## **CLINICAL INVESTIGATION**

### The Impact of a Pediatric Antibiotic Standard Dosing Table on Dosing Errors

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**OBJECTIVES** The goal of this study was to compare the rate of dosing errors for antibiotic orders in pediatric patients before and after the implementation of an antibiotic standard dosing table with precalculated dosage for different weight ranges at a tertiary care hospital.

**METHODS** A retrospective study of 300 antibiotic prescriptions for pediatric patients in three different settings (ambulatory care, inpatient, and emergency department) at a tertiary care hospital assessed the appropriateness of antibiotic dosing. The need for an antibiotic dosing standardization policy was identified after finding that more than 30% of patients experienced a dose variation of  $\pm 10\%$  of the recommended daily dose. An antibiotic dosing standardization policy was implemented with an antibiotic standard dosing table for different weight ranges, and a hospital wide-education program was conducted to increase awareness of this new practice and its benefits. Three months after implementation, a random sampling of 300 antibiotic prescriptions collected from the same settings as the pre-intervention period was evaluated for compliance with the new policy and its effect on the number of antibiotic dosing errors.

**RESULTS** Six hundred prescriptions were included in this study (300 in the pre-implementation phase and 300 in the post-implementation phase). Patient characteristics were similar in both groups in terms of sex, age, and weight. Physician compliance with the antibiotic dosing standardization policy after its implementation was 62%. The dosing standardization policy reduced the rate of dosing errors from 34.3% to 5.06% (p=0.0001), and weight documentation on the antibiotic prescription improved from 65.8% to 85.7% (p=0.0001). **CONCLUSIONS** Implementation of an antibiotic dosing standardization policy significantly reduced the incidence of dosing errors in antibiotics prescribed for pediatric patients in our hospital.

**INDEX TERMS** antibiotic dosing, dose rounding, dosing errors, dosing standardization, medication safety, pediatrics

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#### INTRODUCTION

Medication errors are one of the most common types of medical errors and contribute to the mortality and morbidity of hospitalized patients.<sup>1,2</sup> Pediatric patients are at a higher risk of experiencing medication errors than adults because of the need for a dose calculation based on a patient's age, weight (mg/kg), body surface area (mg/m<sup>2</sup>), and clinical condition.<sup>3–5</sup> Kaushal et al.<sup>6</sup> studied medication errors in pediatric patients and found that medication errors that can cause harm were three times more likely in children than in the adult population. In a systematic review of 16 studies that investigated the incidence and nature of medication errors, dosing errors were found to be the most common type of error during the medication use process in the pediatric population.7 Miscalculation of pediatric dosing can lead to a tenfold or greater rate of dosing errors which can have harmful consequences for patients. Another source for dosing errors in children is misplacement of the decimal point after calculating the dose.4,8,9 Antibiotics and sedatives are the medications most widely prescribed in the pediatric population and are the drug classes most commonly reported involved in pediatric medication errors.6,7,10,11 Subtherapeutic dosing of antibiotics has been identified as a frequent problem in the pediatric population as many clinicians do not consider weight when they calculate the dose or they

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simply calculate the pediatric dose as one half of the adult dosing.<sup>6,12,13</sup> Optimizing antibiotic dosing is essential to avoid treatment failure and minimize the emergence of resistant organisms.<sup>14</sup>

Strategies that reduce the rate of dosing errors are essential to minimize harmful consequences. Implementing dosing standardization and polices that guide the medication use process in the hospital setting were found to be important in minimizing medication errors and promoting medication safety and control.1,15-17 Antibiotic dosing standardization refers to unified antibiotic doses that are based on therapeutic ranges within child weight-based dosing without the need for dose calculation. Dosing standardization removes the risk of calculation errors and reduces the amount of time required for dose calculation by the prescriber. Dose standardization is safer than dose calculation in the pediatric environment because of the milligram per kilogram dosing method that is used for pediatric patients. Furthermore, dose calculation with the milligram per kilogram dosing method often leads to a dose value to the 10th or 100th decimal place, which is impractical and impossible to measure with accuracy.<sup>18</sup> The primary objective of this study was to evaluate the impact of a dosing standardization policy that includes an antibiotic standard dosing table with precalculated dosages for different weight ranges on antibiotic dosing errors for pediatric patients in our center. The study furthermore looked at the level of prescribers' compliance with weight documentation on the prescription and writing the appropriate dosing intervals, as secondary endpoints.

