Impact of Clinical Pharmacist Intervention In Rational Antibiotic Use In Pediatric Patients

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Abstract

Irrational use of antibiotics and the major complication of the rapid growth of antibiotic resistance are widely acknowledged. Irrational practice of antibiotics comprises prescription of incorrect dose, duration, route of administration, and regimen frequency and are influenced by certain interrelated factors and drivers. The primary complications of irrational antibiotic use are antibiotic resistance with an increase in poorer health outcomes, increased healthcare costs, more extended hospitalization, and higher mortality, particularly more in the pediatric population. The scope of clinical pharmacy delineates the promising use of antibiotics more rationally than ever. Clinical pharmacists are responsible for achieving goals by spreading awareness and educating about optimal drug use to govern pharmaceutical promotions at the hospital, subsequently progressing outcomes. The narrative review aimed to discuss major influencing factors and compilations associated with irrational antibiotic use, concerns on the pediatric population regarding pharmacokinetic/pharmacodynamic characteristics, and the contribution of clinical pharmacist intervention in addressing the global concern of irrational antibiotic use.

Keywords: Irrational use • Antibiotics • Complications • Antibiotic resistance • Clinical pharmacist • Pediatrics

Introduction

The pharmacy profession is an essential and fundamental part of the healthcare system. The traditional role of pharmacists has been expanded from dispensing medications to a long way of ensuring the quality of healthcare by playing a direct role in providing care to patients as integral members of the medical management system. Community pharmacy services have been a boon to rural areas with a lack of physicians; having said, the general physician services are expensive to afford for the healthcare requirements. Numerous reformations have improved job gratification among Indian pharmacists for advanced salaries, supplementary job opportunities, and recognition in healthcare [1].

The drastic changes regarding the growth in demand for pharmacists in healthcare and patient needs have been significant in parallel to the redefinition of educational and professional responsibilities of pharmacists. The Pharmacy Council of India introduced a Doctor of Pharmacy (Pharm D) program in 2008, emphasizing clinical and patient-oriented aspects of the clinical pharmacy profession. India is yet to encounter the significant job role and recognition of Pharm D in meeting international standards for pharmacy practice [2]. Milap C Nahata et al. conducted a prospective study to evaluate pharmacy practice in 6 hospitals in India and observed that drug availability, selection of best generic drug concerning bioavailability/pharmacokinetic data, presence of formularies, calculated unit dose/IV admixture services, maintenance of patient profiles, providing professional, educational and clinical services to patient/physicians, drug therapy monitoring were optimal in private hospitals with clinical pharmacists. There was an overall limited resource in the current status of pharmacy practice at government hospitals [3].

There is a considerable variation in the delivery of pharmaceutical services offered by clinical pharmacists from one setting to another. The differences are visible in diverse aspects of pharmacy practice, pharmaceutical care, and public health. Clinical pharmacists specialize inpatient care to evaluate medication-related needs and supervise complex/specialized regimens comprehensively [4]. The defined CP scope is not limited to drug information, drug utilization, drug distribution, drug selection, drug evaluation, medication therapy management, disease state management, and pharmacy education/training. The recent effect of the COVID19 pandemic has brought significant improvement in the services offered, such as; identification of triage, individualization of drug dosage regimen, drug monitoring concerning patient parameters, dose regulation of narrow therapeutic agents, drug intelligence, dosage calculation, ADR monitoring, reduction in rates of antimicrobial resistance, detailed history collection/medication reconciliation, patient counseling, Tele counseling services and implementation of national and international guidelines.

