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Comparative analysis of clinical pharmacy interventions in a pediatric intensive care unit

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Abstract

***Objective*: The objectives of this study were 1) to describe and characterize interventions performed by a clinical pharmacist and 2) provide a comparative analysis of length of stay, mortality, and drug charges in control and intervention groups.**

***Design*: This was a retrospective analysis of clinical pharmacy interventions performed in a Pediatric Intensive Care Unit (PICU) over two years. The clinical pharmacy faculty member was a dual-residency trained specialist in pediatric critical care, and was on-site in the PICU for approximately 0.5 full time equivalents.**

***Setting and patients*: The interventions occurred in an 18-bed medical-surgical PICU in a tertiary care children's hospital. All patients admitted to the PICU during the study period were included.**

***Interventions*: The intervention group was comprised of patients admitted to the PICU during the study period for which the clinical pharmacist suggested changes in medication therapy. All other PICU patients were included in the control group. Interventions suggested were varied, including drug dosing adjustments, antibiotic recommendations, sedation recommendations, and discontinuation of drug therapy.**

***Measurements and main results*: On average, there were 4.4 interventions per patient (0.35 interventions per patient-day). Dosing recommendations, pharmacokinetic recommendations, and discontinuation of medications were the most common types of interventions performed. Antibiotics and sedation/analgesia were the most common drug classes for intervention. There were statistically significant differences in the length of stay and mortality of groups, with both higher in the intervention group. Notably, the intervention group also had higher Pediatric Risk of Mortality (PRISM) scores and drug charges, signifying increased severity of illness compared to the control group. Estimated annual cost savings in the intervention group was $ 86,000.**

***Conclusions*: Antibiotics and sedation/analgesia dosing were the most common areas for pharmacy interventions. Patients with higher PRISM scores had increased interventions. Cost savings were considerable even with a part time pharmacist.**

Key words: Pharmacy practice, pediatrics, pharmacy interventions, pharmacists, pharmacy service.

Introduction

In both adult and pediatric populations, studies have shown a positive impact by pharmacists on patient care. (1-3) The American Academy of Pediatrics and the Society of Critical Care Medicine have also described the importance of having pharmacists involved in the care of patients. (4,5)

In previous work, our group conducted a descriptive study, which detailed the types and numbers of clinical interventions suggested by our pharmacist. (6) This work included detailed descriptions of the interventions suggested and changes made by the medical team, as well as baseline characteristics of the patient population. In our current study, we expanded the time frame of the original study and included a control group for an in-depth comparison of outcomes.

The objectives of this study were twofold: 1. To describe and characterize the interventions performed by the clinical pharmacist; 2. Provide a comparative analysis of the length of stay, mortality, and drug charges for patients in the control and intervention groups. Estimated cost savings for pa-

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tients in the intervention group were also calculated. Institutional Review Board approval was granted by each of the author's academic affiliation and the hospital.

Methods

A clinical pharmacy faculty member with 2-year specialized residency training in pediatrics participated in the care of children in an 18-bed tertiary-care medical-surgical Pediatric Intensive Care Unit (PICU) located in a free-standing children's hospital. The faculty member was fully funded through a primary academic appointment and provided services in the PICU through a contractual agreement with the hospital. The clinical pharmacist was present during interprofessional rounds and in the afternoons approximately 25 hours each week and 12 days per month. Activities included patient rounds, participation in medical emergencies, and adjusting drug therapies as needed, but did not include order entry interventions. Outside of the PICU, no clinical services or interventions were performed by the pharmacy faculty in this hospital.

We conducted a retrospective review of all patients admitted to the PICU from May 1, 2009 to April 30, 2011. The study start date coincided with the arrival of the clinical pharmacist at the institution. Prior to this date there were no clinical pharmacist. Inclusion criteria were all patients admitted to the PICU during the study period. Exclusion criteria included patients not admitted to the PICU during the study period. While the pharmacist was present, all patients and medications were reviewed. Only patients requiring interventions by the pharmacy faculty member in the PICU were included in the intervention group. All other admitted PICU patients during the study period were included in the control group. Basic patient demographic data was collected including age, gender, PRISM score, hospital length of stay, PICU length of stay, total drug charges, and mortality rate. Specific collected information about the interventions performed included medication class and type of intervention.

Data on intervention acceptance by the medical team and intervention time were also collected. Cost savings were calculated based on Pharmacy One Source Quantify data and previous reports in the literature. (7-9)

Statistical analyses were performed using SPSS version 23.0. (10) The Mann-Whitney U test (i.e., Nonparametric Independent t-Test) was used for age, weight, length of stay, drug charges, and PRISM score because the data was not normally distributed in each group. The Chi-Square Test of Association was used for gender and mortality.