#### **METHODS**

This study was conducted at a tertiary care hospital in the western region of Saudi Arabia, with a capacity of 400 beds. The pediatric services at this hospital include a general pediatric floor (28 beds), a pediatric surgery floor (20 beds), a neonatal intensive care unit (24 beds), a pediatric intensive care unit (10 beds), and a pediatric oncology unit (24 beds). The ambulatory care clinics at this facility have four half-day general pediatric clinics per week that see 20 to 30 patients per clinic. A retrospective cohort study of 300 randomly collected, physician-prescribed antibiotic order sheets was performed over a 2-week period within three different settings in our hospital (inpatient unit = 100; ambulatory care clinic = 100; emergency department = 100). The order sheets were evaluated for dosing errors, dosing interval, and weight documentation. Antibiotic prescriptions for pediatric patients (14 years old or younger) were included in this study. In this study, a dosing error was defined as the presence of a daily antibiotic dose that was 110% or more of the maximum recommended daily dose or below 90% of the minimum recommended daily dose.<sup>19</sup> Additionally, the appropriate dosing interval for the prescribed antibiotic was evaluated and compared with the recommend dosing interval provided by the up-to-date version of two pediatric drug references, the Harriet Lane Handbook (Custer J, Rau RE (eds). 18th Edition, Elsevier Health Sciences, New York, NY) and the Pediatric & Neonatal Dosage Handbook (Taketomo C (ed). 18<sup>th</sup> Edition. Lexi-Comp, Inc., Denver, CO).

This study found dosing errors in 34.5% of the prescribed antibiotics. In response, we created a departmental policy and procedures that included an antibiotic dosing table with precalculated dosages for different pediatric weight ranges to address antibiotic dosing standardization for pediatric patients in our hospital. All physicians in our hospital who treat pediatric patients were instructed to write orders for antibiotics using the standardized dosing table for oral and parenteral antibiotics (Figures 1 and 2). The pediatric standardized dosing table for oral and parenteral antibiotics was created by clinical pharmacists and received the approval of the antimicrobial subcommittee at this hospital. Dosing of 10 oral and 5 parenteral antibiotics, including the antibiotics most commonly prescribed at our hospital and those associated with the most dosing errors (based on our study), was standardized according to pediatric weight. All standard doses provided in these tables were within the therapeutic range for a child's weight; in addition, the standard oral antibiotic dosing table provided the appropriate strength and volume of medication to be dispensed in milliliters.

Pediatric infectious disease consultants in our hospital suggested preserving this dosing practice for patients who present with mild-tomoderate infections. Patients who present with severe infection or sepsis or who are immunocompromised should not be candidates for this dosing policy as providers must use the maximum recommended daily dosing. Furthermore,