The aim of clinical pharmacists comprises functions necessary to discharge a set of social responsibilities regarding the proper therapeutic use of drugs (prescribing, dispensing, and administration), documenting professional services, direct involvement with patients, review of drugs, and education consultation and counseling. The objective lies in ensuring the patient's optimal well-being resulting from the safe and rational use of drugs. The goals are to effectively provide the appropriate maintenance of documentation related to medical incidents to maximize patient compliance with drug use [5]. Antimicrobial resistance is a spontaneous phenomenon and many features influence its rise and spread. One among the chief factors of AMR threat is the irrational practice of antibiotics [6]. Irrational practice of antibiotics involves prescribing incorrect doses, polypharmacy, self-medication practices, off-label use, inappropriate ROA, and overuse/abuse of antibiotics [7]. These elements increase the exposure of bacteria to suboptimal levels of antibiotics resulting in therapeutic inefficiency and facilitating resistance against the drug [8]. Irrational use of antibiotics has been evolving as a global threat in healthcare in escalating numbers in well established countries. It is measured to be 80% in community settings of low- and middle-income countries that lack guidelines and principles [9]. The outcomes are frequently associated with longer hospitalization, poorer health consequences, increased charge to patient/government, and increased mortality and spread. Several pieces of literature have described the incidence of irrational practice of antibiotics in industrialized countries. Southern and Eastern Europe have recorded 30% and 19% of irrational antibiotic use, respectively. Other studies conducted in the Southern province have reported similar results. Northern countries like Austria, Belgium, Denmark, Ireland, and the Netherlands have reported a prevalence of 3% and 6% in central countries [10]. Recent study reports from Tanzania have observed 88.8% of irrational antibiotic purchases with more non-prescription use and incomplete dosage purchases and concluded relatively higher prevalence.

WHO identified India as one of the top countries with higher rates of antibiotic resistance globally with proven reports of inappropriate and irrational use of antibiotics resulting in increased incidence and the threat of antimicrobial resistance [11]. Hence, the rational and judicious use of antibiotics is required and the strategies for achieving the goal and addressing the challenges must be well communicated. The lack of awareness among the general public regarding the (in)appropriate use of antibiotics must be addressed with a good monitoring and surveillance system. Standard treatment guidelines have been generated in developing countries stressing limiting the use of antibiotics by improving the quality of water, sanitation, and immunization. The key is preventing the intake of antibiotics in cases that do not demand them. Two approaches have been stimulated to reduce/prevent the spread of antibiotic resistance - 1) better targeting of antibiotics and 2) thorough vaccination against pneumonia and H. Influenza B virus. In hospital settings, reducing the spread of infections can be implemented, such as isolation rooms, hand washing, use of PPE, and in-service training for physicians to improve prescribing behavior by infection control committee practices. Employment of broad-spectrum antibiotics for empirical therapy to out patients is a significant feature in the development of resistant bacterial strains [12]. Analysis of prescribing patterns of antibiotics in the pediatric population is more effective for better rationality [13]. Generally, pediatrics are more prone to infectious conditions like diarrhea, RTI, unspecified fever and acute gastroenteritis demanding for short-term antibiotic use.

Inappropriate antibiotic treatment regimens are usual and communal in pediatrics like misapplication during viral RTIs and abuse of broad-spectrum antibiotics in RTI,s and UTIs [14]. Reducing the needless use of antibiotics should be a step to decelerate ABR. Studies on pediatric antibiotic use concluded plentiful with irrational antibiotic use. 93.4% of inpatients received IV/IM antibiotics, with the utmost common antibiotics being cefoperazone, cefixime, and azithromycin. LTRI was the foremost reason for antibiotic misuse in pediatric units (56.8%) followed by URTI (22.2%). Unpredictably antibiotic prescription quantity of URTI in tertiary hospitals was higher than patient care (8.1%) (P<.001). A cross-sectional experiment of hospitalized infants has demonstrated investigations of irrational use of antibiotics observed 66.9% compared to tertiary children's hospitals (46.1%) (P<.001) [15]. Thus, it is necessary to identify and implement the WHO recommendations of the Indian Academy of Pediatrics list of Essential Medicines (IAPEM) to avoid the irrationality.

Adherence to guidelines needs a thorough understanding of antibiotics and outcomes to childs' parents. Clinical pharmacists are indispensable in promoting the selection and appropriate use of antibiotics depending on provable microbiological examinations in pediatrics with special care. Additionally, monitoring with pertinent intervals with verifiable use of rational dose antibiotics can result in precise therapy to avoid complications. The present narrative review was developed to discuss the causes and complications of irrational use of antibiotics, pediatric concerns, and the clinical pharmacist's role in addressing the concerns.

