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Review Article

A systemic review on antibiotic use evaluation in paediatrics

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ABSTRACT

Drug utilization is the marketing, distribution, prescription, and use of drug in a society, with special emphasis on the resulting medical, social and economic consequences. Antibiotics are valuable discoveries of modern medicine and their definitive and or appropriate use has led to a decline in the morbidity and mortality associated with various infectious diseaseswhile inappropriate use of antibiotics can increase morbidity, mortality, patient cost and bacterial antibiotic resistance.Antimicrobial agents are among the most commonly prescribed drug in Paediatrics. Because of an overall rise in health care costs, lack of uniformity in drug prescribing and the emergence of antibiotic resistance, monitoring and control of antibiotic use are of growing concern and strict antibiotic policies should be warranted. The caution use for antimicrobial agents is very important as their unavailability or resistance can be life threatening. Irrational drug use is a common practice in developing countries. In India, clinician often prescribe three or four drugs to treat the most trivial conditions for the sake of satisfying the patients need to receive drugs or the drug sellers need for profit. Thus drug use evaluation studies are required for all drugs in general and particularly for antibiotics.

Key words: Drug use evaluation, antibiotic resistance, irrational use, antimicrobial agents.

INTRODUCTION

Drug Utilization Evaluation (DUE) has been defined by the American Society of Health System Pharmacists (ASHP) as a "Criteria-based, ongoing, planning and systemic process for monitoring and evaluating the prophylactic, therapeutic and empiric use of drugs to help and assure that they are provided appropriately, safely and effectively."[1,2]It is an ongoing, authorized and systemic quality improvement process, which is designed to review the drugs which are prescribed to the patients, provide a right feedback to the clinician/other relevant groups, develop criteria and standards that describe optimal drug use, promote appropriate drug use through education and council the patients.

In the realm of pediatric pharmacotherapy, the investigation of drug utilization is used to examine numerous outcomes, including the examination of prescribing trends in various clinical settings, the extent to which best practices in children differ from drug monographs/labelling and adult dosing guidance, the cost-effectiveness of hospital formularies, and the correlation between medication errors and utilization. Pharmacoepidemiology can be a useful tool for evaluating the appropriateness of drug prescriptions and for estimating therapeutic needs. In particular, pharmacoepidemiology can be valuable in the paediatric setting, which is characterized by the availability of only limited information on the safety and effectiveness of drug use. Recent years have seen growing concerns about the incompleteness of the evidence relating to the efficacy and safety of drugs used in children. Almost all of the drugs prescribed to children are the same as those originally developed for adults. They are often prescribed on an unlicensed or "off label" basis usually by extrapolating clinical data of adults, without conducting any pediatric clinical, kinetic, dose finding, or formulation studies in children.[3]Diseases in children, however, might be different from their adult equivalents, and the

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processes underlying growth and development might lead to a different effect or an adverse drug reaction unseen in adults (Reye's syndrome is an outstanding example). To provide legitimate and appropriate treatment for children's diseases, a legislation was approved in the European Union in 2007 [4]and in United states in 2003.Both the Food and Drug Administration (FDA) and the European Medicines Agency for the Evaluation of Medicinal Products (EMEA) now offer drug licenses to those pharmaceutical companies who provide sufficient clinical evidencesregarding the safety and efficacy of new drugs in childrens.[5,6]In December 2007,The World Health Organization emphasizes the need for these actions and launched a global campaign "make medicines child size" to address the need for improved availability and access to safe child specific medicines for all children.[7]

The rational use of drugs demands prescription of appropriate drugs; availability of drugs at the right time, at a price people can afford, that it be dispensed correctly and that it be taken in the right dose at the right intervals and for the right length of time.Irrational drug use is a common practice in developing countries. In India, a baseline hospital survey showed that poly-pharmacy was common, in hospitalised inpatient and outpatient departments.[8]Clinician often prescribe three or four drugs to treat the most trivial conditions without any laboratory investigations for the sake of satisfying the patients or for the benefit of the drug seller.[9]Thus DUE studies are required for all drugs in general and particularly for antibiotics in children because use of antibiotics in hospitals account for 20% to50% of drug expenditures.[10,11]It is found that about half of the antibiotics prescribed to the children are unnecessary.