Medication	Weight (kg)							
	5-9	9.1-15	15.1-20	20.1-30	30.1-40	>40		
AMOXICILLIN (25-60 mg/kg/day)	100 mg q 8 hr (250 mg/5 mL) 2 mL	150 mg q 8 hr (250 mg/5 mL) 3 mL	250 mg q 8 hr (250 mg/5 mL) 5 mL	350 mg q 8 hr (250 mg/5 mL) 7 mL	500 mg q 8 hr (500 mg cap)*	500 mg q 8 hr (500 mg cap)*		
AMOXICILLIN (large dose) for Acute Otitis Media	40-45 mg/kg/dose q 12 hr							
AMOXICILLIN AND CLAVULANATE (20-45 mg/kg/day; based on amoxil)	75 mg q 8 hr (156 mg/5 mL) 3 mL	125 mg q 8 hr (156 mg/5 mL) 5 mL	200 mg q 8 hr (312 mg/5 mL) 4 mL	250 mg q 8 hr (312 mg/5 mL) 5 mL	375 mg q 8 hr (312 mg/5 mL) 7.5 mL	625 mg q 8 hr (Tab. 625 mg)*		
<b>BACTRIM (TMP)</b> (6-13 mg/kg/day; based on TMP)	32 mg q 12 hr (40 mg/5 mL) 4 mL	60 mg q 12 hr (40 mg/5 mL) 7.5 mL	80 mg q 12 hr (40 mg/5 mL) 10 mL	100 mg q 12 hr (40 mg/5 mL) 12.5 mL	160 mg q 12 hr (Tab 160mg TMP)*	160 mg q 12 hr (Tab 160mg TMP)*		
<b>CEFPROZIL</b> (15-33 mg/kg/day)	75 mg q 12 hr (250 mg/5 mL) 1.5 mL	125 mg q 12 hr (250 mg/5 mL) 2.5 mL	250 mg q 12 hr (250 mg/5 mL) 5 mL	300 mg q 12 hr (250 mg/5 mL) 6 mL	500 mg q 12 hr (250 mg/5 mL) 10 mL	500 mg q 12 hr (Tab 500 mg)* Cefuroxime tab		
<b>CEPHALEXIN</b> (50-100 mg/kg/day)	150 mg q 8 hr (125 mg/5 mL) 6 mL	300 mg q 8 hr (250 mg/5 mL) 6 mL	500 mg q 8 hr (250 mg/5 mL) 10 mL	500 mg q 8 hr (250 mg/5 mL) 10 mL	500 mg q 8 hr (Tab. 500 mg)*	500 mg q 8 hr (Tab. 500 mg)*		
CLINDAMYCIN (10-30 mg/kg/day)	45 mg q 8 hr (10 mg/mL) 4.5 mL	90 mg q 8 hr (10 mg/mL) 9 mL	150 mg q 8 hr (10 mg/mL) 15 mL	200 mg q 8 hr (10 mg/mL) 20 mL	300 mg q 8 hr (Cap.150 mg)*	450 mg q 8 hr (Cap.150 mg)*		
<b>CLOXACILLIN</b> (50-110 mg/kg/day)	125 mg q 6 hr (125 mg/5 mL) 5 mL	250 mg q 6 hr (125 mg/5 mL) 10 mL	375 mg q 6 hr (125 mg/5 mL) 15 mL	500 mg q 6 hr (125 mg/5mL) 20 mL	500 mg q 6 hr (Cap. 250 mg)*	500 mg q 6 hr (Cap. 250 mg)*		
<b>METRONIDAZOLE</b> (15-33 mg/kg/day)	50 mg q 8 hr (125 mg/5 mL) 2 mL	100 mg q 8 hr (125 mg/5 mL) 4 mL	150 mg q 8 hr (125 mg/5 mL) 6 mL	200 mg q 8 hr (125 mg/5 mL) 8 mL	500 mg q 8 hr (Tab 250)*	500 mg q 8 hr (Tab 250)*		
PENICILLIN V (25 mg-60 mg/kg/ day)	100 mg q 8 hr (250 mg/5 mL) 2 mL	150 mg q 8 hr (250 mg/5 mL) 3 mL	250 mg q 8 hr (250 mg/5 mL) 5 mL	325 mg q 8 hr (250 mg/5 mL) 6.5 mL	500 mg q 8 hr (Tab 250 mg)*	500 mg q 8 hr (Tab 250 mg)*		

Figure 1. Standardized Dosing for Pediatric Oral Antibiotics

Cap, capsule; Tab, tablet; TMP, trimethoprim

\* If patient can tolerate solid dosage form physician should specify tablet, capsule or suspension

patients with abnormal kidney or liver function should not be candidates for this dosing policy. Those patients who were not candidates for the standardized dosing policy were excluded from the study.

To improve the acceptance of the new policy and practice, we printed the dosing tables in a card-sized format that easily fit into a physician's laboratory coat pocket. Additionally, dosing tables were printed in  $8.5 \times 11.5$  inch size format and posted on the walls of each inpatient care unit. At the time of this policy implementation, the hospital did not have computerized prescriber order entry, and we created these simple, low-technology tools to improve the accuracy of antibiotic orders.

The pharmacy and therapeutic committee approved this policy for implementation. A team of 10 members (2 clinical pharmacists, 5 nurses, 3 pediatricians) was established and given the responsibilities of teaching the hospital staff how to use the policy and overseeing the implementation process. The educational program was presented to physicians, pharmacists, and nurses.

