

Prescription Pattern Monitoring and Off-label Use of Medicines in the Pediatric Department at Tertiary Care Teaching Hospital

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Citation

Pandey S, Yadav CK, Ghimire P, Shrestha AC. Prescription Pattern Monitoring and Off-label Use of Medicines in the Pediatric Department at Tertiary Care Teaching Hospital. *Kathmandu Univ Med J.* 2020;72(4):367-71.

ABSTRACT

Background

Off-label use means the use, concerning dosage, indication, route of administration, or age, of pharmaceutical products which are beyond the terms of the product license. For regulatory bodies and physicians, the global challenge is to achieve optimum pediatric drug therapy.

Objective

This prospective observational work was carried out in the paediatric department to evaluate the prescribing pattern of medicines and to identify the use of off-label drugs.

Method

A cross-sectional study was carried in 200 paediatric patients of ages between 0 and 12 years at the paediatric outpatient department of Universal College of Medical Sciences, Bhairahawa. Data were collected by reviewing the prescription paper and the required information was recorded using a structured data collection sheet prepared for study. The prescribing pattern was assessed by using the World Health Organization (WHO) Prescription Indicators and off-label use was assessed using the WHO Children Formulary 2010.

Result

Among 413 total prescriptions, only 5.56% of drugs were found to be prescribed by generic name, 16.7% of prescriptions were found to be antibiotic and 57.62% of prescribed drugs were from essential drug list. Out of 413 prescribed drugs, 16.46% of drugs were found to be off-label. The maximum extent of off-label prescribing was 51.47% in the child, followed by infants (42.6%) and neonates (5.8%). Fexofenadine; antihistaminic (23.56%), Amoxicillin+clavulanic acid; antibiotic (22.06%) had higher off-label use. Off-label dose (71.8%) was the most common cause of off-label prescribing.

Conclusion

Off-label prescribing among pediatric patients is common. More evidence data on the safety and efficacy of off-label medicines must be generated to rationalize paediatric pharmacotherapy.

KEY WORDS

Child, Neonates, Off-label drug use, Pediatric, Prescription pattern monitoring studies (PPMS)

INTRODUCTION

Children are treated with medications that have not been tested for safety and efficiency and are also accompanied by evidence of poor quality.¹ Clinician administer medications in an off-label way, in the absence of standard prescribing details. Off-label use involves the use, concerning the route of administration, dosage, indication or age, of pharmaceutical goods which are away from the scope of the product license.² Off-label prescribing is estimated to be 18% to 60% in infants, but in newborns, it can be up to 90 percent.³⁻⁹ In Nepal, there is a strong shortage of study into off-label prescribing. Hence, the purpose of the research analysis was to measure the use of off-label based on the World Health Organizations (WHO) Model List of Essential Medicines for children, different predictors and several methods are addressed to track it.

METHODS

The prospective observational research was performed for six months at a tertiary care hospital in Bhairahawa (Nepal). The study included all pediatric patients aged less than 12 years who received at least one medication and were admitted to the pediatric ward. The patients were not regarded as they were older than 12 years of age and severely ill pediatric patient. Data were collected by reviewing the prescription paper and the required information was recorded using a planned data collection sheet prepared for study. There were seven off-label categories which were shown in table 1.¹⁰ Model List of Essential Medicines for children was used as the sole reference material for determining the prescribing of off label medicines.

Table 1. Off-label categories¹⁰

Off-label Category	Description
Age	The drug not recommended in the product license below a certain age
Weight	The drug not recommended in the product license for children below a certain weight
Absence of pediatric information	No mention at all in the product license regarding pediatric use
Lack of pediatric clinical Data	Stated lack of evidence of efficacy and safety in pediatric patients in the product license
Contraindication	Statement in the product license that the drug is contraindicated in children
Indication	Drug prescribed for indications outside of those listed in the product license
Route of administration	Drug administered by a route not described in the product license

The collected data were filled using MS Excel. Descriptive values were presented as mean values and percentages using statistical tools SPSS (Ver 20.0, IBM SPSS, Inc., NY, USA) for Windows.

