The American Journal of Surgery 217 (2019) 1099–1101

Contents lists available at ScienceDirect

The American Journal of Surgery

journal homepage: www.americanjournalofsurgery.com

Evaluation of white blood cell count at time of discharge is associated with limited oral antibiotic therapy in children with complicated appendicitis

Patrick C. Bonasso*, Melvin S. Dassinger, Deidre L. Wyrick, Samuel D. Smith, Jeffrey M. Burford

University of Arkansas for Medical Sciences, Division of Pediatric Surgery, 1 Children's Way, Slot 837, Little Rock, AR, 72202, USA

ARTICLE INFO

Article history:
Received 8 March 2018
Received in revised form
20 December 2018
Accepted 29 December 2018

Keywords:
Perforated appendicitis
Oral antibiotics
White blood count at discharge

ABSTRACT

Background: Variation exists for postoperative antibiotics in children with complicated appendicitis. We investigated the impact of white blood count (WBC) at discharge on oral antibiotic therapy, abscess rate, and readmission rate.

Material/Methods: We conducted a two year review of children with complicated appendicitis. In the pre-protocol group, total antibiotic therapy was ten days (IV and oral) and home oral antibiotics at discharge. In the post-protocol group, children with leukocytosis were prescribed oral antibiotics to complete seven days of total antibiotic therapy and children without leukocytosis were not prescribed oral home antibiotics.

Results: There was no difference between mean hospital days after operation (3.52 vs. 3.24, $p = 0.5111$), means days of inpatient intravenous antibiotics (3.13 vs. 2.58, $p = 0.5438$), post-operative abscess rates (20.7% vs. 19.6%, $p = 0.9975$), or readmission rate (13.4% vs. 12.4%, $p = 1.000$).

The post-protocol group had a shorter average total antibiotic duration (4.24 vs. 9.52 days, $p < 0.001$) and were more likely to be discharged without oral antibiotics (71.1% vs 8.5%, $p < 0.001$).

Discussion: Limiting home antibiotics at discharge to children with leukocytosis significantly decreases home antibiotic use.

Introduction

The lifetime incidence of appendicitis is 9% and children younger than 15 years of age have the highest risk of complicated appendicitis.[1] Care in children with this disease remains highly variable with research focusing on diagnostic imaging, timing of operative intervention, preoperative and postoperative antibiotic management, and discharge criteria.[2–4] The national readmission rate following appendectomy for complicated appendicitis is estimated to be 12.8% and the post-operative intra-abdominal abscess rate is approximately 20%.[5,6]

Variation exists for the administration of perioperative intravenous (IV) and oral antibiotics for appendicitis. Treatment regimens have been driven by both efficacy of the medications and cost comparisons. Previous triple IV antibiotic regimens dosed multiple times daily have progressed to double IV antibiotic treatment dosed twice daily that are reliably effective.[6] Monotherapy regimens such as piperacillin/tazobactam have been found to be equally advantageous; however, they are more expensive than the dual antibiotic regimens.[7,8] Our current regimen of ceftriaxone and metronidazole dosed once daily was adopted from St Peter et al.[6] Some studies support a defined length of antibiotic treatment whereas others follow institutional clinical practice guidelines.[6,9–11] No defined consensus on treatment length exists for the administration of oral antibiotics at home. We transitioned our pathway in the management of complicated appendicitis to include evaluation of a white blood cell count (WBC) when the child met discharge criteria. The purpose of our study was to investigate the impact of WBC at discharge on oral antibiotic therapy, abscess rate, and readmission rate. We hypothesized that evaluation of WBC at the time discharge criteria were met would decrease use of home

* Corresponding author.
E-mail addresses: pbonass3@hsc.wvu.edu (P.C. Bonasso), DassingerMelvinS@uams.edu (M.S. Dassinger), DLWyrick@uams.edu (D.L. Wyrick), SmithSamuelD@uams.edu (S.D. Smith), JMBurford@uams.edu (J.M. Burford).

https://doi.org/10.1016/j.amjsurg.2018.12.071
0002-9610/

oral antibiotics and total length of antibiotic treatment.

