International Journal of Research in Medical Sciences
Vaghela MM et al. Int J Res Med Sci. 2016 Aug;4(8):3498-3503
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: http://dx.doi.org/10.18203/2320-6012.ijrms20162319

Research Article

An analysis of ear discharge and antimicrobial sensitivity to the bacteria used in its treatment

Mukund M. Vaghela*, Hiren Doshi, Sneha Rajput

Department of ENT, Smt. NHL MMC, Ahmedabad, Gujarat, India

Received: 19 June 2016
Accepted: 08 July 2016

***Correspondence:**
Dr. Mukund M. Vaghela,
E-mail: akansha_prajapati@yahoo.com

ABSTRACT

Background: Children are unique population with distinct development and physiological differences from adults, clinical trials in children are essential to develop age-specific, empirically – verified therapies and interventions to determine and improve the best medical treatment available. The aim of this study was to find out the appropriateness and accuracy of the dose of drugs prescribed and compares it with standard dose.
Methods: Total 400 prescriptions were collected from the OPD of the paediatrics of Shree Krishna Hospital, Karamsad. Calculation of standard total daily dose for each drug was done by using Clark's formula and was compared with that of prescribed dose of that particular drug.
Results: Total 1042 drugs were prescribed. Among antibiotics (22%) statistically significant difference in the prescribed and standard total daily dose was observed with cefexime [t-value 28.6>1.96 for 95% confidence interval] and metronidazole [t-value2.03>1.96 for 95% confidence interval], NSAIDs (31%), Paracetamol [t-value11.14>1.96 for 95% confidence interval] and antihistaminics (22%), phenylephrine [t-value7.1>1.96 for 95% confidence interval], cetrizine [t-value2.4>2.00 for 95% confidence interval].
Conclusions: Results show that prescribed doses of commonly used drugs were higher than the standard dose. This is directly related to the occurrence and severity of adverse drug reactions.

Keywords: Prescribed drugs, Dose and body weight

INTRODUCTION

Children are unique population with distinct development and physiological differences from adults, clinical trials in children are essential to develop age-specific, empirically – verified therapies and interventions to determine and improve the best medical treatment available.[1] Even widely used pediatric medications may have the potential for serious adverse effects. Indeed, many of the medications that are being used currently for children have never been tested rigorously for pediatric safety and efficacy, a problem that federal regulators have been attempting to resolve over the past decades.[2] Calculation of dose of drugs prescribed for pediatric population remains the major challenge for paediatricians. Iatrogenic injuries occur frequently in hospitalized patients and often remains the serious sequelae.[3] As the pharmacokinetics in infants and children are different, simple proportionate reduction in the adult dose may not be adequate to determine a safe and effective pediatric dose.[4-6] A large number of children's drug dosage rules have been described, almost all using percentage of an adult dose to calculate an appropriate child's dose. An advantage of these rules is that modifications to adult doses to allow for sickness in adults are appropriately incorporated in to calculations for children.[7-9] Reports in the literature quote many examples of prescription errors in children, of 2-10 times the recommended dose.[10-14] This study was designed to analyze the appropriateness of dose of drugs prescribed in pediatric age group of patients visiting outpatient department (OPD).

METHODS

This was an open label cross-sectional study spreaded over a period of one year and three months May 2012 to August 2013, conducted in Shree Krishna Hospital and Medical Research Centre, a 550 bed tertiary care teaching rural hospital attached to Pramukh Swami Medical College, Karamsad. Patients of either sex falling into different age groups according to ICH guidelines attending outpatient department (OPD) of pediatrics were included in the study. Patients coming for only vaccination were excluded from the study. A total 400 patients were included in the study. Parents or guardians of the eligible patients were explained about the research study and written informed consent was obtained in the native language of the patient. Analysis of demographic data and medication details were done separately. Prescribed total daily dose and its mean standard deviation were calculated according to frequency of administration for each drug. Standard dose was calculated according to Clark's formula.