RESULTS

Among 200 patients, 109 (54.5%) were males and 91 (45.5%) were females. The age ranges of pediatric patients were Neonates 13 (6.5%), Infant 41 (20.5%) and Child 146 (73%). The dominant age group was child age ranges from 1-12 years. A total of 413 medicines were prescribed for 200 patients. The average medicine prescribed for 200 patients was 2.065.

Table 2. Demographic Data of Patients in the Pediatric Department of Universal College of Medical Sciences

Demographic	N=200(%)
Gender	
Males	109 (54.5)
Females	91 (45.5)
Age	
Neonates	13 (6.5)
Infants	41 (20.5)
Child	146 (73)

Table 3 reveals the different WHO prescribing indicators for prescription pattern monitoring of drugs. The average number of medications prescribed per patient was found to be 2.06 out of 413 prescriptions in total. It was discovered that only 5.56% of drugs were prescribed under the generic name. Likewise, 17.43% of prescriptions are antibiotics and the proportion of medicines prescribed from the list of essential drugs was found to be 57.62%.

Table 3. Prescribing Indicator for Pediatric Patients in UCMS, (N=200)

Prescription Indicators	Value Obtained
Average no. of drugs prescribed per patients	2.06
% of drugs prescribed by generic name	5.56
% encountered with antibiotics	17.43
% of drugs prescribed from essential drug list	57.62

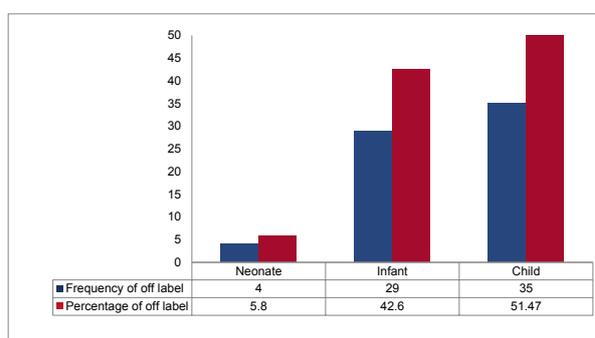


Figure 1. Off-label prescribing in different age groups

Figure 1 shows the off-label prescribing in different age groups. The extent off-label prescribing was highest (51.47%) in the age group of 1 to 12 years i.e. child, followed by age group of 1 to 12 months i.e. infants which accounted for 42.6% of off-label use followed by neonates (0-28 days) which comprises of 5.8%.

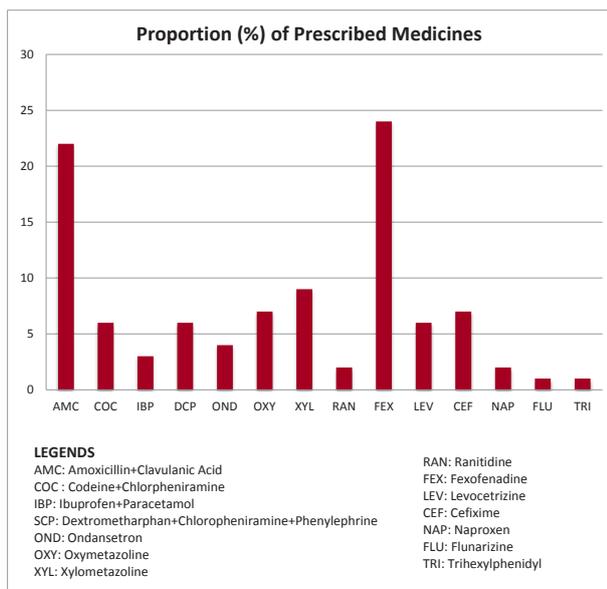


Figure 2. Off-label prescribing of different drugs

Figure 2 shows the highest proportion of off-label medicine prescribed was found to be Fexofenadine; antihistaminic 16 (23.56%) followed by Amoxicillin + clavulanic acid; antibiotic 15 (22.06%) followed by Xylometazoline; nasal decongestant 6 (8.8%). The least proportion of off-label prescribed drugs were ranitidine, naproxen, flunarizine.