Antibiotics

Irrational use of antibiotics is increasing worldwide. Associated complications include antimicrobial resistance, antibiotic-related toxicity, gut-microbiome-mediated properties, and expensive health care costs. Study conducted to evaluate the irrational use of antibiotics in hospitalized children revealed 66.9% of prevalence, with consistently higher percentages than other studies. The point prevalence data from another survey has reported 40.9% irrationality, with data collected only on one selected day of hospital stay. A cross-sectional study in Ethiopia showed 74% of prevalence, and it can be concluded that geographical differences in antibiotic use should be further evaluated through future research. According to the Chinese national management strategy, not more than 60% of hospitalized children should receive antibiotics. Moreover, the research states that approximately 90% of irrational antibiotic use with indications of overprescribing were obvious. The reasons for divulging might be triggered by poorer and suboptimal acquaintance on antibiotic use of doctors and pediatric-specific sources.

Parenteral route of administration has been widely reported for antibiotics such as amoxicillin, azithromycin, and cefuroxime. In contrast, certain studies have reported an oral route of administration ranging for an average of 21.5% in hospitalized children. Parenteral routine is preferable in certain circumstances for antibiotics with restricted oral bioavailability, CNS infection, complex infections, and children with GI distress. The route of administration be subject to solemnly on the form and severity of the disease, and the best effective course must be decided. Various RCTs revealed equivalent safety and efficacy of oral and parenteral penicillin aimed at pediatric patients clinically diagnosed with community-acquired pneumonia. Oral routes can be considered for potential benefits such as avert the suffering of children, minimizing the risk associated with hospital infection, reducing nursing burdens, decreasing medical expenses, and shortening hospital stay.

Causes of irrational antibiotic use

Antibiotics are life-saving, cost-effective medications and contribute to an extended lifespan. The contributing factors to the irrational use of antibiotics include 1. Lack of community knowledge and responsiveness, 2. Access to antibiotics without prescription, 3. Use of unused antibiotics, 4. KAP of healthcare professionals regarding antibiotic use and resistance, 5. Lack of adequate knowledge for healthcare providers, 6. Effect of pharmaceutical preferment, 7. Lack of rapid/adequate diagnostic tools, and 8. Patient doctor interface.

Public understanding and awareness

Regarding antibiotics are powerful determinants contributing to the irrational practice of antibiotics. A recent Eurobarometer statement has revealed 34% of unreasonable antibiotic use. Of these, 57% were unmindful that antibiotics are useless against viruses, and 44% were unaware that antibiotics have no effect against sore throat, cold, and influenza. These varied attitudes and beliefs between countries and social groups impact and increase the higher levels of irrational antibiotic use. Certain studies have shown significant associations with lower literacy levels and worse economic circumstances related to irrational antibiotic use. In Other studies in Sweden, socioeconomic factors have reflected higher antibiotic use, especially amongst children aged 0-6 years. The data suggest that antibiotic use among children are of parental affluence and cannot be solely described by economic factors.

Awareness regarding complications

Awareness regarding complications of irrational use of antibiotics, such as antibiotic resistance and its misconceptions, are high-level contributors. The cause is the cultural variances in public attitudes, opinions, and knowledge regarding antibiotic practice, resistance and self-medication practices. Lithuanian study revealed that two-thirds of contributors with inadequate knowledge tend to overestimate their knowledge due to higher rates of non-adherence and self-medications. Eurobarometer participants have reported that 32% of the population received information regarding doctors' correct use of antibiotics. Efforts must be taken to develop policies regarding advancing knowledge and drug information through TV advertisements, news and newspapers.

Antibiotic use as over-the-counter medications

Antibiotic use as over-the-counter medications is one of the major driving factors with a potential lack of access to the appropriate diagnosis. In Greece, 79% of respondents received antibiotic prescriptions from medical prescribers, whereas in Sweden, it is 98%. Spain showed that antibiotics are easily dispensed in Catalonia without prescriptions for UTI-infected cases. Most OTC dispensed antibiotics are mainly used as topical preparations or eye drops and should not be disorganized with an illegal supply of antibiotics. The occurrence of ABR can bound the availability of licensed antibiotics, and monitoring mustt be made mandatory. Issues regarding telemedicine are the lack of medical examination. There is no possible source of antibiotic resistance from teleconsultation, and thus, lack of proper inspection and significant testing before antibiotic prescription leads to irrational antibiotic practice. The effortless and straightforward dispensing process greatly influences the irrational use of antibiotics.