$$\text{Clark's formula} = \frac{\text{Child's weight in kg}}{\text{70 kg}} \times \text{adult dose in mg} = \text{Paediatric dose in mg}$$

Standard total daily dose and its mean standard deviation were calculated and was compared to that of with prescribed. Data were entered in to the Microsoft Excel 2007 and separate master chart was prepared and analysed using SPSS version 16.0. Mean±standard deviation for prescribed total daily dose and standard total daily dose of all the drugs was calculated and was compared using independent Student's t-test. Standard error of mean was calculated and degrees of freedom was calculated for each drug. Prescribed total daily dose was considered statistically significantly different than standard total daily dose if t-value was greater for that degrees of freedom according to the probability table for t-test at 95% confidence interval. Before starting this study, necessary permission was taken from the Human Research Ethics Committee (HREC), H M Patel Centre for Medical Care and Education, Karamsad. Confidentiality of all participants was maintained at all levels.

RESULTS

Total 400 prescriptions were collected from outpatient department (OPD) of pediatrics of Shree Krishna Hospital, Karamsad.

Table 1 shows distribution of enrolled patients according to age and weight. Out of 400, 244 (61%). Patients were in the age group of 2-11 years. As weight is one of the parameter for calculating the standard dose according to Clark's formula it was one of the most important detail to be recorded. Majority of the patients weighed between 1-10kg (169, 42.25%), followed by 11-20kg (146, 36.5%), 21-30 kg (61, 15.35%), 31-40 kg (18, 4.5%) and 41-50 kg (6, 1.5%).

Total 1042 (100%) drugs were prescribed. Out of these 616 (59.12%) drugs were prescribed by brand name and 425 (40.88%) were prescribed by generic name, 593 (56.94%) oral liquid (syrup, suspensions) formulations and 441 (42.93%) oral solid (tablet, capsule) formulations were prescribed. 19 (1.83%) inhalational (metred dose inhaler, rotahaler) formulations were prescribed. We were not encountered with any prescription containing injectable dosage forms (Figure 1 and 2).

Table 1: Distribution of patients according to age and weight.

Parameters	No. of patients (n =400)	% of patients
Age		
0-27 days (newborns)	0 (0%)	0%
28 day-1 year (infants)	89 (22.25%)	22.25%
1-2 years (toddlers)	50 (12.5)	12.5
2-11 years (children)	244 (61%)	61%
12-18 years (adolescents)	17 (4.25%)	4.25%
Weight (kg)		
1-10 kg	169 (42.25%)	42.25%
11-20 kg	146 (36.5%)	36.5%
21-30 kg	61 (15.25%)	15.25%
31-40 kg	18 (4.5%)	4.5%
41-50 kg	6 (1.5%)	1.5%

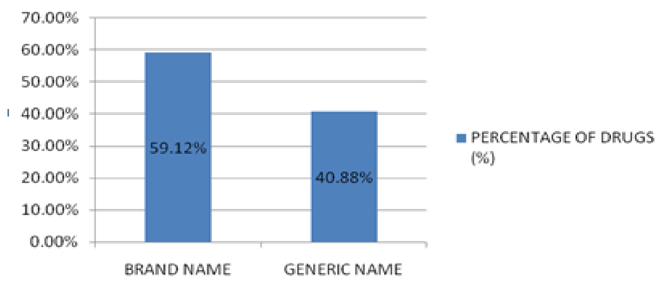

Figure 1: Distribution according to brand/generic name.