We conducted an ad-hoc analysis of patients who had multiple admissions during the study period. Age and weight were compared using an independent T-test. Gender and mortality were compared using Chi-Square Test of Association. Hospital and PICU length of stay, PRISM scores, and drug charges were compared using Mann-Whitney U tests because the data were not normally distributed in each group.

Results

There were a total of 1450 patients admitted to the PICU during the 2-year study period. There were 111 patients (7.7% of total patients) who had multiple admissions totaling 292 admissions for the multiple admissions group. Sixty patients and 192 admissions of the 111 multiple admission patients had interventions performed. Four hundred nine patients of the single admission group had interventions performed (30.5% of single admission patients).

There were a total of 2073 interventions performed during the study. This is an average of 4.4 interventions per patient, 0.35 interventions per patient per PICU day and 0.17 interventions per hospital day. There were 207 total days in which the pharmacy faculty member (approximately 0.5 full time equivalents) performed these interventions for an average of 10 interventions per day.

Dosing recommendations (26.6%), pharmacokinetic recommendations (20.1%), and discontinuation of medications (17.5%) were the most common types of interventions performed. See **Table 1** for all intervention types. Dosing recommendations included both increases and decreases of dose or frequency to optimize therapy or minimize side effects. Pharmacokinetic recommendations included dose adjustments, additional monitoring parameters, or discontinuation of unnecessary tests of which vancomycin accounted for approximately 60% of the recommendations (11.4 % of all interventions). Antibiotic recommendations included changing a particular agent to optimize coverage, discontinuation or addition of antibiotics. Renal recommendations included dose or agent changes based on patient's renal function. Laboratory evaluation included additional monitoring parameters for non-pharmacokinetic interventions. Any intervention performed by the clinical faculty member that was not described by a particular category was placed in the category of other. This category included interventions such as participation in cardiac arrests, intubations, addition of therapies to manage side effects, discontinuation of duplicate therapies, and home medication reconciliation.

Antibiotics (29.4%), and sedation/analgesia (23.1%) were the most common drug classes in which interventions were made. **Table 2** lists the drug classes by number of interventions. Within the antibiotic group, vancomycin pharmacokinetics (35.6%), dosing (22.2%) and suggesting a specific agent (13.6%) were the most common interventions made. Within the sedation/analgesia drug classification, discontinuation of agents (24.9%), weaning (23.5%) and suggesting agents (20.1%) were the most common interventions made.

Patient information was compared after separating into a control group and intervention group. **Table 3** compares the 2 groups for age, gender, weight, and PRISM score. There were no statistically significant differences for age, gender, or weight between the two groups. The PRISM scores were significantly higher in the intervention group ($p<0.001$, 95% CI -2.00 - 0.00).

Table 4 compares the control group and intervention group for PICU length of stay, hospital length of stay, mortality, and drug charges. There were significant differences between the groups for all indicators. PICU length of stay ($p<0.001$, 95% CI -2.88 - -2.02), hospital length of stay ($p<0.001$, 95% CI, -6.29 - -4.41), and mortality ($p<0.001$, 95% CI 1.70 - 5.46) were higher in the intervention group. Drugs charges were approximately 9 times lower in the control group as compared to the intervention group ($p<0.001$, 95% CI -298.00 - -208.00). In a logistic regression analysis, controlling for length of stay, hospital length of stay, drug charges, and PRISM scores, there was no statistically significant relationship between intervention group and mortality ($p=0.086$). The results of the logistic regression should be interpreted with caution as the percentages of mortality were less than 10%.

Ninety nine percent of all interventions were accepted by the medical staff. Each intervention took on average 7 minutes for completion, which included extended time spent in emergency situations such as cardiac arrest. The estimated cost savings for the study period was $173,273 or $86,636 per year with the 0.5 full time equivalent pharmacist.

Multiple admissions: There were a total of 111 patients in the multiple admission groups. Forty patients had 3 admissions or more. The maximum number of admissions during the study period was 7. Sixty patients had interventions on the first admission, 70 had interventions on the second admission and 32 on the third admission.

There were no differences in age, weight, or gender between the intervention group and the control group for the 1st, 2nd and 3rd admissions ($p>0.05$). There was a difference in hospital length of stay for only the third admission with the control group average of 7.6±11 vs 33±52.8 in the intervention group ($p=0.04$). For PICU length of stay, there was a longer stay for the first 3 admissions in the intervention group over the control group. First admission was 4.8 days in the control vs 8.4 days in the intervention ($p=0.02$). For mortality and PRISM scores, there were no differences between the groups across all admissions ($p>0.05$ for all). There were a higher number of drug charges in the intervention group for the 3rd admission (1199 vs 100) ($p=0.12$).

