**Evaluation of a pediatric ceftriaxone dose rounding protocol on time to administration in an emergency department**

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Abstract:

**Background**

Pediatric doses utilize weight-based dosing, which results in doses not available in commercially available products. Dose rounding can round doses to commercially available products, which may be stored in patient care areas and thereby expedite acquisition time. These commercially available products may then be prepared in a patient care area and prepared for administration. In the emergency department (ED), antibiotics are regularly administered empirically. At the Renown Regional Medical Center (RRMC) ED, ceftriaxone is used as a broad-spectrum cephalosporin for the empiric coverage of various infections. Doses of ceftriaxone were prepared at bedside if the dose was available commercially. Otherwise, doses were prepared in the pharmacy IV room and given as an infusion. Workflow is more intense for doses prepared in the IV room, as this utilizes pharmacy technician hours, a double-pharmacist check on the compounded product, and then delivery of the patient specific dose to the patient care area.

**Methods**

This is a quasi-experimental, retrospective study at RRMC. A pharmacy-driven pediatric dose rounding protocol (See Appendix A) was accepted by The Pharmacy & Therapeutics Committee in October 2022 to round doses in accordance with product availability, as well as expedite administration time. Ceftriaxone is the only medication from the protocol investigated. The review compared a total of 6 months of administrations in the pediatric ED – 3 months before (pre-implementation) and 3 months after (post-implementation) the approval of pediatric ceftriaxone dose rounding. The primary outcome was the time to first administration. Secondary outcomes included adverse events, doses prepared by the central pharmacy intravenous (IV) room, and in-hospital mortality.

**Results**

The study included 157 patients in the final analysis, 52 in the pre-implementation group and 105 in the post-implementation group. There was no difference in the time to administration (41.5 minutes versus 43 minutes, p = 0.48). There were 3 adverse events (0 versus 3), and no in-hospital mortality was reported. The number of doses prepared by the pharmacy IV room decreased after implementation (40.4% versus 10.5%, p <0.0001).

**Conclusion**

Time to antibiotic administration was not different before and after implementation of a pediatric ceftriaxone dose rounding protocol. The number of doses prepared by the IV room significantly decreased in the post-implementation group. There were higher ED volumes in the post-implementation group, as well as seasonal spikes of viral infections such as respiratory syncytial virus (RSV) and influenza-A. While there was no difference in time to administration, administration times are anticipated to decrease as ED volumes return to historical averages.

Keywords: pediatric dose rounding, ceftriaxone, pharmacist

1. Background

Pediatric doses utilize weight-based dosing, which results in doses not available in commercially available products. These doses must then be individually prepared, commonly done in a central pharmacy intravenous (IV) room. Dose rounding can round doses to commercially available products, which may be stored in patient care areas within an automated dispensing cabinet (ADC). These commercially available products may then be prepared in a patient care area and prepared for administration. In the ED, antibiotics are regularly administered empirically. Ceftriaxone is a broad-spectrum cephalosporin commonly given for the empiric coverage of infections.

In the ED at RRMC, ceftriaxone doses were prepared at bedside if the dose was available in commercially available products. Vials were prepared and pushed at bedside. Otherwise, doses were prepared in the pharmacy IV room and given as an infusion. Workflow is more intense for doses prepared in the IV room, as this utilizes pharmacy technician hours, a double-pharmacist check on the compounded product, and then delivery of the patient specific dose to the patient care area.

This study compares the time to first dose administration before and after implementation of a pediatric ceftriaxone dose rounding protocol in an ED.

**2. Methods**

This was a quasi-experimental retrospective chart review of patients presenting to Renown Regional Medical Center between July 1, 2022 to September 30, 2022 in the pre-implementation group and December 1, 2022 to February 28, 2023 in the post-implementation group. This was done by collecting charts of pediatric patients who received their first dose of ceftriaxone in the RRMC emergency department.

***2.1 Data Collection***

*Original Methods:*

* Inclusion criteria: First ceftriaxone dose administered in the RRMC ED
* Exclusion criteria: Patients equal or greater than 18 years of age, or less than 17 kilograms

*Outcomes:*

The primary outcome was the difference in time to administration between groups. Secondary outcomes included adverse events, the number of doses compounded in the central pharmacy IV room, and in-hospital mortality.

***2.2 Data Analysis***

Nominal variables were analyzed using Fisher’s Exact Test. Continuous outcomes were analyzed using Wilcoxon signed-rank test. A p-value less than 0.05 was considered statistically significant.

**3. Results**

Of 508 charts initially collected, 351 were excluded (235 administrations outside the ED, 116 less than 17 kilograms). Of the remaining 157 charts, 52 were in the pre-implementation group, and 105 in the post-implementation group.

