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Early transition to oral antibiotics for treatment of perforated appendicitis in pediatric patients: Confirmation of the safety and efficacy of a growing national trend

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ABSTRACT

Purpose: We performed a quality improvement initiative to monitor the change in protocol from purely intravenous therapy for perforated appendicitis to oral antibiotics at discharge once patients could tolerate eating.
Methods: Standardized prospective data were gathered on all children with perforated appendicitis treated under the new oral protocol from January 1 to December 31, 2014. Retrospective data through chart review were gathered on all children treated for perforated appendicitis during 2013. We compared demographics, clinical parameters, and hospital charges.
Results: Comparing 115 patients in 2013 and 144 in 2014, demographics and clinical characteristics were similar. In 2014, 95% of patients were discharged on oral therapy. Compared to the intravenous group, the enteric group had statistically lower rates of repeat ultrasound imaging (49.6% vs 35.1%) and PICC placement (98.3% vs 9.1%) and similar rates of intraabdominal abscess (20.9% vs 16.0%) and antibiotic change (26.1% vs 22.2%). In 2014, 55% of patients were discharged by postoperative day 5, compared to 33% in 2013. Total antibiotic days and readmission rate were similar, while hospital charges decreased by half.
Conclusion: Our results reaffirm that transition to oral antibiotics is safe, effective, and cost-efficient in treatment of perforated appendicitis in the child.

According to the Healthcare Cost and Utilization Project's Nationwide Inpatient Samples of the Agency for Health and Quality Research (AHRQ), there were 76,874 cases of appendicitis in children age 1–17 years in 2010, 26.6% of which were perforated. Based on their cost data, this translates into a burden of US$303 million annually. Additionally, the rate of perforated appendicitis in children remained unchanged from 2001 to 2010, despite declines in the rate of perforation in adults during that interval [1].

Pediatric surgical textbooks continue to delineate intravenous (IV) antibiotic therapy as the gold standard in treatment of perforated appendicitis [2,3]. Several recent retrospective studies, however, have established safety and efficacy of early transition to oral (PO) antibiotic therapy in patients tolerating a regular diet [4,5,6]. The efficacy of such a pathway was confirmed by a prospective randomized, controlled trial from the Kansas City group [7]. In practice, some pediatric surgeons have changed their postoperative protocols to include discharge with oral antibiotics as standard practice. In many institutions, however, children still remain on IV antibiotics in the hospital for days after oral intake has been re-established.

At Miami Children's Hospital, our former protocol for perforated appendicitis included insertion of a peripherally-inserted central catheter (PICC) and IV antibiotics for at least 5 days, or until tolerance of regular diet, complete resolution of abdominal tenderness, lack of fever >100.5 for 48 h, and demonstration of a normal white blood cell (WBC) count. As part of a quality improvement initiative begun after reviewing the relevant literature in a departmental journal club, we felt compelled to transition to PO antibiotics once food intake was normalized. We proposed a prospective data collection for one year, with quarterly reviews to ensure the safety and efficacy of the new pathway in our patient population, which is 65% Hispanic, 19% African-American, and 15% non-Hispanic white [8]. We instituted the new protocol on January 1, 2014, expecting that the regimen would prove equally safe, more efficient and more cost effective for perforated appendicitis than the PICC line/IV protocol employed previously.

1. Methods

1.1. Patient population

Beginning January 1, 2014 and using standardized data forms, we prospectively collected information on each patient presenting with perforated appendicitis. The data sheet followed the child through the hospital stay to the office visits until discharge from care. Our data

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collection ended with the last patient presenting to our institution prior to midnight on December 31, 2014. For comparison purposes, we performed retrospective chart review using the same data sheet for all patients presenting during the 2013 calendar year.

Perforated appendicitis was defined as a visible hole in the appendix at operation or an extraluminal fecalith in the peritoneal cavity. Four attending surgeons (CAB, LM, CR, CK) performed or directed all operations. For all patients, the initial surgical approach was via a single site, single instrument laparoscopy, with conversion to standard three port laparoscopy in cases of severe adhesion, purulence, phlegmon, bleeding or nonstandard anatomy.

1.2. Clinical management protocols

In the 2013 cohort, patients were postoperatively managed with IV piperacillin/tazobactam 100 mg/kg every six hours with routine PICC line placement. Home health nursing and antibiotics were arranged by our social work team, and the patients were discharged home when tolerating a regular diet, after training the parents on antibiotic administration. These patients were seen approximately every five days until completion of their antibiotic course. Patients without insurance were maintained in the hospital until their antibiotic course was completed. Cessation of antibiotics was considered once the patient had been afebrile for >48 h, with a nontender abdominal exam. At this time, a WBC count was sent, and if normal, the PICC line was removed and antibiotics discontinued. If abnormal, antibiotics were continued for five more days.

