Impact of a pediatric antimicrobial stewardship program in an academic medical center

Jason T. Wong*, Diana Yu, Lam H. Nguyen, James Lewis and Dawn L. Nolt

Abstract

Purpose: To evaluate the clinical and financial impact of a pediatric infectious disease pharmacist, during the initiation of an inpatient antimicrobial stewardship program (ASP) at an academic pediatric institution, to support judicious antimicrobial use through restricted antimicrobial approval, prospective-audit-and-feedback of patients receiving antimicrobials, and review of microbiology laboratory results.

Summary: A pediatric ASP utilizing prospective audit and feedback was developed and implemented at Doernbecher Children's Hospital (DCH) at Oregon Health & Science University (OHSU) in October 2017. As a key contributing member of the pediatric ASP, the pediatric infectious disease pharmacist demonstrated value to the pharmacy enterprise by making clinical optimization interventions related to antimicrobial therapy. Measures included antibiotic utilization and associated cost as well as intervention type and potential cost avoidance to the health-system.

Conclusion: The implementation of a pediatric ASP at DCH consists of leadership commitment, accountability, drug expertise, action, tracking, reporting, and education. Tracked and trended data since program implementation has demonstrated high rates of proposed interventions from the pediatric clinical pharmacist, and high acceptance rates of those interventions by physician clinical teams. This has resulted in a decrease in days-of-therapy per 1000 patient days and significant cost avoidance to the pharmacy enterprise without increasing hospital readmission rates.

Keywords: Prospective-audit-and-feedback; stewardship; pediatric; intervention; utilization

Background

Twenty to fifty percent of all antibiotics prescribed in the United States acute care hospitals are either unnecessary or inappropriate [2]. When patients are given unnecessary antibiotics, they are placed at risk for serious adverse events with minimal clinical benefit and possible fiscal irresponsibility. The misuse of antibiotics has contributed to the growing epidemic of antibiotic resistance that has is a serious and growing threats to public health [3].

In order to increase patient safety, reduce financial costs, and address the public health threat, healthcare organizations must improve the utilization of antibiotics. To date, there is a significant amount of literature that supports hospital-based antimicrobial stewardship programs (ASP) dedicated to improving antibiotic use to optimize the treatment of infections and reduce adverse events associated with antibiotic use [4, 5]. ASPs have shown to improve health-related quality and safety, and to result in cost savings [6-8]. Benefits of ASP have been documented for not only adult, but pediatric patient populations [9]. In response to the published benefits of ASPs, major medical societies such as the Infectious Disease Society of America, the Pediatric Infectious Diseases Society and American Academy of Pediatrics endorse the development of a pediatric ASP.

Problem

Effective January 1, 2017, The Joint Commission (TJC) announced a new Medication Management standard requiring antimicrobial stewardship for hospitals, critical access hospitals, and nursing centers [10]. At the time, Oregon Health & Science University (OHSU) had a dedicated adult ASP but lacked a pediatric specific ASP for its pediatric hospital, Doernbecher Children's Hospital (DCH).
Analysis and Resolution

Program Development

Doernbecher Children’s Hospital (DCH), the pediatric hospital within Oregon Health & Science University (OHSU), has 145 licensed beds and is recognized by the U.S. News & World Report as one of the nation’s best pediatric hospitals [1]. DCH serves a catchment area of the entire state of Oregon, southern Washington, northern California, western Idaho, and Alaska.

The pediatric ASP at DCH launched October 16, 2017. The ASP incorporated best practices from TJC, CDC, and CMS to create a robust stewardship program to optimize the treatment of infections, reduce adverse events, and improve antibiotic related financial stewardship. The CDC priorities include seven elements that consist of leadership commitment, accountability, drug expertise, action, tracking, reporting, and education [11]. The purpose of the pediatric ASP at DCH is to support judicious antimicrobial use through prospective audit and feedback (PAF) of hospitalized patients receiving antimicrobials, restricted antimicrobial approval, and review of microbiology laboratory results, intravenous to oral conversion (IV to PO), discontinuation of double anaerobic coverage, formulary management, education of patients and healthcare staff, development of antimicrobial guidelines, and monitoring outcome measures. The pediatric ASP at DCH is composed of a leadership team that consists of a faculty member from the Pediatric Division of Infectious Disease and the pediatric infectious disease pharmacist from the Department of Pharmacy (hereby named “pediatric ASP pharmacist”).