Asia is one of the region where the problem of resistance is most prominent. In particular, the rates of resistant pneumococci in Asian countries have been alarming. In India, almost 100% of the healthy population carries bacteria that are resistant to ampicillin, ciprofloxacin trimethoprim, nalidixic acid and chloramphenicol.[12] The International Network for the Rational Use of Drugs (INRUD) was established with an objective to promote the rational use of drugs in developing countries. The INRUD in collaboration with WHO has developed various indicators for assessment of drug use practices.[13] Poor patient compliance or noncompliance with medications is particularly important in clinical practice. It has been found to be related with treatment failure and all its consequences, namely, deterioration of patients' health, the need for additional consultations, the use of extra drugs, additional hospital admissions and increase in direct and indirect costs of disease management.[14] Infants and children represent a large part of the population in developing countries.

Pediatric population is prone to suffer from recurrent infections of the respiratory tract and gastrointestinal system. Although most of the common childhood infections such as diarrhea and upper respiratory tract infections are caused by viruses,and large volumes of antibiotics are prescribed for these infections in children in the primary care settings. It is estimated that 90% of upper respiratory tract infections are selflimiting viral illnesses and even bacterial infections like acute otitis media often run a self limiting course. Clinical trials have shown that antibiotic use to treat common upper respiratory tract infections like sore throat, nasopharyngitis and otitis media has no or minimal benefit on the clinical outcome. Lower respiratory tract infections are one of the leading cause of death in children below 5 five years of age.[15] Acute respiratory infection, acute watery diarrhea and viral fever are the common childhood illnesses accounting for the major proportion of pediatric visits. [16]Respiratory syncytial virus (RSV) is the most common cause of bronchiolitis in infants, infecting most children by two years of age. Approximately 1% to 2% of infected children will require hospitalization. Acute respiratory infections accounts for 20–40% of outpatient and 12–35% of inpatient attendance in a general hospital. In the 2004, World Health Report, the World Health Organization (WHO) estimated that respiratory infections generated 94.6 disability adjusted life years lost worldwide and were the fourth major cause of mortality, responsible for 4 million deaths or 6.9% of global number of deaths in 2002. It is interesting to note that maximum levels of antibiotics are used in the community and primary care, which account for 80% of all human antimicrobial use, yet these antibiotics are inappropriately used for mostly self-limiting upper respiratory tract infections (URTI). Antimicrobial are among the most commonly prescribed drug in Pediatricpatients. They are mostly prescribed as empirical therapy, rather than prophylactic or definitive therapy.The excessive and inappropriate use of antibiotics are believed to be associated with the development of antibiotic resistance in the community.The caution use for AMAs is very important as their unavailability or resistance can be life threatening in certain conditions. Krivoy N et al. has reported that the continuous, indiscriminate, and excessive use of antimicrobial agents may promote the emergence of antibiotic-resistant organisms The International network of surveillance system monitoring data on antibiotic use in Europe through the ESAC project (European