In the 2014 cohort, patients were postoperatively managed with IV piperacillin/tazobactam until they had tolerated one full meal, at which time they were switched to oral metronidazole and sulfamethoxazole/trimethoprim. Patients with intolerance or allergy to this regimen were trialed on amoxicillin/clavulanate. PICC line placement only occurred if a patient required total parenteral nutrition (TPN) or if oral antibiotic therapy proved impossible, requiring completion of treatment with intravenous antibiotic therapy. Failure of oral antibiotics was defined as intolerance of two different oral regimens, manifested mainly by vomiting. Patients on the oral regimen were seen in the surgical offices approximately every five days until the antibiotic course was completed, using the same criteria for cessation as for the previous cohort.

We included patients undergoing interval management in the data set, with the decision for interval management being made by the attending surgeon at presentation. The criteria for interval management were symptom duration more than 5–7 days, palpable right lower quadrant mass consistent with phlegmon, and/or discrete intraperitoneal abscess on imaging. Antibiotic treatment continued until resolution of symptoms as for postoperative treatment, and we offered interval appendectomy at the parents' discretion 6–12 weeks thereafter.

For both cohorts, we changed antibiotics if there was no improvement of symptoms (fever, abdominal pain, intolerance of oral intake) by postoperative day 5, or if a trial of oral antibiotic produced vomiting. Postoperative ultrasound was ordered in any child who by postoperative day 5 failed to tolerate oral intake or continued to have spiking fevers, pain, diarrhea or dysuria.

All but one patient undergoing interval management did eventually undergo appendectomy; some required additional postoperative antibiotics for intraoperative perforation and contamination, and these days were included in the calculation of total antibiotic days.

All patients presenting with appendiceal perforation (suspected in the interval management cases or confirmed at operation) were therefore included in the data collection. One patient was excluded from the 2013 cohort for perforated appendicitis as an initial manifestation of unrecognized Crohn disease. Three patients in the 2014 cohort were excluded owing to the majority of their treatment being performed at another institution, limiting ability for secure data collection. To ensure the best possible follow-up in patients sent home on oral antibiotics, we instituted a dual-language, bright pink discharge information sheet that stressed the importance of continuing the antibiotic therapy until the office visit and clearly identified before discharge the follow-up appointment date and time.

1.3. Demographics, clinical observations and outcomes

Data collected included age at presentation, gender, insurance status, management strategy, utilization of postoperative radiologic exams, length of hospital stay, emergency department visits, readmission rates, total days of antibiotic usage, complications and interventions, and length of follow-up. Total antibiotic days included antibiotic use for any indication related to appendicitis up to 90 days after the definitive operation. Patients were deemed lost to follow-up if they did not visit the office postoperatively, or if they missed a scheduled office appointment and did not reschedule. In patients lost to follow-up prior to completion of antibiotics, we calculated antibiotic days based on intention of completion of the prescribed course of treatment.

Complications were defined strictly in an attempt to avoid bias in the retrospective chart review. Intraabdominal abscess was defined by a combination of persistent fever, abdominal tenderness and fluid collection on ultrasound (US) or computed tomography (CT) scan. PICC complication was any complaint related to the PICC line after its initial placement that resulted in an extra visit from the IV nurse specialist.

In order to analyze the financial impact of our protocol change between 2013 and 2014, we utilized the hospital charges made to patients for all encounters related to their appendicitis. We used the charges made by our hospital for analysis rather than using actual reimbursement amount which varies greatly between insurance companies thereby introducing a confounding factor in the analysis. The total charges to the patient on their initial presentation and during any subsequent readmission or emergency room visit were recorded. We initially intended to include the home health nursing charges and the cost of home IV antibiotic use, but we were unable to extract solid figures for charges from our survey of home health companies to complete the outpatient side of the analysis.

1.4. Statistical analysis

Continuous variables were compared with Student *t*-test. Discrete variables were compared with Chi-square test. P values <0.05 were considered to be statistically significant.

2. Results

2.1. Demographics and protocol adherence

The cohorts comprised 115 patients in 2013 and 144 patients in 2014. Percentage male and age of patients were similar between groups, as were type of management (immediate operative vs interval). Demographic and clinical variables are delineated in Table 1. Mean total days of antibiotic usage were identical between cohorts (15 days). In 2013, owing mainly to lack of home IV antibiotic insurance coverage, 9% of patients were discharged home with oral antibiotics (in violation of protocol) while 15% of patients finished their IV antibiotic course in the hospital and were discharged home without further antibiotics. In 2014, 95% of patients were discharged home with oral antibiotics. Two patients failed oral antibiotic therapy (1.3%), and one completed IV therapy while remaining in the hospital for hemorrhagic gastritis. Four were discharged with IV antibiotics for other clinical and social reasons (one with neutropenia undergoing active chemotherapy for medulloblastoma, one with perforated appendicitis complicated by contaminated ventriculoperitoneal shunt requiring externalization, two owing to parent preference).

Repeat ultrasound imaging declined significantly in our 2014 cohort, while repeat CT scanning stayed about the same. PICC line placement