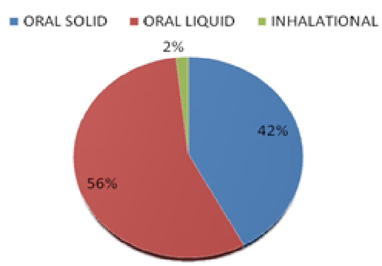

Figure 2: Distribution according to different dosage forms

Out of 1042 maximum number of drugs were prescribed from the group of non-steroidal anti-inflammatory drugs (NSAIDs) 322 (22%) followed by antibiotics and antihistaminics 232 (22%) each. Among NSAIDs Paracetamol and Ibuprofen were prescribed most frequently. Out of 322 (31%) NSAIDs paracetamol was 270 (83.8%) and ibuprofen was 52 (16.14%) times prescribed. Next groups of drugs with second highest frequency of prescription were antibiotics (232, 22%) and antihistaminics (232, 22%). Amoxcillin (65, 28.01%), azithromycin (56, 24.13%), cotrimoxazole (35, 15.08%) were most common antibiotics prescribed. Other antibiotics like cefixime, metronidazole, ciprofloxacin, cefpodoxime and linezolid were also prescribed (Table 4). Chlorpheniramine maleate (95, 40.94%) and pheniramine maleate (81, 34.91%) were most common antihistaminics prescribed, followed by diphenhydramine (32, 13.79%) and cetrizine (24, 10.34%) (Table 4).

Table 2: Frequency of prescribed NSAIDs and comparison of dose.

NSAIDS 322(100)					
Sr. No.	**Drugs and categories**	**Frequency of prescription (%)**	**Prescribed total daily dose (mean±standard deviation)**	**Standard total daily dose (mean±Standard deviation)**	**t- value (independent t-test)**
Ia	Paracetamol	270(83.85)	878.212±415.657	521.090±323.04	**11.14**
Ib	Ibuprofen	52(16.14)	692.307±395.086	626.923±372.162	0.5

Table 3: Frequency of prescribed antibiotics and comparison of dose.

Antibiotics 232 (100)					
Sr. No.	**Drugs and categories**	**Frequency of prescription (%)**	**Prescribed total daily dose (mean±standard deviation)**	**Standard total daily dose (mean±Standard deviation)**	**t- value (independent t-test)**
IIa	Amoxicillin	65 (28.01)	939.538±598.727	787.477±868.131	0.0068
IIb	Azithromycin	56 (24.13)	265.892±168.316	165.535±102.288	5.27
IIc	Cotrimoxazole	35 (15.08)	534.857±206.851	507.43±205.025	0.22
IId	Cefixime	29 (12.5%)	410.345±30.132	264±65.791	28.61
IIe	Metronidazole	20 (8.62)	975±974.999	495.231±407.329	2.03
IIf	Ciprofloxacin	18 (7.75)	491.667±361.67	530±736.884	0.3
IIg	Linezolide	6 (2.58)	733.333±37.91	800±326.597	0.4
IIh	Cefpodoxime	3 (1.29)	666.667±690.667	300±141.417	0.9

Table 4: Frequency of prescribed antihistaminics and comparison of dose.

Antihistaminics 232(100)					
Sr. No.	**Drug**	**Frequency of prescription (%)**	**Prescribed total daily dose (mean±standard deviation)**	**Standard total daily dose (mean±standard deviation)**	**t-value (independent t-test)**
IIIa	Chlorpheniramine maleate	95(40.94)	17.72±16.79	9.8±5.63	0.5
IIIb	Pheniramine maleate	81(34.91)	42.25±21.85	26.48±13.39	**7.1**
IIIc	Diphenhydramine	32(13.79)	39.06±22.45	21.87±10.43	**3.9**
IIId	Cetrizine	24(10.34)	9.12±5.37	6.25±1.91	**2.4**

Prescribed total daily dose was statistically significantly different from the standard total daily dose of paracetamol [t-value 11.14>1.96 for 95% confidence interval] (Table 2). t-value for azithromycin was 5.27, which was higher than 1.96 for 95% confidence interval suggested that prescribed total daily dose was statistically significantly higher than the standard total daily dose. Similarly, prescribed total daily dose was statistically significantly different than the standard total daily dose of cefixime as t-value 28.61>1.96 for 95% confidence interval. Statistical significant difference between prescribed total daily dose and standard total daily was also found with metronidazole [t-value 2.03>1.96 for

95% confidence interval]. Prescribed total daily doses were not statistically significantly different from the standard total daily doses for other antibiotics like, cotrimoxazole, ciprofloxacin, linezolid, cefpodoxime and amoxicillin (Table 3).

t-value for pheniramine maleate was 7.1 which was higher than 1.96 for 95% confidence interval suggested that prescribed total daily dose was statistically significantly different than the standard total daily dose. Prescribed total daily dose was statistically significantly different from the standard total daily dose of diphenhydramine and cetrizine also, as t-value for diphenhydramine was 3.9 which was higher than 2.00 for 95% confidence interval and t-value for cetrizine was 2.4 which was higher than 2.02 for 95% confidence interval (Table 4).

