



## Japanese Journal of Surgery & Medicine

Available Online: <http://ijgms.edwiserinternational.com>

### *The Strategy of a Shorter Course of Postoperative Intravenous Antibiotics for Advanced Appendicitis in Children*

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#### Article info

Received 30 March 2018

Revised 11 April 2018

Published 18 April 2018

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#### Abstract

**Objective:** Antibiotic treatment is standard after appendectomy for advanced appendicitis in children with the aim to reduce postoperative complications. However, the evidence for deciding the duration of administration of the intravenous antibiotics (IVA) is limited. We present our experience focussing on the duration of IVA and the strategy for managing the complications.

**Methods:** Retrospective review of patients undergoing an emergency appendectomy supervised by the senior surgeon (TT) over an 11-year period (2006-16) was done. Patient records were reviewed for operative findings, duration of IVA and oral antibiotics and post-operative complications. All patients diagnosed with advanced appendicitis were included. Post-operatively for the initial 3 days all received IVA viz. amoxicillin, metronidazole and gentamycin; continuing them further was based on the clinical course. The outcome and complications were analysed with respect to the duration of the (IVA) required.

**Results:** 79 patients with advanced appendicitis were included in this study; 74 done laparoscopically and 5 open. There were 52 males and 27 females, with a mean age of 9.2 years (2.5-16). Median postoperative hospital stay was 4 days (3-24). 38 (48%) and 4 (5%) patients were able to stop IVA after 3 and 4 days respectively, the rest 37 (47%) required a longer course of IVA. 15 were discharged home with oral antibiotics completing a total of 10 days antibiotics. The overall complications was 11.4%, wound infection in 4 patients and abscess in 5. On statistical analysis, the higher incidence of complications in the 5 or more days IVA group was not significant comparing to those who received for shorter duration.

**Conclusion:** In our experience children operated for advanced appendicitis early review and consideration of short course (minimum of 3 days) IV antibiotics based on clinical status is a safe and efficient method to treat with minimal complication rates.

**Keywords:** Appendicitis; Advanced appendicitis; Perforated; Gangrenous; White blood cell count; C-reactive protein IV antibiotics; Intra-abdominal abscess.

## Introduction

Antibiotic treatment is standard after appendectomy for perforated and gangrenous appendicitis in children with the aim to reduce postoperative complications. However, the evidence for deciding the duration of administration of the intravenous antibiotics is limited. Restriction and proper use of antibiotics is important to preventing harmful adverse effects and developing antibiotic resistance. We present our experience with the management of perforated and gangrenous appendicitis with regards to the duration of the intravenous antibiotics required.

## Materials and Methods

A retrospective review of patients undergoing an emergency appendectomy supervised by the senior surgeon (TT) over an 11-year period (2006-2016) was done. Patient records were reviewed for operative findings, duration of intravenous (IVA) and oral antibiotics and post-operative complications. All patients diagnosed with advanced appendicitis (i.e.

perforated or gangrenous based on macroscopic intra-operative appearance) were included in the study. All resected specimens had histopathological evaluation. As a routine, pus from the peritoneal cavity was collected intra-operatively for microbiology and antibiotic sensitivity. The postoperative management was in accordance to the strategy as shown in Figure 1. The patient is started empirically on the intravenous triple antibiotics, amoxicillin, metronidazole and gentamycin for the initial three days. Reasons for continuing antibiotic treatment longer than 3 days were determined by the clinical course of persistent temperature >37.5°C, delay in return of bowel function and continuing pain with limited mobility. Any signs of secondary infection, such intra-abdominal abscess or wound infection will be treated with an extended period of IV antibiotics. The outcome and complications were analyzed with respect to the duration of 3 days, 4 days and 5 or more days of the intravenous antibiotics (IVA) required.

**Table 1:** Preoperative complications.

Patients treated	No. of patients with perforated appendix	No. of patients with gangrenous appendix	WCC, Median (range)	p-value	CRP, Median (range)	p-value
3-day IV	15	16	17.0 (4.3-34.8)	0.6745 (3-day cf 5-day)	80.0 (15.0-198.0)	0.0658 (3-day cf 5-day)
3-day IV+oral	4	3	15.0		60.0	
4-day IV	2	1	22.5 (19.0-26.0)	0.3789 (4-day cf 5-day)	78.3 (55.0-84.0)	0.1443 (4-day cf 5-day)
4-day IV+oral	1	0	-		-	
≥ 5 days IV	19	11	17.6 (8.8 – 26.0)		184 (79.0-315.0)	
> 5-day IV+oral	5	2	14.0 (9.0-23.0)		155.5 (5.0 -200.0)	

The preoperative serum inflammatory markers, median C-reactive protein (CRP) was more elevated in the 5 or more days IVA group while the median white cell count (WCC) was similar in all 3 groups and no statistical significance is demonstrated.