Baseline characteristics were similar and are listed in Table 1. The pre-implementation group had a greater number of positive COVID-19 tests, whereas the post-implementation group had a greater number of positive viral tests, influenza A, and RSV cases. Primary and secondary outcomes are listed in Table 2 and 3, respectively.

Table 1: Baseline Characteristics

|  |  |  |
| --- | --- | --- |
|  | Pre-Implementation (n=52) | Post-Implementation (n=105) |
| Age, years, median (IQR) | 15 (7.5-16) | 9 (6-15) |
| Weight, kg, median (IQR | 47.9 (25.9-68.2) | 36.0 (21.3-58.3) |
| Height, kg, median (IQR) | 154.9 (129.5-167.6) | 139.7 (118-160) |
| Temp, Celsius, median (IQR) | 37.2 (36.6-37.7) | 37.2 (36.7-38.0) |
| HR, bpm, median (IQR) | 114 (89-126) | 121 (101-133) |
| RR, bpm, median (IQR) | 20.0 (20-26) | 24.0 (20-30) |
| O2, %, median (IQR) | 97 (96-100) | 96 (93-98) |
| MAP, mmHg, median (IQR) | 83 (75-96) | 84 (78-91) |
| WBC, cellsx103, median (IQR) | 12.5 (8.6-15.9) | 10.6 (7.3-15.6) |
| Positive culture, % (n) | 25 (13) | 15.2 (16) |
| Positive viral test, % (n) | 17.3 (9) | 22.9 (24) |
| Influenza A, % (n) | 1.9 (1) | 13.3 (14) |
| Influenza B, % (n) | 0 (0) | 0 (0) |
| RSV, % (n) | 1.9 (1) | 7.6 (8) |
| Covid-19, % (n) | 15.4 (8) | 1.9 (2) |

*HR: heart rate, IQR: interquartile range, MAP: mean arterial pressure, O2: oxygen, RR: respiratory rate, WBC: white blood cell count*

Table 2: Primary Outcome

|  |  |  |  |
| --- | --- | --- | --- |
| Outcome | Pre-Implementation  n = 52 | Post-Implementation  n = 105 | P-value |
| Time to administration, minutes, median (IQR) | 41.5 (29-59) | 43 (26-73) | 0.48 |
| Order to verification,  minutes, median (IQR) | 6.4 (3.2-11.2) | 6.8 (3.7-11.5) | 0.78 |
| Verification to administration, minutes, median (IQR) | 36.0 (20-45) | 36.0 (17.6-63.9) | 0.96 |

*IQR: interquartile range*

Table 3: Secondary Outcomes

|  |  |  |  |
| --- | --- | --- | --- |
| Outcome | Pre-Implementation  n = 52 | Post-Implementation  n = 105 | P-value |
| Adverse events | 0 | 3 | - |
| Anaphylaxis | 0 | 1 | - |
| Administration error | 0 | 1 | - |
| Dosing error unrelated to dose rounding | 0 | 1 | - |
| Doses prepared in pharmacy IV room (%) | 40.4 | 10.5 | < 0.0001 |
| In-hospital mortality | 0 | 0 | - |

**4. Discussion**

After implementation of a pediatric ceftriaxone dose rounding protocol, there was no difference in the time to first administration (41.5 minutes vs 43 minutes, p-value = 0.48). There were three reported events in the pre-implementation group. The doses prepared by central pharmacy was significantly decreased after implementation (40.4 vs 10.5%, p-value < 0.0001). There were no cases of in-hospital mortality.

A separate 2019 retrospective study investigated the correlation between door-to-antibiotic time and mortality in patients with sepsis in the ED. Door-to-antibiotic administration times were correlated with significantly lower odds of mortality during the hospital visit, at 30 days, and 90 days. Additionally, each hour in delay to antibiotic administration correlated with 10% increased odds of one year mortality.1 There were approximately 2400 more visits in the post-implementation group of this study. While there was no difference in time to administration, during times of normal admission volume it is anticipated the findings would be corroborated.

A 2013 retrospective study reviewed the effect of antibiotic dose rounding before and after implementation of a pediatric antibiotic standard dosing table in three healthcare settings (ambulatory care, inpatient, and emergency department). The investigators found dose errors significantly decreased (34.3% to 5.06%) and weight documentation significantly increased (65.8% to 85.7%).2 A proposed explanation is the improved ability to identify incorrect doses, as they are more readily recognizable if they deviate from an institutions dose rounding protocol. This study did not evaluate the effect of pediatric ceftriaxone dose rounding in regard to weight documentation, and should be considered an opportunity for future research.