Discussion

Few studies have described clinical pharmacy interventions in pediatrics. The previous publication from our group reported that antibiotic and sedative/analgesic agents were the most common drug classes with dosing and pharmacokinetics as the most common types of interventions. (6) This current study showed similar results with a larger sample size. Other studies have shown similar results with drug dosing, drug interactions, and drug information as the most common activities. (1,2,11,12) Our study specifically looked at individual characteristics of the drug classes to gain a better understanding of where a clinical pharmacist can have the most impact. Sedation and analgesia along with infectious disease issues are common in PICU patients, and our study supported that pharmacists can offer interventions in these areas, especially on appropriate dosing of these agents.

On average there were 4.4 interventions performed per patient. This was higher than the approximately 2.5 interventions/patient as reported in previous studies. (1,11,12) Reasons for this lower rate in other studies may include their focus on particular categories of drug dispensing and patients having a lower PRISM score indicating less illness severity than in this study. Our data also demonstrated that approximately 0.35 interventions occurred per patient PICU day which was similar to previous reports. (1) This showed that most patients admitted into the PICU required more than one intervention by a pharmacist and these continued as the patient remained in the PICU.

One of the major differences in the previous research was that regular order entry and medication review, which was done by staff pharmacists, was also included in their analyses. (11-13) For example, order clarification could include indications for a PRN order and documented as an intervention. (12) Our study looked specifically at only clinical interventions at the point of direct patient

care and did not include the interventions performed by the other pharmacists. If these order verification interventions had been included the intervention data would have been much larger than what we currently report.

Limited previous studies that compared demographics between the intervention and control groups showed no differences in age, gender, and weight. (1,11) Similarly, there were no differences found in demographics between our two groups. Our study showed that patients who had a clinical intervention performed had a significantly longer length of stay in both the PICU and the hospital as compared to the control group. Previous studies comparing length of stay found similar results, however our average length of stay was longer than other reports, possibly signifying sicker patients. (1,11) Reasons for our control group having lower length of stays include a lower severity level of disease. Since the hospital is a surgical center as well, many patients are admitted for post-operative observation and increased nursing care. In these patients that are often only receiving pain medications and prophylactic antibiotics, it follows that there may be less need for clinical pharmacy interventions. Also when there is a shorter length of stay there would be less opportunity for the pharmacist to intervene due to part time scheduling necessitated by the pharmacist's academic appointment responsibilities and lack of presence of the clinical pharmacist during the patient's brief stay (i.e. weekends). We used PRISM scores to assess severity and found that the patients with clinical interventions had a significantly higher PRISM score and therefore an increased risk of death due to severity of illness. Only one other study used a standardized scale to evaluate illness severity in patients. (1) Krupicka, et al showed a higher PRISM score in the intervention group as compared to the control group, however the difference was not statistically significant. (1) Our PRISM score average was higher (6.8 vs 4 in that study) and we were able to show significance in that the intervention patients had a higher risk of mortality over the control group. As a surrogate marker, we used the total number of drug charges to assess severity as well. The intervention group showed significantly higher drug doses administered over the control group indicating that they had more severe disease.

Previous studies have shown no difference in mortality between intervention and control groups. (12,14) In our study, there was a significantly higher mortality rate in the intervention group as compared to the control group. This could be explained by multiple mechanisms. The study by Ho, et al was performed in adults and showed a significantly higher mortality rate of over 25% which was not seen in pediatrics. (14) In the pediatric study, there was a much larger sample size which may have given them the statistical power to truly detect a difference. (12) Our patients may have been sicker than the pediatric study, however the authors did not evaluate a severity score so no true comparisons could be made. (12)

The multiple admission analysis revealed similar results as the single admission data. The major differences were in mortality and PRISM score as we found no differences. Since this was a relatively small sample size of 111 patients and no real differences were found, conclusions regarding this sub population of PICU patients could not be made. Larger studies may be able to show a difference in this group or even reductions in multiple admissions.

A true pharmacoecomomic study was beyond the purview of this study and estimated cost saving contained hard and soft costs based on our previous work. (6) Hard costs include direct drug costs such as discontinuing an unneeded medication. Soft costs include costs such as additional ventilator days. For instance, if a patient was switched from a more expensive medication, which caused less sedation, the patient may have been weaned from mechanical ventilation in less time, decreasing hospital costs. Previous reports of cost savings were scarce for pharmacy interventions in a PICU. One previous study estimating cost at about 10% of our findings was published almost 15 years ago. (1) An annual estimated cost saving in our study from the interventions of a clinical pharmacist was valued at $86,000. This was especially significant as the clinical pharmacist was only practicing in the PICU approximately 50% of a full time position due to the primary academic appointment. One would expect the cost savings for a full time position to greatly exceed this estimate likely justifying the salary for a full time clinical pharmacist.

Overall acceptance rates for pharmacy interventions in the literature ranges from 51% to 98%. (2,6,11,12,15) The wide range may be due to difference in study methodology, physician pharmacist rapport, and order entry/staff pharmacist vs clinical pharmacist interventions. The acceptance rate in this study was 99%, which represented all discussions regarding patient, care regardless of the likelihood of being accepted.