## Results

Seventy-nine consecutive patients underwent emergency appendectomy, 74 laparoscopic and 5 open, with advanced appendicitis were included in this study. There were 52 males and 27 females, with a mean age of 9.2 years (range: 2.5-16). The median postoperative hospital stay was 4 days (range: 3-24). The culture of the peritoneal pus grew *Streptococci milleri* (15),

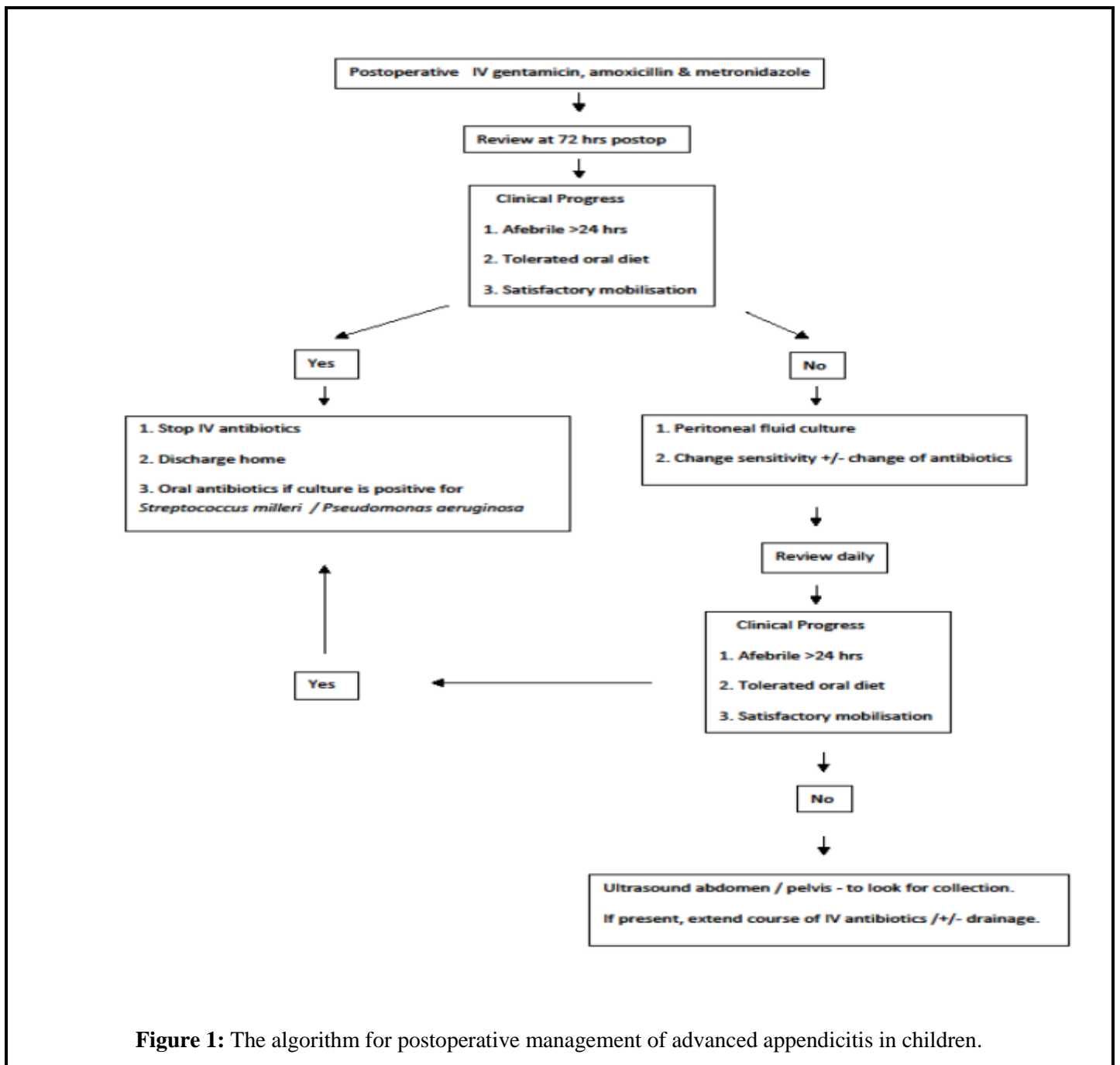
*coliforms* (13), anaerobes (9), alpha-haemolytic *Streptococcus* (3), *Pseudomonas* (2), non-haemolytic *Streptococcus* (2) and combination of growth in 13 and no growth in 4 patients. According to the clinical progress (Figure 1), 38 (48%) and 4 (5%) patients were able to stop IVA after 3 and 4 days respectively. The rest 37 (47%) required a longer course of IVA, 5 or more days. Because of the *Streptococci milleri* or *Pseudomonas aeruginosa* positive peritoneal pus culture, 7 (18.4%), 1 (25.0%) and 7 (18.9%) patients of

each of the 3 days, 4 days and 5 or more days IVA groups were given additional days of oral antibiotics to

take at home after discharge completing a total of 10 days antibiotics treatment (Tables 1 and 2).