On the other hand, **pharmaceutical promotions** increase irrational prescribing. Universally, even developing countries with suitable resources for pharmaceutical regulatory oversight varies significantly. Pharmaceutical manufacturing promotions manipulate and influence health care authorities to prescribe and dispense. Various research with systematic review analysis published in 2010 disclosed that physicians' exposure to pharmaceutical data is accompanying with higher prescribing frequency, increased expenses, and lower prescribing excellence. In fact, sales representatives are highly skilled and skilled in influence and prompting talks. A study from Germany revealed that general physicians subject to medical sales had a increased number of total prescriptions than general physicians who visited less regularly.

The **patient-doctor interaction** are essential for recommending antibiotics. An observational research from the UK presented that doctors overestimate patients' hopes for antibiotics just to preserve the relationship. Some surveys have also shown that 55% out of 1000 GPs were under compression to prescribe antibiotics eventhough when it is not necessary and 44% acknowledged that they had to write antibiotics to get the patient to leave the hospital. The complications of antibiotic abuse are severe and have a major impact and the development of antibiotic resistance, thereby increasing healthcare costs.

KAP of community pharmacists

KAP of community pharmacists influence antibiotic practice. The roles of community pharmacists is to adhere to the standard dispensing process and also to provide counseling in regard to effects and safe administration of the drug in promoting appropriate use of antibiotics. WHO shows that community pharmacists are the best-suited public-health related professionals to manage development of antibiotic resistance. Community pharmacies are the primary contact for general public to health-care system for symptom relief and should be referred to practitioners for further consultation. In most developed countries, supply of drugs without a prescription is still a communal exercise. A recent research from Spain revealed that attitudes and factors related to antibiotic resistance are a major accountability of general physicians, dental doctors, and the National Health Service. A study from the Portuguese community revealed that pharmacist knowledge on attitude could influence the partiality to dispense antibiotics without a medical prescription and were satisfactory among patients, the responsibility of others and distress with caution. Community pharmacists had agreement to dispense without prescription in cases for dental diseases/ailments (38.4%) and UTIs (36.2%). Certain studies from Romania evaluated the pharmacist toward antibiotic management and encountered many barriers in their activities. The economic condition of the patient contributes a important role in antibiotic consumption and seek and when combined with operational barriers created by regulations and policies, leads to moral predicaments for ntibiotic management. Considering the patients' economic condition and health consequences, pharmacists dispense antibiotics without prescription.

Complications of irrational antibiotic use

Complications of irrational use of antibiotics in pediatrics are immense, and compulsory attention must be paid to antimicrobial resistance, clostridium difficile infection, hepatotoxicity, renal toxicity caused by overdose, and adverse drug reactions that can be fatal. Other superficial complications include more severe diseases, increased hospital stay, the risk of complications, mortality rate, healthcare costs, reinfection, and the medicalization of self-limiting infectious conditions.

Clostridium difficile

Clostridium difficile is a severe condition more frequently causing nosocomial antibiotic-associated diarrhea with increasing incidence, morbidity, mortality, and healthcare costs worldwide. Centers for Disease Control and Prevention have identified C. Diff as one of the five urgent antibiotic resistance threats. Antibiotic use is not indicated in C. Diff colonization and only to be treated in the presence of CDI with symptoms ranging from mild foul-smelling watery diarrhea to pseudomembranous colitis and toxic megacolon. However, CDI is developed due to irrational antibiotic exposure, especially in the elderly population. Other factors such as alcohol consumption, previous hospitalizations, previous exposure to antibiotic treatments and urban residents are found to be contributing to the development of C. Diff patients who require higher doses of vancomycin and are prone to recurrent disease. According to scientific literature, increased concern for hand hygiene, sterilized environment, proper patient isolation, and duly use of PPE during the initial pandemic have decreased healthcare-associated infections of CDI. Regarding the increase in the irrational use of antibiotics and significant GI symptoms reported in patients, prolonged attention to symptom monitoring is mandatory. Following established therapeutic guidelines of antimicrobial stewardship should remain vigilant for unsolicited adverse reactions.