DISCUSSION

Infancy and childhood is the period of rapid growth and development. Compared to adult medicine, drug use in paediatric patients is not extensively researched, specially the dose of the prescribed drugs. Weight based dosing is needed for drugs prescribed in paediatric patients and involves extensive calculations than for adults. Thus children are particularly more vulnerable to medication dosing errors. All 400 patients were classified in to different age groups according to ICH classification of children by age in newborns, infants, toddlers, children and adolescents.[15] Out of 400 patients 244 (61%) patients were in the age group of 2-11 years (children). In this study there were more male children (227, 56.75%) than females (173, 43.25%). In a similar study by Kaushal R et al, 2001, in 1120 admissions and 3932 patient-days during which 10778 orders were written.[3] The patients included 183 (16%) neonates, 326 (29%) infants, 223 (20%) preschoolers, 161 (14%) school-aged children, 191 (17%) teenagers and 36 (3%) adults. In same study 525 (49%) were female patients. In a study by Domecq C et al, 1980 in Santiago, Chile, it was shown that 83% of ADR in males and 93% of ADR in females were dose related effects.[16] It shows that may be females are more prone to dose related errors, but association of dosing errors with sex is not carried out in our study so it can not be confirmed. Out of 400 patients 169 (42.25%) patients had weight between 1-10 kg. One prospective cohort study carried out by Kaushal R et al, 2001 in 1120 patients in two academic institutions showed that 3.7% of institutions' medication errors were due to missing or wrong weights.[3] This depicts the importance of recording of weight accurately. Out of total drugs 1042 drugs 616 (59.12%) were prescribed by brand name and 593 (56.94%) were prescribed by oral liquid dosage form. In a study by Mirza NY et al, showed that of total 1483 medicine formulations prescribed 1027 (69.3%) were prescribed by brand names, which shows inclination of prescriber to prescribe a drug by brand names.[17] In a similar type of study by Pramil T et al, showed that out of total drugs prescribed 90% were administered by oral route and out of that 75% of the prescribed dosage forms were syrups followed by tablets (7.2%), capsules (0.4%) and inhalation (1.6%).[18] These similar findings suggest more common use of oral liquid dosage form in paediatric patients in outpatient setting. The possible reasons for less prescribing by generic name could be prescribers' doubt about bioavailability and efficacy of generic formulations, prescriber's ignorance about the price variations between generic and branded and lack of information on the availability of various generic formulations. Another possible reason could be the easy availability, easy recall of branded. Most commonly used dosage form was oral liquid. Children are more comfortable with the dosage forms like syrup and drops than tablets or capsules and this finding is well taken. The administration of liquids can be a major contributing error in dosing in children. The use of different size of spoons may lead to under dosing and over dosing of medication.[18] Of total 1042 drugs 322 (22%) drugs were prescribed from NSAIDs group followed by 232(22%) antibiotics and antihistaminics. Pramil T et al, 2012, found that only 79 (6%) drugs of 1331 were antibiotics.[18] Where as in a study by S Dimri et al, showed that percentage encounter with an antibiotic prescribed was found to be 29.1% and NSAIDs (paracetamol) contributed to the majority (76%) of drugs prescribed.[19] These findings correspond with our study. In our study we observed out of total 1042 drugs 322(31%) were NSAIDs and out of these 270 (83.8%) were paracetamol and 52 (16.14%) were ibuprofen. Dimri S et al, found out that out of 254 prescriptions paracetamol was most commonly prescribed drug, 83 cases.[19] This was similar to our study. A study carried out by Shamshy K et al, 2011[20], observed significant use of antimicrobials. Among those cephalosporins (38, 83%) contributed highest, followed by aminoglycoside (22.78%) and penicillin derivatives (18, 87%). Cephalosporins like cefotaxim and ceftriaxone were antimicrobial agents of choice for pediatric patients which accounts for 20.03%. In contrast to these findings in our study among antimicrobial agents penicillin derivative like amoxicillin (28.01%) and aminoglycoside like azithromycin (24.13%) were major contributors. In our study out of all prescribed antibiotics statistical significant difference between prescribed and standard total daily doses was observed in azithromycin (t-value 5.21>1.96 for 95% confidence interval), cefexime (t-value 28.61>1.96 for 95% confidence interval) and metronidazole (t-value 2.03>1.96 for 95% confidence interval). A study carried out by Elias GP et al, showed that standard doses calculated by Clark's formula for amoxicillin and erythromycin was not statistically significant (p>0.05) in three groups of children, group 1: age 1-3 years, group 2: age 3-5 years and group 3: age 6-12 years.[21] This finding is similar to our study. In a study by Lesar TS et al, showed that errors most commonly involved children (69.5%) and that too because of antibiotics (53.5%).[22] Our study, we observed the statistically significant difference in the prescribed and total daily doses in pheniramine maleate, dphenhydramine and cetrizine.