**Table 2:** Postoperative Complications

Number of days received IV antibiotics	Number of patients	Postoperative wound infection	Postoperative intra-abdominal abscess	Overall Complications
3 days	38 (48.0%)	2	1	3 (7.9%)
4 days	4 (5.0%)	0	0	0 (0%)
5 or more days	37(47.0%)	2	4	6 (16.2%)
p value	-	1.0	0.2	0.6



**Figure 1:** The algorithm for postoperative management of advanced appendicitis in children.

## Discussion

In the postoperative course of antibiotic treatment for advanced appendicitis, it is very much desirable to keep it as minimum as possible without incurring any added morbidity in order to lower the risk of rising bacterial resistance, minimize toxicities, and furthermore increase patient compliance. It is logical to follow the trend to be away from the use of therapeutic courses of fixed duration, and to stratify the infective processes and tailors the duration of IVA to the clinical progress [1]. In 2014, the importance of restricting antibiotic treatment when possible was also highlighted in the report by the World Health Organization stating that the most important reason for antibiotic resistance is the misuse of and over-treatment with antibiotics [2]. Traditionally, postoperative IVA for advanced appendicitis has been given for as long as 10 days covering Gram-positive, Gram-negative, and anaerobic bacteria [3] and can contribute to a longer length of hospital stay. Use of clinical criteria such as fever, pain, return of bowel function and white blood cell count and a 5-day course of IVA for children with perforated Appendicitis was recommended by the American Pediatric Surgical Association Outcomes and Clinical Trials Committee in 2010 [4]. A significant shorter hospital stay has also been reported in a series of 47 children with advanced appendicitis treated with postoperative IV antibiotics until each satisfied a set of bed side clinical parameters, core temperature <38°C for 24 hours, tolerated two consecutive meals, mobilizing independently, requiring only oral analgesics, suggesting resolved intra-peritoneal infection [5]. Furthermore, there was no difference in the postoperative complications comparing to the historical controls. In our study, with strict adherence to the criteria of being afebrile for 24 hours, tolerating oral diet and satisfactory mobilisation, nearly half of them (48%) did not required IVA after 3 days and a further few (5%) completed by the 4th day. These patients were discharged within the median postoperative period of 4 days, keeping hospital stay down to a minimum. As a routine, oral antibiotics were given to 15 (19%) patients to complete a total of 10 days, including the in-patient period of IVA for peritoneal pus cultures positive for *Streptococcus milleri* and *Pseudomonas* because of the susceptibility of persistent intra-abdominal abscess reported by Madden et al. [6], Hardwick et al. [7] and Leeuwenburgh et al. [8]. This seemed to have mitigated the risk of developing abdominal abscess to only 6% among our patients. There is a noticeable but no significant higher incidence intra-abdominal

abscess among the 5 or more days group (10.8%) as compared to the shorter IVA groups (2.3%) indicating the discrete and cautious use of shorter duration of IVA does not incur higher risk of postoperative abscess formation. There is no evidence of any significant difference in the raised inflammatory markers, white cell count or C-reactive protein, among the two groups. Our experience is also shared by Henry et al. [9] and van Wijcket et al. [10] in no correlation between lengths of postoperative antibiotic treatment and abscess formation in children operated on for advanced appendicitis. The markedly raised CRP, also echoed by Stefanutti et al. [11], could be helpful in pre-empting the possibility of longer duration of IVA which seemed necessarily in the few patients complicated with intra-abdominal abscess. We managed to keep the overall complications to 11.4%, wound infection in 4 patients and abscess in 5. Only one abscess required drainage and the rest responded to an extended course of antibiotics following the initial postoperative period of IVA. There is no significant difference between the shorter and 5 or more days groups and this is in agreement with Snelling et al. [12] in their systematic review of antibiotic use in children who had undergone appendectomy for complicated appendicitis showing 3 days did not appear to associate with higher rates of intra-abdominal abscess or wound infection.

## Limitations

This was a retrospective study with its inherent limitations. The sample size of children with advanced appendicitis (79 patients over a period of 11 years) may be relatively small. We are aware that some centres [13] have reported equivalent results using the combination of other antibiotics such as ceftriaxone and metronidazole with shorter course of IV administration.

## Conclusion

Our experience suggests that in children operated for advanced appendicitis early review and consideration of short course (minimum of 3 days) IV antibiotics based on clinical status of the patients is a safe and efficient method to treat with minimal complication rates. For persistent fever, abdominal pain and/or delay in the return of bowel function, a vigilant search should be done for possible source of infection such as of the wound and/or intra-abdominal pus collection. The total duration of the antibiotics can be optimised primarily on the clinical grounds as per the response to the treatment. Further study with a multi-centre

randomised controlled trial is necessary to determine the optimal duration of the course of antibiotic use in childhood advanced appendicitis.

### Ethical Approval

The study was done as an audit based on standard hospital trust guidelines for clinical audits and hence ethically approved.

### Conflict of Interest

None declared.

### Funding

None declared.

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*This manuscript was peer-reviewed*

*Mode of Review: Single-blinded*

*Academic Editor: Dr. Gulnur Gollu*