In hospitalized patients, acute kidney injury and liver injury

In hospitalized patients, acute kidney injury and liver injury increase the risk of mortality and morbidity. The causes of divulging include direct cytopathogenic effects, secondary damage caused by the coexistence of inflammatory responses, or the effect of the patient's drug therapy. The presence of chronic conditions and off-label antibiotic use are the underlying risk factors that exacerbate liver and kidney damage. During COVID-19, there was an increase in the irrational use of azithromycin and other broad-spectrum antibiotics, which were associated with AKI and liver damage in vulnerable populations. Antibiotic-induced hepatotoxicity is usually asymptomatic, transient, and only causes minor hepatic dysfunction. However, acute liver failure has resulted in significant morbidity and death in rare cases. Hepatocellular injury, cholestasis, stenosis, and zonal injury are all common side effects of antibiotics, impairing liver function. ACE-2 receptors on cholangiocytes and hepatocytes have been demonstrated, suggesting that the liver could be a potential access point for SARS-COV-2, resulting in direct liver damage and inflammation/immune reactions manifested as fibrosis and liver dysfunction. Off-label and irrational use of antibiotics is linked to intratubular crystal deposition, interstitial nephritis, and proximal and distal tubulopathy, exacerbating the direct effects of comorbid infections. To avoid complications, it is recommended that antibiotics be used with caution as per protocols and guidelines that specialize in specific comorbid infections and a rational manner in patients. Antibiotic rationing should be promoted in patients to avoid further organ damage and serious long-term complications.

Clinical pharmacists support and contribute to better patient care by monitoring the medication regime, dose, duration, and drug-drug interactions with corticosteroids to actively control ADR development**.** Drugs such as aminoglycosides and cycloserines can potentiate drug induced renal toxicity so they should be given with great caution. Pneumonia is a life-threatening disease and is a chief source of childhood morbidity and mortality. Empirical medications with broad-spectrum antibiotics can reduce significant complications before determining the acute pathogenic cause from results of cultural sensitivity. Recommendations from WHO have mentioned using oral amoxicillin, parenteral ampicillin, and gentamicin as first-line treatment for severe pneumonia. Despite the guidelines and international recommendations, some studies have identified misuse of antibiotics such as cephalosporins (60.3%) with overall antibiotic use escalating to 56.8% in children clinically diagnosed with LRTI. Practicing ntibiotic de-escalation is mandatory as a part of antibiotic stewardship following post culture sensitivity reports. The introduction of pneumococcal vaccines and Hi conjugate vaccines can excellently reduce the prevalence of pneumonia.

Inappropriate antibiotic practice in pediatrics (misuse and overuse) with unnecessary use of antibiotics should be avoided to maintain antibiotics' rationality. Regional antimicrobial stewardship programs (s) are implemented and proved to be effective in optimizing antibiotics in children. Educational programs on antibiotic use in pediatrics to manage secondary and primary children's care settings should be further improved.