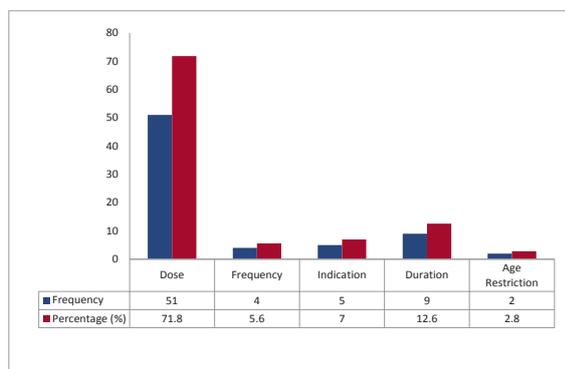


Figure 3. Frequency of prescribed off-label drugs based on different off-label categories

Figure 3 shows the frequency of prescribed off-label drugs based on different off-label categories. Among all prescribed off-label drugs, dose off-label was found to be highest 51 (71.8%) followed by duration off-label 9 (12.6%) followed by indication off-label 5 (7%). Whereas the least off-label category was frequency off-label 4 (5.6%) and age restriction off-label 2 (2.8%).

DISCUSSION

Irrational use of drugs is common in developing countries with a high rate of polypharmacy, overuse of antibiotics, injections, use of 'off-label' drugs and drugs with poor efficacy. Several studies have recorded prescribing

practices among adults in different countries. But there is still the death of information on the prescribing practices in pediatrics. Drugs administered to children are the same as those for adults that were originally created. However, in addition to the disease profile, growth and development processes in children may subject them to multiple adverse effects. In recent years, there has been a growing interest in researching the efficacy and safety of medicine use in children. For example, in 2007, the WHO initiated a global initiative called "make medicines child size" to resolve medicine use concerns in pediatric patients.¹¹

The findings of this current study were based on data from 200 patients. Out of 200 patients, 54.5% of the patients were male and 45.5% of the patients were female. Our findings were comparable to the studies carried out by Thiruthopu et al. and Jose et al. which showed male 65.55%, female patients 34.45% and male (55%), female (45%) respectively.^{12,13} The dominant age group was child age ranges from 1-12 years (73%). Of the total of 413 drugs prescribed in 200 prescriptions, the average number of drugs per prescription was 2.065. This finding was similar to that of the study conducted in Sweden by Olsson et al. in 2011.¹⁰ At another study conducted by Jose et al. average no. of drugs per prescription were 2.29 which were similar to our study.¹²⁻¹⁴

In our study, Antibiotics comprised the highest percentage i.e. 17.43% followed by Antihistaminic 13.8%. Anticonvulsant, antitussive/expectorant, NSAIDs, nasal decongestants, and minerals and vitamins were other commonly prescribed drugs. Antibiotics prescription was less in our study when compared to the study of Thiruthopu et al. (33.29%) and Jose et al. (31.43%).^{12,13} The over-prescription of antibiotics is a challenge that is the main goal of the antibiotic stewardship programme to reduce drug resistance.^{12,13}

Just 5.56% of medications were found to be prescribed under the generic label in this report which is very less as compared to the study conducted by Thiruthopu et al. in India.¹² In tertiary care teaching hospitals, Nazima et al. found that the medications prescribed with generic names were 30.7%. The study conducted by Jose et al. found out that 98% of the drugs were prescribed in a generic name. It is known that prescribing a generic name reduces the cost of drug treatment and rationalizes drug therapy.^{12,13,15} But due to the lack of effective policy by the government the scenario of generic prescription is very low in Nepal.