Materials and methods

We conducted a retrospective review of all pediatric patients (<18 years) who underwent appendectomy at a freestanding children's hospital from August 2014 to July 2016. Two sequential one year groups were compared. Appendectomy was performed by one of five pediatric surgeons in a single clinical practice. Subjects were also excluded for a diagnosis at the time of appendectomy other than complicated appendicitis, clinically defined as perforated or gangrenous by the attending surgeon via review of operative notes. Additionally, subjects were excluded if they presented with complicated appendicitis with a well formed abscess and were managed with initial percutaneous drainage by Interventional Radiology (IR) and interval appendectomy.

All children received a fluid bolus and IV antibiotics (ceftriaxone and metronidazole) pre-operatively in the emergency department. Ceftriaxone (50 mg/kg) and metronidazole (30 mg/kg) were given every 24 h while inpatient. All patients were evaluated at least twice daily, on morning and afternoon rounds, to determine if they met discharge criteria. Discharge criteria included being afebrile (<38.5 °C), tolerating a diet, and pain controlled with oral medications. Prior to the protocol change all patients were discharged home with oral antibiotics to complete 10 days of treatment. In 2015, the protocol was changed to include evaluation of the WBC at the time of discharge. If the WBC was elevated, the patient was sent home with oral antibiotics to complete 7 days of treatment. If the WBC was not elevated, all antibiotics were discontinued.

Information on demographics, operative findings, length of stay, antibiotic administration (time, type, and dose given), imaging studies, readmissions, complications, abscess rate, and hospital charges were collected. Length of stay was calculated from date of admission to date of discharge. Comparisons between pre- and post-protocol groups were made using t-tests for continuous variables and chi-square tests for categorical variables. P-values less than or equal to 0.05 indicated statistical significance.

Results

A total of 520 children with appendicitis underwent appendectomy during the two year study period; 179 (34.4%) had complicated appendicitis. 82 (46%) children were in the pre-protocol group and 97 (54%) children were in the post-protocol group. There were no differences in age or gender between patients in the pre- and post-protocol group (See Table 1). There was 95% adherence to the protocol in the latter group.

There was no difference in mean days of hospitalization after operation (3.52 vs. 3.24, $p = 0.5111$), mean days of inpatient IV antibiotics (3.13 vs. 2.58, $p = 0.5438$), post-operative abscess rate (20.7% vs. 19.6%, $p = 0.9975$), readmission rate (13.4% vs. 12.4%, $p = 1.000$), or day of readmission (7.4 vs. 7.5, $p = 1.000$) between the two cohorts (See Table 1).

For the 17 patients with a postoperative abscess in the pre-protocol group, 9 were inpatient on IV antibiotics, 7 had been discharged home with PO antibiotics, and 1 had been discharged home without PO antibiotics. Regarding abscess treatment, 7 were treated with antibiotics alone and 10 were treated with drainage by Interventional Radiology (IR). For the 19 patients with a post-operative abscess in the post-protocol group, 9 were inpatient on IV antibiotics, 7 had been discharged home with PO antibiotics, and 1 had been discharged home without PO antibiotics. Regarding abscess treatment, 7 were treated with antibiotics alone and 12 were treated with IR drainage (See Table 1).

Those in the post-protocol group were more likely to be discharged without oral antibiotics (71.1% vs 8.5%, $p < 0.001$). The post-protocol children who were discharged with oral antibiotics had a shorter duration of oral therapy compared to the pre-protocol group (5.75 vs 7.50 days, $p = 0.001$). The average duration of total antibiotic therapy (IV + PO) was shorter in the post-protocol group compared to the pre-protocol group (4.24 vs. 9.52 days, $p < 0.001$) (See Table 1).