Pediatrics

Understanding differences between children and adults regarding anatomy and physiology is supreme in apprehension and conception of drug dosing and rational use of antibiotics. Several crucial differences develop and change over time in preschool age and adolescence. At the age of 18; anatomy and physiology is said to be complete. Recent clinical findings have evaluated the infant subcutaneous tissue of 30% and infant epidermis 20% thinner than compared to adults. Moreover, baby skin is more smooth, permeable, and prone to dryness and infection than adult skin. In addition, a baby's volume/weight ratio is higher comparatively which rises the baby's skin susceptibility to any applied materials/UV exposure. The sebaceous glands are large and the fat content is higher in children than in adults. Body fat percentage in humans peaks at the age of 3-6 months and the nails are soft/thin in contrast to hard/thick in adults. Total amount of water is 75-80% of the body surface area and neonates/infants lose heat more rapidly. Young children have underdeveloped hypothalamus with impared temperature regulation. Drug administration through injections into the rectus femoris/vastus lateralis is the most communal exercise amongst pediatric practice. Due to the larger muscle dimensions; vastus lateralis muscle is usually recommended (<12 months of age) and deltoid muscle (>12 months of age) for IM injections. The liver and spleen lower levels and are less protected by the rib cage. In children, the liver is large, has a wider abdominal cavity, and is protected by undeveloped abdominal muscles. Trachea has a small diameter; the respiration rate is faster, and the airway mucosa is very gentle. Cardiovascular health is generally good and enables them to compensate well for hypervolemia and dehydration. The bladder is less protected by the pelvis, and bladder capacity is 500 cc maximum and not affected by stress.

PK/PD characteristics

The anatomy and physiology establishes the pharmacokinetic outline of the drug. The variations and variations in anatomical and physiological will affect pharmacokinetics and pharmacodynamics characteristics. The pharmacokinetics varies with age, with rapid change in size, body composition, and organ function. The therapeutic value of understanding differences in PK/PD characteristics of pediatrics is to better understand the dose vs. concentration vs. effect profile for a specific drug in patients and improve clinical trial designs on drug disposition and efficacy. Factors influencing **pharmacokinetics** are absorption, distribution, metabolism, and excretion.

The **absorption** of a drug differs in regard to formulation type of manufacturing, especially in pediatrics since the gastric emptying time and intestinal transit time are significantly different with drug disintegration and dissolution rates. In young children with decreased drug absorption, the intestinal transit time has been shorter, particularly with poorly soluble drugs (e.g., theophylline). Gastric pH is neutral at birth, reduced within 24-48 hours to pH 3 with a further rise to neutral again after 72h. The effect of gastric pH in drug absorption is significant, especially for weak essential drugs such as itraconazole (pKa = 3.7). Bile secretion in 2-3 weeks of birth is decreased, with luminal concentrations less than adults respectively. The drug solubility rises with an increase in bile salt concentration. The difference in concentration alters the absorption rate, particularly with poorly soluble drugs (e.g., hydrocortisone). Intestinal permeability is comparatively more at birth with a gradual lessening during the first week of birth and depends on surface area and volume of intestinal villi. Extended GET and condensed intestinal motility are responsible for parallely observed total mass absorbed regardless of D(+)xylose absorption rate in younger patients. Further study was conducted to measure the effects of intestinal motility on absorption, with results showing an increase in Ka in both newborns and infants with Ka: age remained constant. Usually, the absorption rate of most drugs are reduced in newborns and infants; although the cause is unknown.

The drug **distribution** affects the efficacy/duration and dose of the drug and its action. Studies have reported larger distribution volumes in children than that in adults. Drug distribution depends on the body composition, and lipophilic drugs have a higher volume of distribution in infants associated with comparatively higher fat levels. Protein binding with physiological variables influences drug distribution, and the same in newborns is 86% in that of adults. The drug distribution can be higher with a high degree of protein binding (>95%) in newborns and infants.

Drugs are highly **metabolized** in children at lowest dose of mg/kg due to the variances in enzyme concentrations. Although, the hepatic clearance of drugs is increased due to the increase in liver blood flow associated with a larger ratio of liver to total body mass. The increased blood flow to the liver can elevating first-pass metabolism rates, and age-dependent clearances are observed. This has significant outcomes in relations to dosage adjustment whenever necessary. Enzymes are accountable for gut wall metabolism, and thus, variations in enzyme expressions and activity can affect the systemic metabolism in a variety of medications.

Elimination of drugs predominantly occurs via the kidneys. The GFR is 2-4ml/min in neonates and is doubled by one week of birth, attaining adult values after turning one year. The unchanged free drug elimination is less in newborns due to immaturity of renal function, and a greater elimination rate is observed in infants and school-going children. The ontogeny of renal tubular transport mechanisms can impact the excretion of drugs (e.g., digoxin). Creatinine clearance is the estimate of GFR, and a significant reduction in drug dosing is advised with a drop in creatinine clearance from normal GFR. Urinary pH influences the reabsorption of weak acids and bases and is usually lower than in adults.