	Weight (kg)						
Medications	5-7	7.1-10	10.1-15	15.1-20	20.1-30	30.1-40	>40 (Adult dose)
<b>CEFAZOLIN</b>	150 mg	200 mg	300 mg	500 mg	600 mg	1000 mg	1000 mg
(50-100 mg/kg/day)	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr
<b>CEFTRIAXONE</b>	500 mg	750 mg	1000 mg	1000 mg	1000 mg	1000 mg	1000 mg
(50-100 mg/kg/day)	q 24 hr	q 24 hr	q 24 hr	q 24 hr	q 24 hr	q 24 hr	q 24 hr
<b>CEFUROXIME</b>	250 mg	350 mg	500 mg	750 mg	750 mg	750 mg	750 mg
(75-150 mg/kg/day)	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr
CLINDAMYCIN	75 mg	100 mg	125 mg	200 mg	250 mg	400 mg	600 mg
(25-40 mg/kg/day)	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr
METRONIDAZOLE	50 mg	75mg	100 mg	150 mg	200 mg	300 mg	500 mg
(20-30 mg/kg/day)	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 8 hr	q 12 hr

Figure 2. Standardized Dosing for Pediatric Parentral Antibiotics.

It took 8 weeks to implement the new policy and apply it throughout the hospital. Three months after the implementation phase was completed, we evaluated the impact of the standard dosing table to determine whether there was a reduction in dosing errors for the selected antibiotics.

We assumed the rate of dosing errors prior to implementation of antibiotic dosing standardization to be 20%, and we aimed for a poststandardization dosing error rate of 5%. We needed at least 113 antibiotic order sheets for each group to detect significant differences between the two groups, with level of significance of at least 5% with 90% power. We anticipated that some order sheets would lack documentation of patient weight, so we decided to increase the sample size and we collected a total of 300 order sheets. Data were entered into an Excel 2007 spreadsheet (Microsoft, Redmond, WA) and were analyzed using SPSS version 19 statistics software (IBM, Armonk, NY) for descriptive statistics. Differences in rates of dosing errors, appropriateness of dosing intervals, and weight documentation prior to and following implementation of the antibiotic dosing standardization policy were analyzed using the Pearson chi-square test.

#### RESULTS

We reviewed 600 antibiotic order sheets for pediatric patients; 300 sheets were collected before the implementation of the antibiotic dosing standardization policy, and another 300 sheets were collected during the postimplementation phase. Patient characteristics for both groups were similar, as shown in Table 1. The rate of physician compliance with the antibiotic dosing standardization policy following implementation was 62%. The preimplementation phase data showed 68 of 197 antibiotic order sheets had a dose variation of 10% more or less than the recommended daily dose. The magnitude of dosing errors for the preimplementation phase was as follows: dose variations more/less than or equal to 30% from the recommend daily dose = 34 order sheets (17.3%); dose variations between 20 and 29.9% = 2 order sheets (6.1%); dose variations between 10% and 19.9% = 22 order sheets (11.02%). The antibiotic dosing standardization policy dramatically improved various aspects of patient care in our hospital, compared with that during the preimplantation phase: there was significant reduction in the overall rate of dosing errors (34.5%–5.8%; p=0.0001), the appropriateness of antibiotic prescribing interval improved (91.7%–98%; p=0.002), and there was an increase in physician documentation of patient weight on the antibiotic order sheets (65.6%–85.7%; p= 0.001). Table 2 shows the impact of the dosing standardization policy for pediatric patients compared with that in the pre-implementation period. We appreciated a significant increase in weight documentation after the implementation of this policy in the emergency department (17%-81%; p=0.0001).

#### DISCUSSION

This quality improvement project of implementing an antibiotic dosing standardization JPPT

Table 1. Characteristics of Fatients in the Field and Fost-implementation Gloups					
Characteristic	Pre-implementation (n=300)	Post-implementation (n=300)	p Value		
Sex no. (%)	Males = 166 (55.3%) Females = 134 (44.7%)	Males = 161 (53.7%) Females = 139 (46.3%)	0.743		
Mean age ± SD (yr) Mean weight ± SD (kg)	4.67 ± 3.24 17.68 ± 8.75	5.19 ± 3.76 17.45 ± 8.44	0.080 0.811		

Table 1. Characteristics of Patients in the Pre- and Post-implementation Groups

policy resulted in an overall statistically significant reduction in the rate of antibiotic dosing errors for pediatric patients at our hospital. Dosing errors for antibiotic prescriptions were the most common type of medication error in our hospital, and these errors were often not detected by the pharmacy or nursing staff prior to medication administration. Additionally, this project has significantly improved physicians' prescribing behaviors: weight documentation on antibiotic prescriptions has increased, and dosing interval for antibiotics is more often appropriately prescribed according to the treatment indication.

