid (clarithromycin) 500mg and a tablet of Paracetamol (acetaminophen). His vitals were checked. His physical examination showed temperature 102°F, pulse rate 120 beats/min, respiratory rate 45/min and B.P 120/90 mmHg. He weighted 42 Kg. His previous medical history shows the excessive use of antibiotic Claritek (clarithromycin) dose up to 500 mg BID (two times in a day) with recur of infection again and again. Now in the present situation, patient didn't response to this class of antibiotic probably due to the development of antimicrobial (drug) resistance. On the basis of his condition and response to primary treatment physician moves toward the secondary treatment and prescribe him tablet Zinacef (cefuroxime) 500 mg TDS (three time in a day) for seven days, Syrup DrKoff TDS (three times in a day), Paracetamol (acetaminophen) BID (two times in a day) for two days, Nimaran 100 (nimesulide) BID (two times in a day) for five days. The patient recovers from the symptom of upper respiratory track infection (URTI) but complaint diarrhea and nausea. For the treatment of Diarrhea,

doctor prescribes Entamizole DS (Diloxanide 500mg, Metronidazole 400mg) BID and tablet Cipro (ciprofloxacin) 500 mg BID (two times in a day).

The above mentioned treatment was irrational as the doses of certain drugs were found to be incorrect and some unnoticed drug interactions were also found. The excessive use of antibiotics leads toward drug resistance. There is no need of Cipro (ciprofloxacin) because the complaint of Diarrhea is already due to excessive use of antibiotics. Doctor must have to prescribe vitamins with antibiotic to avoid diarrhea. Care must be taken while treating a patient with adjunct therapy of antibiotics along with Gravinate (Dimenhydrinate). Vigilant monitoring should be required other wise situation moves toward ototoxicity because Dimenhydrinate is capable of masking ototoxic symptoms.

Discussion

The four main mechanisms by which microorganisms exhibit resistance to antimicrobials are [10]: Drug inactivation or modification: for example, enzymatic deactivation of *penicillin G* in some penicillin-resistant bacteria through the production of β -lactamases.

Alteration of target site: for example, alteration of PBP—the binding target site of penicillin—in MRSA and other penicillin-resistant bacteria. Alteration of metabolic pathway: for example, some sulfonamide-resistant bacteria do not require para-aminobenzoic acid (PABA), an important precursor for the synthesis of folic acid and nucleic acids in bacteria inhibited by sulfonamides, instead, like mammalian cells, they turn to using preformed folic acid.

Reduced drug Accumulation: by decreasing drug permeability or increasing active efflux (pumping out) of the drugs across the cell surface [11].

With regard to use of antibiotics in the Region, it was found that [12]:50% of viral upper respiratory tract infection cases are treated unnecessarily with antibiotics, yet only 53% of pneumonia cases receive an appropriate antibiotic, 54% of acute diarrhea cases are treated unnecessarily with antibiotics, yet only 55% receive oral rehydration solution as recommended in the guidelines; and 40% of prescribed antibiotics are prescribed in under-dose. This report is exactly in accordance to the case presented above in which irrational therapy with antibiotic leads toward antimicrobial resistance as well as severe adverse effect.

In the case presented above, the Gram-positive microbe develop resistance against Clarithromycin (macrolides) that might be due to acquisition of the *erm* (B) gene, which confers high-level resistance to all macrolides [13]. During initial treatment of upper respiratory infection (URTI), the dose of clarithromycin increases incorrectly. It should not exceed 250mg/dose two times in a day [14].

The first line therapy for the treatment of upper respiratory track infection (URTI) includes penicillin V, penicillin G and benzathine. Alternative antibiotics include amoxicillin, cephalosporin and macrolides [15]. The above mentioned therapy is completely irrational. Dose of Zinacef (cefuroxime) was found to be overdose. It should not exceed 30mg/kg/day in children's [16]. Cephalosporin was prescribed only for the treatment of infectious Diarrhea [17]. For therapy with more than one antibiotic, vigilant monitoring and protocols should be required to provide maximum benefit to the patient.

Conclusion

In appropriate antibiotic dispensing and use owing to commercial interests and lack of knowledge about rational use of antibiotics and antibiotic resistance to the physicians were the main finding of this case report. Lack of patient-pharmacist and physician-pharmacist interaction, unavailability of pharmacist at all pharmacies in developing countries like Pakistan, negligence of drug regulating authorities, lack of awareness among people and not keeping the record of previous medication taken by the patient are the key reason that provoke the irrational use of medicine.

Recommendations

Implementation and enforcement of rules for dispensing of drug to assure standard drug monitoring i.e. Prescription review, Dose Calculation, Therapeutic evaluation, medical history and previous medication record.

Make sure the availability of Clinical pharmacist round the clock in all public as well as private hospitals to ensure the rational use of antibiotics and other medicine.

Implementation of the six major contributing elements of hospital pharmacy section designed by the international pharmaceutical federation (FIP) with the collaboration of World Health Organization, UNESCO, World Health Professions Alliance, Regional Pharmaceutical Forums and all other partners. Retail

Pharmacist must be present in all Pharmacies at the time of dispensing of drug to prevent abuse of any kind of drug.

Community pharmacists must arrange educational programs aimed at improving use of antibiotics. Such programs should be initiated within a multidisciplinary framework including doctors, pharmacists, social scientist, government agencies and Multinational pharmaceutical industries.

Pharmacist should consult with the patient's physicians and other health care providers in selecting the medicational therapy that best meets the patient's needs and contributes effectively to the overall therapy goals.

It's the responsibility of Government of Pakistan and health concern authorities to make Prescription Drug Monitoring Program (PDMP) that ensures vigilant monitoring of correct diagnosis of disease, rational prescription, safe dispensing and administration of drug to eliminate the chances of Antimicrobial Resistance (AMR).

For making these programs more successful Government should take guidance from developed countries. E.g. USA, Australia, Canada, Europe. Such type of programs (PDMP) should be extended through out the country including villages because most of the population lives in villages.

Along with restriction policy, additional interventions such as Postgraduate training programs, elaboration of local prophylactic guidelines, an independent and sovereign committee comprising of pharmacists, clinical microbiologist and infectious disease specialist could be beneficial in order to idealize rational use of antimicrobial agent in future.

Following the recommendations of the European Conference "The Microbial Threat" a Committee for the Coordination of Antibiotic Policy (BCCAP) was created in 1999 by Royal Decree in order to improve the situation. The recommendations are as under. Collection and organization of all available information on antibiotic use and resistance

Publication of reports on antibiotic use and resistance that provide information to scientists and increase of public awareness on antibiotic resistance and the risks associated with the irrational use of antibiotics Making recommendations on relevant points such as detection of resistance, cross-resistance mechanisms, use and consumption of antibiotics in man and animal, etc ...

Making recommendations for research on antibiotic

resistance and on the transfer of resistance among bacteria and among ecosystems International Conferences on Antimicrobial Resistance (AMR) should be regularly arranged to promote rational use of antimicrobial agent and to update knowledge of Physicians, pharmacist and other health care workers.

Extensive use of antibiotic as prophylactic should be prevented. Antibiotic reduction campaigns do not necessarily reduce resistance [18]. So in order to reduce antimicrobial resistance (AMR), all the information provided by the scientist, physician, microbiologist, pharmacist and other health care worker on that particular matter must be considered to make a solid policy.

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