Pharmacodynamics includes functional and biological responses to drugs. The balance between pharmacokinetics and pharmacodynamics is essential for rational dosing, and analysis of biological samples is necessary to quantify serum drug concentrations over time.

Dose adjustments are undertaken to rationalize the use of drug dosing in children. The drug dosing parameters and age and physiology are dependent. Most realistic practices are based on simple algorithms; rather than valid pharmacokinetic figures that not just involves body weight, height, and surface area. Analysis of drug dose must be made by scaling models to predict the loading and maintenance doses in regard to weight and surface area in case of slightly older children. British National Formulary (BNF) in March 2006 stated that "childrens' doses maybe calculated from adult doses by using age, body weight and body surface area or by a combination of all these factors" was replaced with "consult BNFc or seek advice from medicines information centre" in regard to drug dosing in children. The unavailability of sufficient data regarding drug dose and medication supply makes it tedious to treat a pediatric patient. In such cases; the efficacy, safety, toxicity profile, age and the route of administration should be carefully examined. The FDAs pediatric decision tree highlights the importance of analizing disease progression similar to adult populations and measurement of response in terms of extrapolation of pharmacokinetics of adults into pediatric populace.

Antibiotic monitoring in pediatrics is essential in view of the fact of the differences between adult and pediatric anatomy/physiological characteristics, PK/PD parameters and challenges in the management of complications caused by irrational antibiotic use.

Role of Cp Intervention In Rationalization of Antibiotics In Pediatrics

Rational use of antibiotics in pediatrics can be identified and controlled by clinical pharmacists. The goals are to minimise further development of antibiotic resistance and recommend instantaneous actions to improvise the rational use of antibiotics. The clinical pharmacist put forward the following activities to ameliorate antibiotic use in pediatrics;

Achieving public/healthcare awareness about antibiotic use and its complications

Providing standard education regarding antibiotic use and antibiotic resistance at all stages of general public, health care and individuals can bring about a change to guarantee rational use of antibiotics and to prevent the spread of antibiotic resistance. Awareness campaigns are shown to effective in shifting attitudes, perception and knowledge in all aspects [75]. Spreading of awareness to healthcare professional has lead to huge changes in optimizing prescribing patterns of antibiotics with special emphasis to health care students and junior residents. Additionally, education on pharmaceutical promotions should be provided. Clinicians and hospital administrations should come forward to support the initiatives thus by implementing effective strategies of decision making.

Optimization of antibiotic use

Prevention of using leftover antibiotics is effective way of reducing self-medication rates. This must be implemented through technical measures such as promotion of rational use during dispensation and providing patient-information leaflet. Drug Utilization Evaluation (DUE), Therapeutic Drug Monitoring (TDM) is practiced by clinical pharmacists to monitor the serum drug concentrations appropriately to tapper the doses respectively. Identification of drug-drug interactions in the antibiotic prescriptions will help identify synergistic and antagonistic effects. Other miscellaneous advise by American Academy of Pediatrics has proposed 3 principles for judicious use of antibiotics in children: [76]

1. Determining the likelihood of bacterial infection in accordance with clinical signs and symptoms.
2. Weigh risks and benefits of antibiotics on final diagnosis.
3. Decision regarding application of strategies depending on severity of diseases.

Antibiotic data surveillance

Surveillance is the cornerstones of preventing antibiotic resistance. Lack of surveillance can lead to misdirected policies and surplus of resources. Clinical pharmacists are knowledgeable enough to identify and collect all the relevant recent data regarding treatment guidelines, management strategies, priorities of intervention and individualization of antibiotic regimens. Focused research and clinical trials are necessary to help develop newer and effective antibiotic by pharmaceutical industry to ensure prudent use of antibiotics. Advanced and reasonably priced diagnostic tools are needed to identify the significant infective organisms and support physicians in better decision making.