Weight documentation is one of the most important elements of a prescription for pediatric patients. Without knowledge of the patient's weight, a physician cannot evaluate the appropriateness of dosing. Emergency department physicians often rush to evaluate patients who present with mild to moderate illness and may not document the weight of the child on their prescriptions. According to our physicians, antibiotic dosing standardization has reduced prescribing time because clinicians do not have to use the dose calculation process; rather, they simply need to match the desired antibiotic with the patient's weight.

With the help of this standardization process, there are a greater number of appropriate doses of antibiotics given to our patients. This policy implementation has also allowed prescribers to dispense doses with a whole-number value. Eliminating the decimal point helps to avoid errors and provides a practical dose for parents and caregivers to measure when they administer antibiotics to their children, without going outside the therapeutic window. Calculation errors can be made by pharmacists at the dispensing stage; therefore, this policy additionally included the equivalent dosing in milliliters for oral antibiotics.

Clinicians understand that underdosing antibiotics can lead to negative consequences, such as treatment failure, prolonged hospitalization, more frequent emergency room visits, and increased pathogen resistance; while overdosing antibiotics may result in increased adverse effects. The emergence of pathogen resistance has become a global issue, and one effective strategy to reduce this problem is to administer the appropriate dose of antibiotic that will help to eradicate the causative organism.<sup>14</sup> The American Academy of Pediatrics Committees on Drugs and Hospital Care has published recommendations to minimize medication errors in children and emphasize the importance of system changes to detect and prevent medication errors.<sup>16</sup>These recommendations and suggestions are not only for prescribers but also for pharmacists, nurses, parents, and the hospital system. It is important to understand the risk factors for medication error when prescribing medications to pediatric patients in order to develop effective strategies to reduce its occurrence.15

Evidence in the literature confirms that some pediatric health care practitioners have difficulty calculating an appropriate medication dose, and studies recommend that practitioners should be trained in dosing calculation and demonstrate sufficient competency with observation.<sup>20-22</sup>

The impact of an antibiotic standard dosing table was significant in the emergency department setting. Many of our clinicians in the emergency department were not familiar with appropriate pediatric dose calculation as they are not pediatricians by training. The antibiotic standard dosing table has helped them to prescribe the appropriate dose of medication for children who visit this unit. The initial compliance rate with the dosing table was low (62%) as some of our residents rather to calculate antibiotic doses based on child's weight. The availability of a pocket-sized, institution-specific guide may improve safe and appropriate prescribing practices.<sup>17</sup>

To our knowledge, this is the first published study that evaluated the impact of an antibiotics dosing standardization on dosing error reduction. However, our study has some limitations. First, it was a single-center study, so findings cannot be generalized to other hospitals. Second,

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Parameter	Unit	Pre-implementation (n= 300)	Post- implementation (n=300)	p Value
	Ambulatory Care	85 (85%)	87 (88%)	0.839
	Inpatient Units	95 (95%)	89 (89%)	0.139
Weight documentation*	Emergency Unit	17 (17%)	81 (81%)	0.0001†
	All Units	197 (65.6%)	257 (85.7%)	0.0001†
	Ambulatory Care	95 (95%)	99 (99%)	0.091
	Inpatient Units	82 (82%)	97 (97%)	0.002†
Appropriate dosing interval*	Emergency Unit	98 (98%)	98 (98%)	1
	All Units	275 (91.7%)	294 (98%)	0.002†
	Ambulatory Care	26/85 (30.6%)	8/88 (9.1%)	0.0001†
	Inpatient Units	39/95 (41.1%)	4/89 (4.5%)	0.0001†
Dosing error*	Emergency Unit	3/17 (17.6%)	3/81 (3.7%)	0.029†
	All Units	68/197 (34.5%)	15/258 (5.8%)	0.0001†

\* Number (%) patients

+ Statistically significant difference

the study period was short because of a limitation of resources. Third, there was no follow-up with patients who experienced inappropriate dosing, so we were not able to evaluate the consequences of dosing errors such as treatment failure or an increase in emergency room or clinic visits.

#### CONCLUSIONS

Antibiotic dosing errors are common in children. The use of a pediatric antibiotic standard dosing table with precalculated dosages for different weight ranges has significantly reduced the incidence of dosing errors. Physicians were more vigilant in documenting patient weight on prescriptions and following the standardized dosing policy when prescribing antibiotics for pediatric patients in our center.

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**ABBREVIATIONS** KAMC, King Abdul Aziz Medical City

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