Kaushal R et al, observed that 6% dosing errors with antihistaminics.[3] But they have not mentioned the individual drugs of this group. Authors compared their findings with a similar adult study, the rate of dosing errors was 12 times higher in children than adults in prescribed antihistaminics. The many calculations required in paediatrics to do weight based dosing may be an important factor contributing to the high rates of prescribing errors There was lack of published studies on dose calculation of different antihistaminic drugs in paediatric patients. In our study there was statistical significant difference in prescribed and standard doses of paracetamol which was similar to the study carried out by Elias GP et al.[21] They calculated standard dose of paracetamol with the formula based on body surface area and found out it was statistically significantly different than the prescribed dose. It was much closer to the hepatotoxic dose of paracetamol for children. This was observed in the children of age group of 1-5years. A study carried out in 213 children aged 6 weeks to 16 years by Obu HA et al, observed that dose and frequency of administration of drug was much higher than the standard dosing guideline given in pediatric reference text book.[23] In contrast to our study they did not use any formula to calculate the standard dose according to weight, age or body surface area, it was compared with the standard dosing guideline of the reference text books.

Limitations

It was a cross sectional study, no follow-up was done to identify the adverse drug reactions in patients who had been prescribed over doses of drugs. Moreover, it was conducted at only one tertiary care teaching hospital. Comparison with government and private hospitals will strengthen our findings.