Average home oral antibiotic costs were $212.61 per patient in the pre-protocol group vs. $20.22 per patient in the post-protocol group.

Discussion

Complicated appendicitis is a common diagnosis in children. Still, there is variation in preoperative and postoperative antibiotic management.[2–4] At our institution, tailoring antibiotic therapy based on WBC decreased the length of treatment and number of patients discharged with oral antibiotics while not changing the readmission rate or abscess rate. Additionally, there was no difference in postoperative length of stay or inpatient IV antibiotic days.

Total cost of oral antibiotics per patient was 10 times greater in the pre-protocol group than the post-protocol group. Three reasons contribute to that cost difference. First, patients in the pre-protocol group were prescribed home oral antibiotics to complete a ten day course of total antibiotic treatment compared to a total of seven days in the post-protocol group. Second, all patients were prescribed oral antibiotics in the pre-protocol group (n = 68) versus

Table 1
Comparison of demographics, antibiotic usage, and outcomes between pre-protocol and post-protocol groups.

	Pre-protocol (N = 82)	Post-protocol (N = 97)	p-value
Gender *Count (%)*			
Male	56 (68%)	55 (56%)	0.1114
Female	26 (32%)	42 (44%)	
Mean Age (years)	9.37	9.28	0.8856
Mean Days of IV abs (Days)	3.13	2.58	0.5438
Mean Post-operative days to discharge (Days + SD)	3.52 + 2.63	3.24 + 2.79	0.5111
17 (20.7%)	19 (19.6%)	0.9975	17 (20.7%)
Count (%)	17 (20.7%)	19 (19.6%)	0.9975
Readmission rate			
Count (%)	11 (13.4%)	12 (12.4%)	1
Total antibiotic treatment (Mean Days + SD)	9.52 + 3.62	4.24 + 3.83	<0.001*
Mean days of home oral antibiotics			
Mean + SD	7.50 + 2.76 (n = 68)	5.75 + 2.01 (n = 20)	0.0012*
Discharge home without antibiotics			
Count (%)	7 (8.5%)	69 (71.1%)	<0.001*

*Indicates p-value that is statistically significant.

only those with an elevated WBC in the post-protocol group (n = 20). Third, the pre-protocol group was prescribed two oral antibiotics, augmentin and metronidazole, while the post-protocol group was prescribed only one oral antibiotic, augmentin. Metronidazole was no longer prescribed due to poor patient compliance with the medication.

Previously published clinical trials have showed a postoperative abscess rate of 20% and readmission rate of 12.5% which is similar to our findings.[5,6] The change in protocol did not change the need for an IR drainage procedure.

At the free-standing children's hospital where the study was performed, all five pediatric surgeons supported the development and implementation of a post-operative complicated appendicitis protocol. During the first month after the change, the team identified small inconsistencies in adherence to the protocol, mainly obtaining a WBC at time of discharge. Although the surgical team is in-house 24-h a day, there are inconsistencies in the level of the providers placing orders that may have led to variation in protocol adherence. The presence of advance practice nurses and fellows as well as the unified support for the protocol by all surgeons led to the successful implementation of this pathway at our hospital.

Controversy still remains over the duration of antibiotic course in children with perforated appendicitis and studies focused on the pediatric patient are limited.[10] Other authors use a combination of IV and oral antibiotics for a total of seven days.[12] Our findings support a combination of IV and limited oral antibiotics if the WBC is elevated at discharge. Moreover, our study demonstrates that treatment for a full 7 days with a normal WBC may not be necessary. Interestingly, there are some reports that state oral antibiotic use may not be necessary after an appropriate IV therapy is completed.[13] Our study patients with postoperative abscesses were a mix of antibiotic treatments in that some had both IV and PO antibiotics while others only had IV antibiotic treatment. Additionally, we did not find an association with abscess or readmission rates and an elevated WBC.