More than half (57.62%) drugs were prescribed from essential drug list which is more than the study of Thiruthopu et al. (49.78%).¹² In the study of Jose et al. 100% of drugs were from the essential drug list.¹³ Our study states that the most patients were prescribed with syrup (60%) and tablets (26%) which was similar to the study of Jose et al. which showed syrups (62.73%) and tablets (15.25%).^{12,13}

Owing to the minimal pediatric evidence on most drugs, pediatric patients have also been referred to as “therapeutic orphans”. Despite well-known risks, the use of the off-label drug is very common in children. This is due to the extremely small number of prescription types available and the lack of officially recognized clinical evidence in the pediatric population for dosing decisions.¹⁴

In a study of the pediatric patient, Santos et al. found that 39.6% of medications were used off-label.¹⁵ Our study found out that 16.86% of prescribed drugs were off-label. Another study conducted by Saiyed et al. showed 70% off-label of prescribed medicines which was very high as compared to our study.¹⁶ Langerová et al. showed that 9.01% of drugs were prescribed off-label.¹⁷

Pandolfini and Bonati conducted a comprehensive review of all current findings on off-label and unlicensed medicines usage in children. A total of 30 experiments were included, from 1985 to 2004. Eleven active wards for pediatric hospitals, seven wards for neonatal hospitals, and twelve for the group. The off-label and unlicensed methods of classification vary, making it impossible to compare the findings. Off-label/ unlicensed drug rates, in total, ranged from 11% to 80%. Off-label/unlicensed prescriptions ranged from 16% to 62% in the pediatric hospital wards.¹⁸ Off-label classification techniques, sample sizes, prescribing habits of pediatricians, in-house treatment protocols, and features of diseases, most notably pediatric drug regulation, are an assortment of reasons for diverse rates of off-label use.¹⁶

The level of off-label prescription was greatest in our sample (51.47%) in the age group aged 1 to 12 years i.e. child, followed by age group of 1 to 12 months i.e. infants which accounted for 42.6% of off-label use followed by neonates (0-28 days) which comprises of 5.8%. In the study performed by Saiyed et al., the level of off-label prescribing was highest (76%) in the age group of more than 1 to 2 years, followed by an age group of more than 1 to 12 months, accounting for 69 percent of off-label use. Langerová et al. found that off-label prescription medications were found more frequently found in infants (14.3%), toddlers (13.0%) and preschool-age children (15.3%).^{16,17}

Our study concluded that highest proportion of off-label medicine prescribed was Fexofenadine; antihistaminic (23.56%) followed by Amoxicillin + clavulanic acid; antibiotic (22.06%) followed by Xylometazoline; nasal decongestant (8.8%). The study conducted by Olsson et al. showed that antibiotics for systemic use were among the most commonly prescribed drugs used off-label, as

were antiasthmatics drugs.¹⁰ According to the Saiyed et al. report, several of the off-label medications prescribed were ceftriaxone, amoxicillin, amikacin, and vancomycin in antibiotics class and inhaled corticosteroids, ipratropium, chlorpheniramine, salbutamol, phenylephrine analogous to the respiratory system.¹⁶ Various combinations of antihistaminic, decongestants, and/or analgesics were prescribed to patients in off-label doses for the common cold.¹⁰ But the effectiveness of young children is still questionable.¹⁹

In our study, the most frequent cause of off-label prescription was dose off-label (71.8%) followed by duration off-label 9 (12.6%) followed by indication off-label 5 (7%). Whereas the least off-label category was frequency off-label 4 (5.6%) and age restriction off-label 2 (2.8%), which is similar to the study conducted by Saiyed et al. dose (63%).¹⁶ Our result differs from the study conducted by García-López et al. which shows the main reason for off-label use was by indication, followed by age and dose.²⁰ Several other studies have also stated that dosage and/or dosage duration were the most prominent explanation for off-label prescribing.^{9,21} The key reason behind the off-label dose is the need to measure child dose based on weight, body surface area, age or other body condition for any pediatric patient.

CONCLUSION

The study was carried out to describe the pattern of drug prescribing by the physicians and off-label use of medicines in western Nepal. Effective prescribing practices were practised that adhered to standard WHO prescribing guidelines. However, the prescribing of medications by brand names is a matter of concern rather than the suggested generic names. Our research indicates that, based on the WHO Children Formulary 2010, the rate of off-label drug prescriptions in our patients is not as high as in other trials. In 16.86 percent of all prescriptions, medications prescribed off-label was detected.

ACKNOWLEDGEMENTS

We would like to extend our heartfelt thanks to Mr. Anup Bhusal, Department of Pharmacology, UCMS for the encouragement to carry out the research work. We are thankful for all those who have supported us during this project.

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