Governing pharmaceutical promotion

Stronger regulations in governing pharmaceutical promotions should be carried by the department of clinical pharmacy to improve the rational use of antibiotic and preventing the threat of misuse and overuse. Pharmaceutical products with antibiotics should be made available only on prescription demand.

Clinical settings

The primary aim of **patient's medical/surgical history** collection is to determine the patient's current state of health and to rule out any conditions that could complicate the current diagnosis. Patients' basic information, medication history, surgical history, family/personal/social history, type of allergies, and medications are all part of the detailed history collection process. Obtaining the most complete medical history possible aids in preventing potential patient harm during antibiotic treatment. Patient history collection is a time-consuming and tedious task that requires a well-structured framework and questionnaire. The physician collects the patient's medical history in our country, which adds to the burden and delays the physician's time. Recent evolutions in technologies have necessitated a shift in the delivery of significant healthcare services, with preferences shifting to electronic prescriptions, mail orders, the med to bed initiative, and other services that limit patient contact with healthcare professionals, increasing medication errors and interactions. This uncertainty can be avoided by involving a clinical pharmacist in the design of the framework and the patient interview to obtain the most accurate medical history possible. By doing so, the clinical pharmacist will be able to prevent significant medication errors and drug interactions while also saving the time of the physician. Pharmacists can thus act as a link between the patient and the physician. Obtaining an accurate medication history is the first step of the medication reconciliation process, in which the clinical pharmacist reviews the medications that have been prescribed to patients and compares the list with medication that the patient is already taking and thereby helps in preventing medication errors, adverse drug events (ADEs) medication duplication, dosing errors and drug interactions. The important prerequisite for obtaining such satisfactory results is the presence of a pharmacy-led medication reconciliation team who are well trained to collect the best possible medication history. This process can be eased by involving the clinical pharmacist trained in such specific areas in the teams.

The clinical pharmacist can counsel the people regarding the signs and symptoms, route of transmission, and preventive measures, thereby assisting in clearing the confusion and misconceptions regarding antibiotics the therapeutic advantage. Pharmacists can deliver comprehensive disease education at the community level to minimize unwarranted fears. Noncompliance can result in various outcomes, including underuse, overuse, misuse, and abuse. The type of the condition, numerous drug therapy, frequency, duration of therapy, adverse effects, cost of pharmaceuticals, administration technique, and medication taste are the most prevalent factors related to non-compliance. Noncompliance can be prevented by sufficiently educating patients on medication usage and clearly stating the positive benefits of medication compliance and adherence. A clinical pharmacist has a vital responsibility in providing education and awareness regarding disease symptoms, risks and complications, drug compliance/adherence and its importance inpatient therapeutic outcomes and lifestyle modifications, if any, the necessary measures to be taken in emergencies, and the significance of patient review in promoting a better quality of life of the patient and public health in a whole.

Discussion

The role of clinical pharmacists in healthcare settings is growing worldwide parallelly to the higher incidence of irrational antibiotic practice. The scope of clinical pharmacy services is designed to help healthcare professionals with rational dosing and drug use. Unreasonable use of antibiotics in pediatrics is most prominent and can cause a variety of serious adverse events which are hard to manage. The prevention of ADR occurrence is possible by identifying irrational drug use and promoting various strategies for implementing antimicrobial stewardship. Antibiotic use in pediatrics should be of great concern considering the different anatomical, physiological, and PK/PD characteristics. Clinical pharmacists should intervene to promote the rational use of antibiotics with better therapeutic outcomes, and the importance should be recognized.

Conclusion

The demand for clinical pharmacists in hospitals has been increasing in India, uncommonly in small towns and villages with the maximum population. Clinical pharmacy services can serve as the best source of drug information/ polypharmacy for healthcare workers and patients and play a vital role in reducing drug-related problems and drug interactions. Clinical pharmacist services can help determine appropriate antibiotic dosing regimes in pediatric populations in regard to physiological and anatomical changes. Relevant pharmacokinetic data provide sufficient information to improve the standards of antibiotic use. This study best describes the general characteristics of clinical pharmacy services in regulating antibiotics use and the associated outcomes.

Authorship Statement (as per CRediT)

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