Surveillance of Antibiotic Consumption), published in the Lancet; found that the highest rates of antibiotic resistance were seen in countries with the highest consumption rate of antibiotics.[17]In 2010, the National Institute for Health and Clinical Excellence (NICE) guidelines recommended either delayed or no prescribing of antibiotics for five common diagnoses; acute otitis media, acute sore throat, acute cough/ bronchitis, acute sinusitis and common cold.[18]Several studies focusing on antibiotic prescribing pattern in hospitalized children demonstrate that approximately 35% of infants and children admitted to hospitals receive antibiotics and this indicate the widespread misuse of antibiotics.[19]In the studies conducted by Mohammed Aamer khan et al.[20] and marlies et al.[21]showsthat children below one year and two years respectively are prescribed with antibiotics which is considered as inappropriate by some studies.Higher incidence of infections in infants and children as compared to adultis because of immature immunity leading tohigher use of antimicrobials there by contributing to an overall increase in healthcare costs as well as potentially adverse drug reactions.[22,23,24]Based on clinical and economical criteria, it was found that about 50% of antibiotics prescribed are inappropriate.[25]Most of the studies shows that pediatrics patients are unnecessarily prescribed with antibiotic. According to Hindra I. Satari et al.[25]about 73% of antibiotics are prescribed as empirical therapy rather than appropriate therapy. Similar results were seen in Van Houten et al. study.[26] In a study conducted by Mohammed Aamer khanet al.[20] shows that most of the paediatric patients are treated for infections with two antibiotic followed by three antibiotics .Similarly in studies conducted by Shankar et al[27]and Palikhe et al [28] shows that most of the patientsare treated using two antibiotics whereas in K Shamshy et al. [29] and Shankar et al.[27]study 98% and in Jason Hall,[30] 60.6 % of patients wre treated using single antibiotic.The use of antibiotic for unknown reason is 3.3% in Hindari I et al.[31] when compared to AMRIN study (32%).[32] Since effective medical treatment of a pediatric patient is based upon an accurate diagnosis, which will be usually by obtaining specimens from patients. In studies conducted by Palikhe et al [28]and Mohammed Aamer khan et al[20] very few haematological specimens were obtained from the patients ie. 19.8% and 6.27% respectively whereas in studies conducted by Prakash Katakam et al.[33]and in S. Hu et al.[34]haematological specimens were obtained in 98% and 17.84% patientsrespectively. Because of these reasons there is increase in number of antibiotics per patients to treat the infections.In Jagadish babu et al.[35]Hindra I. Satari et al.[31] and Robin E Huebner[36] study most commonly used antibiotic is cephalosporins whereas in Mohammed Aamer khan et al. [20]and Shamshy et al [29]study it is aminoglycoside and in Al Niemat et al. [37] it is penicillins. For proper absorption of drugs that are administered, route of administration plays a crucial role. It is found that in most of the studies the preferred route of administration is intravenous route.In studies conducted byK Shamshy et al.[29] Ansam swalaha et al.[38] andMohammed Aamer khan et al.[20]the most common route of antibiotic administration is intravenous route and accounts for 80.95% , 61.8%and 84% respectively. The effectiveness of antimicrobial therapy is reflected from the duration of hospital stay.Usually duration of hospital stay depends on disease and its severity.According to Ufer M et al [39]duration of hospital stay is directly proportional to the mean treatment duration.The average hospital stay of patients in Mohammed Aamer khanstudy [20]is 5-10 days.In S K Arulmoli et al[40] study the duration of hospital stay without any antibiotic taken prior to hospital admission is less than 5 days.

CONCLUSION

The main challenges in prescription of antibiotics are to achieve a rational choice and appropriate use of antibiotics and to recognize their potential problems. Consequently, physicians must keep a clear understanding of need for microbiological diagnosis, use of antibiotics and make good judgement in clinical situations despite the financial burden of culture tests on patients. . This may diminish the development of resistant bacteria, reduce health care costs and minimize the potential for adverse events associated with inappropriate antibiotic use.The study concludes that the treatment regimen implemented in most of the cases is without doing much culture sensitivity test which may lead to irrational prescription. Empirical therapy and antimicrobial usage for viral infection can be reduced by the availability of rapid diagnostic method to differentiate between viral and bacterial infection. As in many studies maximum patients are treated with two and more antibiotics it seems that inappropriate empirical and inappropriate definitive therapy antibiotic prescription was more frequent than appropriate empirical and appropriate definitive prescription, respectively. It is hoped that health workers will be carefull in choosing antibiotics, including determining the dose, route of administration, and interval, as well as in evaluating clinical response keeping in view of development of antibiotic resistance.

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