The Program

Prospective audit and feedback/"handshake stewardship": The pediatric ASP pharmacist conducts PAF for all patients receiving systemic antimicrobials Monday – Friday in DCH. The appropriateness of the prescribed antimicrobial therapy is based on the review of clinical presentation, illness course, and laboratory or microbiology data. Each day, the pediatric ASP pharmacist assesses therapy per indication, optimal dosage, and appropriate duration of therapy. If the antimicrobial therapy may be optimized based on clinical syndrome, pathogen, susceptibility data, route, dosage or duration, history of patient allergy, and antimicrobial side effect profile, the pediatric ASP pharmacist provides direct communication with the prescriber to relay recommendations. Acceptance or rejection of the recommendations are recorded in the integrated health record as an ad-hoc intervention and is not a part of the patient’s permanent medical record. Additionally, the pediatric ASP pharmacist performs daily ASP rounds with all of the pediatric medical teams (“handshake rounds”), regardless of need for intervention, where clinicians are encouraged to ask antimicrobial or infectious diseases questions to promote education and discuss antimicrobials plans or alternative therapies [12].

Review and approval of restricted antibiotics: Placement of medication on the DCH restricted antimicrobial list is intended to (1) limit the use of these antimicrobials to the treatment of infections caused by multi-drug resistant organisms (MDRO), patients with multiple drug allergies, or contraindications to first-line agents, (2) to minimize the development of microbial resistance as well as serious adverse effects and maintain the efficacy of these medications. The list of medications is reviewed annually by the OHSU institutional antimicrobial subcommittee and modified as needed (e.g., drug shortages, cost increase/decrease).

Review of microbiology laboratory results: Culture results frequently change, and lack of awareness by the clinician of the most updated information on their patient’s status may not prompt the appropriate intervention for the patient. In order to proactively identify at-risk patients, OHSU utilizes a clinical surveillance tool to alert, report and assess analytics to improve clinical outcomes, lower costs and meet regulatory requirements. During business hours on Monday through Friday, the pediatric ASP pharmacist reviews antimicrobial cultures of every hospitalized pediatric patient receiving antibiotics. The appropriateness of the antimicrobial therapy is based on the review of clinical presentation, illness course, and clinical laboratory and microbiology data.

IV to PO conversion: Pediatric patients with an active order for at least 24 hours of a highly bioavailable antimicrobial agent, who are febrile for 24 hours, not receiving vasopressor therapy, are hemodynamically stable, with white blood cells decreasing toward the normal range, may be transitioned from IV to PO formulations of their anti-infective therapy. Of note, patients who receive continuous tube feeds do not qualify while receiving tetracycline or fluoroquinolone antibiotics. In addition, patients with a disease process that require IV therapy (e.g., meningitis, endocarditis, certain osteomyelitis) are not candidates for IV to PO conversion. Once the pediatric ASP pharmacist determines the appropriateness of a switch, he/she pages the primary care team to inform them of the medication change and document the justification within the integrated health record (IHR).
Discontinuation of double anaerobic coverage: Antimicrobials with intrinsic excellent anaerobic coverage do not require the addition of a second agent such as metronidazole. Redundant anti-anaerobic coverage with metronidazole may result in increased acquisition of vancomycin-resistant enterococci (VRE) and likely increases resistance in anaerobic organisms or failure to respond clinically to treatment for Clostridioides difficile associated diarrhea [13-16]. The pediatric ASP pharmacist reviews all patients receiving double-anaerobic coverage to determine if metronidazole may be discontinued or changed to an alternative agent that lacks anaerobic activity. The pediatric ASP pharmacist pages the primary team to notify them that he/she discontinued therapy per protocol and document their justification in the IHR.

Formulary Management: Members of the pediatric ASP recommend antimicrobial additions and/or deletions to, and participate as members of, an Antimicrobial Subcommittee of the Pharmacy and Therapeutics Committee (known as Clinical Knowledge and Therapeutics Committee at OHSU). Antimicrobial agents with the best efficacy, safety, side effect profile and lowest cost are made available for order within the hospital.

Clinician and Patient Education and Development of Antimicrobial Guidelines: The pediatric ASP team makes an on-going effort to educate practitioners concerning the appropriate utilization of antimicrobial agents. The health-system leverages technology via use of computerized physician order entry (CPOE)/IHR to provide and update guidelines and reminders about acceptable and recommended diagnostics and antimicrobial use. The pediatric ASP pharmacist provides real time antimicrobial education to clinicians through patient-based cases during daily ASP “handshake” rounds. Pediatric ASP team members also contribute during formal education opportunities, including Grand Rounds, to educate medical house staff, members of the medical staff, nursing staff, and learners about the ASP as well as various antimicrobial therapy associated topics.

Measures/Reporting: To quantify the impact of the pediatric ASP at DCH, process measures are used to determine the activity of ASP and whether pharmacist-driven interventions have impacted the utilization of antimicrobials. Process measures include tracking utilization of targeted antimicrobials (Days-of-Therapy (DOT) per 1000 patient-days), number and types of interventions. Outcome measures are used to determine if process changes have reduced or prevented the unintended consequences of antimicrobial use. Outcome measures may encompass susceptibility data, incidence of healthcare associated infections due to antimicrobial-resistant organisms, adverse drug events related to antimicrobial agents, and mortality or readmission rates. Balancing measures are also assessed, to determine if changes may be causing problems in other part of the hospital (decreasing antibiotic use or duration may inadvertently be increasing infection rates or escalation to intensive care interventions). The importance of a dedicated Business Intelligence (BI) division within the pharmacy enterprise cannot be understated. By leveraging BI, the pediatric ASP pharmacist is able to visualize actionable insights on key performance measures that positively impact quality and the financial health of the health-system.