As a retrospective study, the study design has limitations. Our hospital is a tertiary referral center with a large catchment area for the state. Readmission need for additional drainage procedures, and abscess rate could have been missed if a child was cared for at another facility. The effect of this is limited in our study since we are comparing two groups where it is just as likely in either group to seek care elsewhere.

Our results support the evaluation of a WBC at the time of discharge for the postoperative management of complicated appendicitis in the pediatric population as it decreased oral antibiotic use. Future studies will look at the effect of adding a differential to the WBC, other ways to better predict which patients will develop a postoperative abscess, or evaluate the discontinuation of antibiotics postoperatively in pediatric patients with perforated appendicitis.

Conclusion

Limiting home antibiotics to children with leukocytosis at discharge significantly decreases home antibiotic use without increasing abscess or readmission rates.

Conflicts of interest

The authors have no relevant financial disclosures or conflicts of interest to report.

Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

References

1. Anderson JE, Bickler SW, Chang DC, Talamini MA. Examining a common disease with unknown etiology: trends in epidemiology and surgical management of appendicitis in California. *World J Surg*. 2012;36(12):2787–2794, 1995-2009.
2. Rice-Townsend S, Barnes JN, Hall M, Baxter JL, Rangel SJ. Variation in practice and resource utilization associated with the diagnosis and management of appendicitis at freestanding children's hospitals: implications for value-based comparative analysis. *Ann Surg*. 2014;259(6):1228–1234.
3. Lee SL, Islam S, Cassidy LD, Abdullah F, Arca MJ. American pediatric surgical association outcomes and clinical trials committee. Antibiotics and appendicitis in the pediatric population: an American pediatric surgical association outcomes and clinical trials committee systematic review. *J Pediatr Surg*. 2010;45(11):2181–2185, 2010.
4. Muehlstedt SG, Pham TQ, Schmeling DJ. The management of pediatric appendicitis: a survey of North American pediatric surgeons. *J Pediatr Surg*. 2004;39(6):875–879.
5. Rice-Townsend S, Hall M, Barnes JN, Baxter JK, Rangel SJ. Hospital readmission after management of appendicitis at freestanding children's hospitals: contemporary trends and financial implications. *J Pediatr Surg*. 2012;47(6):1170–1176.
6. St Peter SD, Tsao K, Spilde TL, et al. Single daily dosing ceftriaxone and metronidazole vs standard triple antibiotic regimen for perforated appendicitis in children: a prospective randomized trial. *J Pediatr Surg*. 2008;43(6):981–985.
7. Nadler EP, Reblock KK, Ford HR, Gaines BA. Monotherapy versus multidrug therapy for the treatment of perforated appendicitis in children. *Surg Infect (Larchmt)*. 2003;4:327–333.
8. Golden AB, Sawin RS, Garrison MM, Zerr DM, Christakis DA. Aminoglycoside-based triple-antibiotic therapy versus monotherapy for children with ruptured appendicitis. *Pediatrics*. 2007;119(5):905–911.
9. Willis ZI, Duggan EM, Bucher BT, et al. Effect of a clinical practice guideline for pediatric complicated appendicitis. *JAMA Surg*. 2016;15(5):e160194.
10. Slusher J, Bates CA, Johsnon C, Williams C, Dasgupta R, von Allmen D. Standardization and improvement of care for pediatric patients with perforated appendicitis. *J Pediatr Surg*. 2014;49:1020–1025.
11. Skarda DE, Schall K, Rollins M, et al. Response-based therapy for ruptured appendicitis reduces resource utilization. *J Pediatr Surg*. 2014;49(12):1726–1729.
12. Fraser JD, Aguayo P, Leys CM, et al. A complete courses of intravenous antibiotics vs a combination of intravenous and oral antibiotics for perforated appendicitis in children: a prospective, randomized trial. *J Pediatr Surg*. 2010;45(6):1198–1202.
13. Nadler EP, Gaines BA. The surgical infection society guidelines on antimicrobial therapy for children with appendicitis. *Surg Infect (Larchmt)*. 2008;9(1):75–83.