CONCLUSION

There was significant difference in the prescribed and standard doses of antibiotics, non-steroidal anti-inflammatory drugs (NSAIDs) and antihistaminic drugs in OPD based patients. This study illustrates the area where children are vulnerable to medication error, where violations in practice are most likely so increasing the risk and where risk reduction strategies can be introduced. Perhaps reduction in dosing error will reduce drug induced adverse drug reactions in children, which can be done by careful monitoring and employing strategies like e-prescriptions.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Frankking FNJ, Van Der Lee JH, Klassen TP, Offringa M. Survey of current guidance for child health clinical trials. The Star Child Health Project: Standards for research with children. Pg; 5-7.
2. Vernacchio L, Kelly JP, Kaufman DW, Mitchell AA. Medication use among <12 years of age in the United States: Results from the Slone Survey. Pediatrics. 2009;124(2):446-54.
3. Kaushal R, Bates DW, Landrigan C, McKenna KJ, Clapp MD, Frank F, Goldmann D. Medication errors and adverse drug events in pediatric inpatients. JAMA. 2001;285:2114-20.
4. Nicholas H, Holford G. Pharmacokinetics & Pharmacodynamics: Rational dosing & The time course of Drug Action. In: Basic & Clinical Pharmacology. 12th edition. New Delhi. McGraw hill &lange. 2012.p.37-52.
5. McCarthy J. Drug metabolism and disposition in Pediatric and Gerontological stages of life. In: Craig CR, Stitzel RE. editors. Modern Pharmacology with clinical applications. 6th edition. Lippincott Williams & Wilkins; 2003. P.56-62.
6. Koren G. Special Aspects of Perinatal & Pediatric Pharmacology. In Katzung BG, Masters SB, Trevor AJ. editors. Basic & Clinical Pharmacology. 12th edition. New Delhi. McGraw Hill & Lange. 2012.p. 1039-49.
7. Augsberger A. Old and new rules for dosage determination in pediatrics. Triangle (Sandoz). 1962;5:200-7.
8. Allnutt AG. Dosage relation to dispensing medicine for children. London Pharmaceutical Society of Great Britain. 1966;57-66.
9. Ritchell WA. Drug dosage in children. In: Ritchell WA, ed. Handbook of Basic Pharmacokinetics Hamilton, USA: Drug Intelligence Publications, 1976; 254-66.
10. Baris GL, Bailey BJR. Surface area estimation: pocket calculator v normogram. Archives of Disease in Childhood. 1994;70:246-7.
11. Koren G, Brazilay Z, Modan M. Errors in computing drug dosages. Canadian Medical Association Journal. 1983;129:721-3.
12. Wilson ME, Macleod KR. Forum: A nomogram to reduce errors in pediatric drug dosage calculation.” Anaesthesia. 1982;37:951-3.
13. Perlstein PH, Callison C, White M, Branes B, Edwards NK. Errors in drug computations during newborn intensive care. American Journal of Diseases of Children. 1979;133:376-9.
14. Shane R, Quon LM. Prevention of medication errors in pediatrics. American Journal of Diseases of Children. 1981;135:384.
15. Aggarwal R, Sankhyan N, Jain V. Normal Growth & Development. In: Paul VK, Bagga A. Essential Pediatrics. 8th edition. New Delhi: CBS publishers; 2013.p.7-42.
16. Domecq C, Naranjo CA, Ruiz I, Busto U. Sex-related variations in the frequency and characteristics of adverse drug reactions. Indian Journal of Clinical Pharmacology and Therapeutic Toxicology. 1980;18(8):362-6.

17. Mirza NY, Desai S, Ganguly B. Prescribing pattern in a pediatric out-patient department. Bangladesh Journal of Pharmacology. 2009;4:39-42.
18. Pramil T, Rajiv A, Gaurav G. Pattern of prescribing at a paediatric outpatient setting in northen India. Indian Journal of Pharmacy Practice. 2012;5(1):40-4.
19. Dimri S, Tiwari P, Basu S. Drug use pattern in children at a teaching hospital. Indian Peadiatrics. 2009;46:165-7.
20. Shamshy K, Mufida BI, Perumal P. Drug utilization of antimicrobial drug in paediatric population in a tertiary care hospital in Erode, Tamilnadu, India. International Journal of Pharma Tech Research. 2011;3(3):1530-6.
21. Elias GP, Antoniali C, Mariano RC. Comparative study of rules employed for calculation of paediatric drug dosage. Journal of Applied Oral Science. 2005;13(2):114-9.
22. Lesar TS. Errors in the use of medication dosage equations. Archives of Pediatrics and Adolescent Medicine. 1998;152:340-4.
23. Obu HA, Chinawa JM, Ubesie AC, Eke CB, Ndu IK. Paracetamol use (and/or misuse) in children in Enugu, South-East, Nigeria. BioMed Central Peadiatrics. 2012;12:103.

Cite this article as: Vaghela MM, Doshi H, Rajput S. An analysis of ear discharge and antimicrobial sensitivity to the bacteria used in its treatment. Int J Res Med Sci 2016;4:3498-503.