A 2014 systematic review evaluated the feasibility and efficacy of developing a dose rounding protocol. There were 74 medications included in their dose rounding table, all of which were utilized in the neonatal intensive care unit. The rounded doses were considered clinically appropriate for all medications, either by regional or institutional practices.3 While three safety events occurred in the post-implementation group of this study, none were caused by the implementation of the ceftriaxone dose rounding protocol.

***4.1 Limitations***

The limitations of this project include the small sample size, the project being a quasi-experimental retrospective chart review and confounding variables that could not controlled for. Confounding factors include nursing awareness of where to find antibiotics, as well as spikes in RSV and influenza cases. Notably, ED volumes had increased in the post-implementation group, where historically ED volumes had been consistent throughout the year.

**5. Conclusion**

Implementation of a pediatric ceftriaxone dose rounding protocol did not reduce time to first dose administration. The reduced number of doses prepared by the pharmacy IV room translates to more doses immediately available on the unit, and reduced time for pharmacy preparation and pharmacy man-hours. There was no difference in time to administration despite an increase number of emergency visits over the same time interval. As ED visits return to normal, the time to administration is expected to decrease for patients receiving their first dose of ceftriaxone in the ED. Future research has the opportunity to expand dose rounding to other medications, as well as re-examining time to administration during periods of similar ED volumes.

Conflicts of Interest

None of the authors have a conflict of interest to disclose.

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**Appendix A**

Pediatric Dose Rounding Protocol

1. **Background**

Medication dose standardization has been shown to improve interdisciplinary communication, reduce medication errors and expedite medication procurement. This protocol allows certain pediatric medication orders to automatically round to a pre-defined and approved standard dose. Physicians need not change their current dose calculation or order writing practices unless the protocol is deemed clinically inappropriate for a specific patient.

1. **Purpose**

This protocol allows for certain pediatric medication orders to automatically round to pre-defined and approved standard doses. Physicians will order medications as per their current practice and approved medications will be rounded by the electronic medical record (EMR) or per protocol by pharmacy when not automatically rounded by the EMR (ex. in the event of an EMR downtime).

1. **Procedure**
   1. Provider will enter the medication order per usual practice. (Example: 50mg/kg of ceftriaxone \* 17 kg = 850 mg of ceftriaxone)
   2. The EMR will automatically round the medication dose in accordance with the dose rounding rules in the Appendices. (Example: Ceftriaxone 50 mg/kg/dose of 850 mg will be rounded to 1000 mg in accordance with Appendix A)
      1. In the event of an EMR downtime or for doses entered that have not been rounded, the pharmacist round the dose in accordance with the listed Appendices per P&T pediatric dose rounding protocol.
   3. If dose rounding is determined to be clinically inappropriate by either the physician or pharmacist, both physicians and pharmacists retain the ability to use their clinical judgment to override the standardization protocol. The physician will discuss with the pharmacist the need to utilize the exact dose. The pharmacist will enter the order at the desired dose.

# References

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**Ceftriaxone:**

|  |  |  |  |
| --- | --- | --- | --- |
| **Ceftriaxone Dose Rounding** | | | |
|  | **Mild-Moderate Infections and < 80 kg**  **50 mg/kg/dose daily** | **Mild-Moderate Infections and ≥ 80 kg** | **Severe Infections**  **50 mg/kg/dose q12h** |
| **< 400 mg IV** | Round to nearest 20 mg¹ | N/A | Round up to nearest 20 mg¹ |
| **400 mg to < 850 mg IV** | Round to nearest 40 mg¹ | N/A | Round to nearest 40 mg¹ |
| **< 850 mg IM³** | Round up to  nearest 35 mg² | N/A | Round up to  nearest 35 mg² |
| **850 – 1100 mg) IV/IM** | 1000 mg | N/A | 1000 mg |
| **> 1100 mg IV/IM** | 1000 mg\* | 2000 mg\*\* | 2000 mg\*\* |

¹ IV concentration: 40 mg/mL ² IM concentration: 350 mg/mL

³Dose rounding not to include IM dosing for STI treatment

**\*Indications for ceftriaxone 1000 mg dose cap:**

* Cystitis any weight
* Mild to moderate infections and < 80 kg: upper respiratory infection, PNA, intra-abdominal infection, cellulitis

**\*\*Indications for ceftriaxone 2000 mg dose cap:**

* Severe Infections (50 mg/kg/dose q12h): Sepsis, meningitis or other intra-cranial infection, endocarditis, endovascular infection, Salmonella, syphilis, complicated PNA, complicated intra-abdominal infection
* Non-cystitis mild to moderate infections and ≥ 80 kg