Results

The first process measure evaluated was tracking the utilization of antimicrobials (DOT/1000 patient-days) pre- (October 2015 – October 2017) and post- intervention (October 2017 – November 2018). For all antibiotics, there was a significant decrease after the initiation of the pediatric ASP from a median of 659 to 604 DOT/1000 patient-days (p<0.001). Additionally, a significant decrease in broad-spectrum antibiotic usage (defined as 3rd generation and higher cephalosporins, beta-lactams/beta-lactamase inhibitor combinations, carbapenems, aztreonam, fluoroquinolones, vancomycin, linezolid, daptomycin) was also observed, from a median of 362 to 306 DOT/1000 patient-days (p<0.001) (Figure 1). Furthermore, this decrease in antibiotic administration data is may be associated with a significant decrease in monthly antibiotic costs ($12634.47 USD vs $10627.2 USD/1000 patient days, p=0.002) using cost data from First Databank.

Based on recommendations from TJC and CDC, the second process measure assessed was the types of interventions made by the pediatric ASP and their corresponding acceptance rates by the clinical team (Figure 2). The intervention types included education, changing antimicrobial therapy, optimization of

Figure 1: Appendix1. Pre- & Post- DOT/1000 Patient Days
dosing or duration, discontinuation of antimicrobial therapy, additional diagnostic tests or laboratory monitoring, Infectious Diseases consultation, approval of restricted antimicrobial therapy, or order clarification. The overall intervention rate by the pediatric ASP was 14.4%. Education was the most common intervention (n=173) but did not require acceptance, as it was informational. The second most common intervention was a change in antimicrobial therapy; for example, the pharmacist could recommend de-escalation or escalation of antimicrobial therapy based on microbiological results or clinical guidelines. Optimization of dosing or duration was the third most common intervention and had the highest acceptance rate (n=167, 77%). The recommendation to discontinue antimicrobial therapy had the lowest acceptance rate (n=113, 40%).

Outcome and balance measures reviewed in the ASP at DCH included C difficile infection, hospital re-admission rates, and overall mortality. The monthly hospital-associated C. difficile infection rate did not change pre/post intervention (3.3 vs 2.9 cases/10,000 patient-days, p=0.060). The monthly 30-day readmission rate and all cause 30-day mortality rate was unchanged pre/post intervention (13.6 vs 16.3 readmission/100 admissions, p=0.469, and 0.95 vs 0.94 deaths/100 admissions, p=0.770, respectively).

**Discussion**

In addition to the clinical benefits of a health-system implementing a robust ASP, cost avoidance due to antimicrobial therapy optimization directly related to a pharmacist is realized. When using published recommendations from the United States Veterans Administration (VA) hospital system on average cost avoided per recommendation, the pediatric ASP at DCH resulted in $323,265.40 USD health-system savings [16]. The findings support that pharmacist recommendations for antimicrobial drug therapy may decrease health-system costs.

The study was not without limitations. The historical-control study may have a possible imbalance in distribution of patient characteristics, selection bias and temporal bias. The pediatric ASP at DCH had only one pediatric ASP pharmacist Monday through Friday (none on the weekend) and no dedicated data analyst. While the BI division within the pharmacy enterprise provided ample support by integrating data from disparate source systems to assess usage through a user-friendly interface, the United States News and World Report recommends all ASP have a dedicated data analyst to ensure accurate classification of data. The estimated cost avoidance was determined through a study reporting in the VA population, and has not been validated in the pediatric population. Additionally, the direct effect of ASP interventions was not assessed, so the relationship between ASP interventions and patient outcomes is unclear. Although no change was observed in patient readmission rates or morality rates prior to and after the initiation of the ASP, these may not be the ideal safety measures in pediatric patients [17].

**Conclusion**

The implementation of a pediatric prospective audit and feedback ASP in DCH resulted in a decrease of antibiotic DOT/1000 patient days as well as a potential in health-system cost avoidance. As ASPs continue to develop, prospective audit and feedback strategy will likely be a preferred method due to the program’s ability to incorporate behavior change without impeding initiation of therapy from the physician perspective [18]. ASPs that leverage a successful prospective audit and feedback strategy should have dedicated staff, information technology resources to identify the target patient population for review, and business intelligence reports to evaluate the impact of the program.
Key Points

- A successful pediatric antimicrobial stewardship program consists of leadership commitment, accountability, drug expertise, action, tracking, reporting, and education
- Prospective audit and feedback antimicrobial stewardship programs may lead to a decrease in days-of-therapy per 1000 patient days and health-system cost avoidance

References