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Non-operative management of early, acute appendicitis in children: Is it safe and effective?

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ABSTRACT

Purpose: The purpose of this study was to determine if early, acute appendicitis in children can be safely and effectively managed with antibiotics alone.
Methods: A retrospective review was performed of children (<18 yrs) treated non-operatively (NOM) for early, acute appendicitis since May 2012. These were compared to patients treated with appendectomy between January 2011 and October 2011 (OM). Inclusion criteria included: (a) symptoms <48 h, (b) localized peritonitis, and (c) ultrasound findings consistent with early, acute appendicitis.
Results: Twelve patients (66% female, mean age 12.2,SD = 4.2 yrs) were treated non-operatively, while 12 (50% female, mean age 12.5,SD = 3.2 yrs) were treated operatively. Two NOM children (16.7%) required initial appendectomy. One patient developed recurrent appendicitis requiring appendectomy 7 months post-discharge. Four other NOM patients returned with symptoms but did not require admission or surgery. Two OM patients (8.3%) had hospital visits and admissions related to surgical site infections. Mean length of stay (LOS) for the first visit was 1.5 days (SD = 1.0d) (NOM) vs. 1.3 days (SD = 0.5d) (OM) (p = 0.61). Including first and subsequent admissions, mean LOS was 1.8 days (SD = 1.1d) (NOM) vs. 1.7 days (SD = 1.5d) (OM) (p = 0.97).
Conclusion: Early acute appendicitis in appropriately selected children can be successfully treated non-operatively. Randomized trials with longer follow-up are required.

Acute appendicitis (AA) is the most common cause of emergency surgery in children, with a lifetime prevalence of 7%–8% [1]. The annual incidence in Ontario is 75 per 100,000 population [2].

Since the early 20th century, treatment of acute appendicitis has been primarily surgical. The surgical management of AA has greatly reduced the mortality associated with the disease, however the risk of complications is inherent to surgical treatment. Most commonly, these risks include wound infection, intra-abdominal abscess formation, and prolonged ileus. Overall complication rates in adults are 11.1% with open appendectomy and 8.7% laparoscopically [3]. A meta-analysis of appendectomy complications in pediatric studies was as follows: 2.6% (laparoscopic) versus 2.7% (open) for non-perforated disease, and 16.0% (laparoscopic) versus 18.1% (open) in perforated disease [4].

Recent randomized controlled trials in adults have shown that primary non-operative treatment with antibiotics alone may decrease the complications traditionally associated with operative management [5–7]. These suggest an algorithm in which patients are first treated with antibiotics, and only progress to surgery if antibiotic therapy fails. This approach is currently utilized in other intra-abdominal infections, such as uncomplicated diverticulitis in adults, with good success rates. Conversely, in another randomized trial, Vons et al. [8] concluded that primary non-operative management was inferior to surgery, with increased peritonitis and a recurrence rate of 26%. Other risks of antibiotic therapy alone include, nausea, diarrhea, allergic reactions and opportunistic infections, such as *Clostridium difficile*.

To date, there is very little experience in managing AA non-operatively in the pediatric population. Abes et al. [9] published a small retrospective review demonstrating that in select cases of early AA, non-operative management could be used safely in children.

The objective of our study was to determine if early, uncomplicated acute appendicitis in children could safely be managed with antibiotics alone.

1. Methods

After IRB approval (UWO REB File: 103669), the medical records of all patients less than 18 years of age treated non-operatively for AA by a single pediatric surgeon at our institution between May 2012 and February 2013 were reviewed. During this time, this surgeon's practice was to offer non-operative management to all patients diagnosed with early, uncomplicated acute appendicitis. Either the

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attending surgeon or the senior resident discussed the benefits and risks of non operative versus operative management of AA. Inclusion and exclusion criteria were predetermined at the onset of the study period. Patients were included in the non-operative management arm of the study (NOM) if they met inclusion criteria, including a classic presentation of appendicitis, less than 48 h of symptoms at presentation, and the diagnosis of acute appendicitis was confirmed with imaging. Patients were excluded if they showed signs of hemodynamic compromise at presentation or if abscess or phlegmon was diagnosed on imaging. These criteria were chosen prior to the study to limit the groups to patients with early, uncomplicated acute appendicitis.

The operative management (OM) group was obtained by reviewing charts of all patients who underwent appendectomy for non-perforated appendicitis by the same surgeon between January and October 2011. The same inclusion and exclusion criteria as the NOM group were then applied to this list to arrive at the final comparison group. There is a 6 month gap between the 2 groups since the surgeon was on parental leave during that time.

NOM patients were treated with intravenous ciprofloxacin and metronidazole or ampicillin, gentamycin and metranidazole while in hospital, and prescribed amoxicillin/clavulanic acid on discharge, with dosing adjusted for patient weight. Duration of antibiotic therapy was one week. While in hospital, serial examinations were performed, and a clinical decision was made by the attending surgeon to offer operative management if the patient's condition worsened or failed to improve over a 24 h observation period. OM patients were treated with a single dose of preoperative antibiotics, followed by laparoscopic appendectomy.