This study was not without limitations. First, there was a delay from the study period to manuscript submission due to the health system having a paper

charting system. All pharmacy interventions were also documented on paper charts. Every patient's chart was hand accessed to obtain the necessary information including the laboratory values to calculate the PRISM scores. Other limitations included a single center and single clinical pharmacist. As discussed previously the clinical pharmacist was available for approximately 50% of a full time position and results may have been different if employed full time. This was a retrospective review and multiple variables could not be controlled for, however a prospective design of pharmacy interventions would be an unethical practice.

Conclusions

This study showed antibiotics, sedation/analgesia, dosing and pharmacokinetics were the most common interventions. These findings suggested that in facilities with limited resources, allocation of pharmacy personnel might be targeted towards these specific areas for optimal impact including education of providers. Patients that were sicker and had a higher incidence of mortality were more likely to have an intervention. Likely this was due to patients with a longer length of stay being sicker and having more opportunity for a pharmacist intervention. For the control group with a shorter length of stay, the pharmacist was likely unavailable for their short stay and did not have the opportunity to intervene or no intervention was needed since that group received less medications and were less ill. More complex patients with more medications likely had more need for the services of a clinical pharmacist and hence were intervened on more. Due to the nature of critical care and the severity of illness, it may be unlikely that studies investigating clinical pharmacy interventions will show decreases in outcomes of length of stay and mortality. Further investigations of other outcomes, including pharmacoeconomic outcomes, are key areas for future work.

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The authors have no conflicts of interest to declare.

At the time of the study Kayrah Jack and Brent A. Kitto were students at Xavier University, and Aryn Karpinski was faculty at LSUHSC.

Table 1. Intervention by type

Type of intervention	Number	Percent
Dosing recommendation	551	26.6
Pharmacokinetics • Vancomycin pharmacokinetics • Gentamicin pharmacokinetics • Enoxaparin pharmacokinetics • Phenobarbital pharmacokinetics • Other pharmacokinetics	417 • 236 • 92 • 41 • 27 • 21	20.1 • 60.5 • 23.6 • 10.5 • 6.9 • 5.4
Discontinuation	363	17.5
Other	173	8.3
Wean	146	7
Intravenous to oral conversion	107	5.2
Antibiotic recommendations	101	4.9
Sedation recommendation	100	4.8
Drug information	44	2.1
Drug interaction	39	1.9
Renal recommendation	37	1.8
Compatibility/administration	27	1.3
Stress ulcer prophylaxis	23	1.1
Continuous renal therapy/hemodialysis	20	1.0
Lab evaluation	20	1.0
Patient education	8	0.4
Allergy	7	0.3
Liver recommendation	2	0.1
Venous thromboembolism prophylaxis	2	0.1

Table 2. Interventions per drug class

Drug class	Number	Percent
Antibiotics	610	29.4
Sedation analgesia	479	23.1
Other	279	13.5
Gastrointestinal agents	264	12.7
Fluids/electrolyte/nutrition	101	4.9
Antiepileptics	85	4.1
Anticoagulations	63	3.0
Antihypertensives	51	2.5
Diuretics	36	1.7
Steroids	36	1.7
Antifungals	27	1.3
Vasopressors	19	0.9
Pulmonary	10	0.5

Table 3. Patient demographics

Indicator	Intervention (n=409) Mean±SD (range)	Control (n=929) Mean±SD (range)	p value
Age (years)	6.6±6.2 (0.01-35)	6.8±6.2 (0.01-26)	0.418
Gender (number and % male)	231 (59.8%)	513 (55.3%)	0.128
Weight (kg)	28±25.8 (1.97-154.6)	30±26.7 (1.8-252)	0.09
PRISM score	6.8±6.75 (0-40)	5.12±5.5 (0-37)	<0.001

Legend: SD=standard deviation; PRISM=Pediatric Risk of Mortality

Table 4. Patient outcomes

Indicator	Intervention (n= 409) Mean±SD (range)	Control (n= 929) Mean±SD (range)	p value
Hospital length of stay (days)	30.1±91.2 (0-1464.2)	13.3±134.5 (0.08-3657.8)	<0.001
PICU length of stay (days)	14.3±37.4 (0.21-367.6)	2.4±4.8 (0.05-93.9)	<0.001
Mortality (number and percent)	27 (6.6%)	21 (2.3%)	<0.001
Number of drug charges*	2572.4±8897.2 (1-103618)	293.3±849.2 (0-11667)	<0.001

Legend: SD=standard deviation; PICU=Pediatric Intensive Care Unit; Drug charges*=partial patient data available. Intervention group: 358/409=87.5%, Control group: 777/929=83.6%

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