Data collected from the initial presentation included age, gender, time since onset of symptoms, leukocyte count ($\times 10^9$/l), C-reactive protein (mg/l), appendix diameter on ultrasound (mm), and time until management was initiated (hours). Post-treatment data included length of stay in hospital (LOS), repeat visits to hospital, repeat admissions, complications, and recurrences.

The primary endpoints were a) failure of initial treatment and b) complications of initial treatment. In the NOM group, this included worsening or non-resolution of symptoms of appendicitis requiring operation, and perforation while attempting non-operative management. In the OM group this was defined to include peritonitis requiring reoperation, and surgical site infections. Secondary endpoints included a) length of stay (for the initial visit and all subsequent admissions), b) recurrences, and c) repeat visits to hospital with symptoms.

Data were analyzed using IMB SPSS Statistics, version 20. The mean and standard deviation were used to summarize normally distributed continuous variables, whereas the median and range were used for skewed continuous variables. Categorical outcomes were reported as percentages. Group differences in continuous variables were compared using the independent samples t-test or the independent samples Mann–Whitney U test. The Chi-square test or Fisher's exact test was used to contrast differences in proportions between the two groups. A p value < 0.05 was considered statistically significant.

2. Results

Of 17 patients treated non-operatively for acute appendicitis, 12 met the inclusion criteria for the NOM group. Reasons for exclusion from the study (Table 1) included lack of imaging findings to support the diagnosis (4 patients) and duration of symptoms greater than 48 h at presentation (1 patient). Twelve of 24 patients treated with appendectomy for non-perforated acute appendicitis between January and October 2011 met the inclusion criteria for the OM group. Patients were excluded for lack of imaging to support the diagnosis (7 patients), symptom duration greater than 48 h (2 patients), appendectomy performed electively as part of a larger procedure (2 patients), and evidence of perforation on ultrasound (1 patient). Initial patient characteristics are presented in Table 2. Median follow-up for the NOM group was 6.5 months, and OM patients were followed up for 6 months after initial presentation.

Table 1
Reasons for exclusion from study groups.

	NOM	OM
Screened for inclusion	17	24
Excluded	5 (29%)	12 (50%)
Imaging does not support diagnosis	4	7
Duration of symptoms >48 h	1	2
Other indication for operative intervention		2
Evidence of perforation on imaging		1

Two of 12 patients (16.7%) in the NOM group failed initial non-operative management of acute appendicitis (Fig. 1). One failed to improve in hospital, requiring appendectomy within 24 h of admission. Another patient showed initial clinical improvement and was discharged home with oral antibiotics the following day. However, a follow-up visit at 6 weeks revealed that the pain had not completely resolved, prompting elective appendectomy as an outpatient. The patient's symptoms resolved following appendectomy. Of note, initial imaging for this patient demonstrated the presence of a fecalith. Of the remaining 10 patients, 1 developed recurrent appendicitis 7 months post-discharge and required an appendectomy. Finally, one post-operative complication was seen in the NOM group: a deep surgical site infection requiring readmission but no invasive interventions. This complication occurred in the NOM patient who underwent appendectomy for failure to improve in hospital within 24 h of admission.

Two of 12 patients (16.7%) in the OM group developed surgical site infections (SSIs), one deep and one superficial. The patient with a deep SSI required 2 readmissions for pain control and antibiotics, each admission two days in length. Imaging revealed a small intra-abdominal abscess that was not amenable to percutaneous drainage, and the complication was treated with antibiotics. The patient with a superficial SSI was found to have an infected 5 mm left lower quadrant port site, and was treated with antibiotics as an outpatient. No other surgical complications were noted in the OM group.

Mean length of stay at the time of the initial visit was 1.5 (SD = 1.0) days in the NOM group versus 1.3 (SD = 0.5) days in the OM group ($p = 0.61$) (Table 3). Including subsequent readmissions, total mean length of stay per patient was 1.8 (SD = 1.1) days (NOM) versus 1.7 (SD = 1.5) days (OM) ($p = 0.97$). There were 4 (0.3 per patient) repeat visits to the emergency department in the NOM group versus 2 (0.2 per patient) in the OM group (Table 3) ($p = 0.51$).

Table 2
Patient characteristics at inclusion.

	Nonoperative management N = 12		Operative management N = 12		p value
	Mean	SD	Mean	SD	
Age (years)	12.2	4.2	12.0	3.2	0.91
Female:Male Ratio	8:4		6:6		0.68
Hours of symptoms	27.3	9.5	27.5	12.8	0.98
LKC	16.1	4.4	14.0	4.2	0.24
CRP	13.6 (median)	1.2–94.1 (range)	5.4 (median)	0.6–81.6 (range)	0.10
Ultrasound diameter (mm)	8.9	1.7	8.9	3.8	0.97
Follow-up (months)	5.3	2.9	6	0	0.41

Values are reported as mean ± SD unless otherwise noted.