A REVIEW

MANAGEMENT OF ACUTE APPENDICITIS: THE ANTIBIOTICS DEBATE

ALIFIYA GORIAWALA, BSC, BHSC (PA), CCPA
MOUNT SINAI HOSPITAL DEPT OF GENERAL SURGERY

Introduction

Appendicitis is one of the most frequent causes for an acute abdomen requiring emergent abdominal surgery worldwide. It has a lifetime risk of 8.6 percent in males and 6.9 percent in females [(1)]. Traditionally, operative management has been the dominant strategy for managing acute appendicitis. However, in recent times, there is much debate about implementing conservative medical management with antibiotics first to treat uncomplicated appendicitis. This article reviews the treatment strategies for acute uncomplicated appendicitis in light of contemporary research to determine if non-operative management is a feasible alternative.

History of appendicitis

Reginald Fitz first coined the term appendicitis in 1886 distinguishing it as an entity separate from inflammation of the cecum and small bowel [(2)]. He recognized that early diagnosis and prompt surgical treatment were essential to prevent potentially detrimental complications [(2)]. However, as early as the 1950s, medical management with antibiotic therapy was emerging as an alternative to surgery for appendicitis [(3)]. Although patients have been successfully treated for uncomplicated appendicitis with antibiotics alone, the long term effects and full repercussions are still largely unexplored.

Uncomplicated appendicitis

Uncomplicated appendicitis also known as simple or non-perforated appendicitis refers to appendicitis that does not have clinical or radiographic signs of perforation such as an inflammatory mass, phlegmon or abscess [(4)]. Most cases of appendicitis are not perforated at presentation. The current standard of care for adult patients with uncomplicated appendicitis that are fit for surgery is an immediate appendectomy, either laparoscopic or open [(5)]. Adult patients that are deemed unfit for surgery are admitted to hospital, started on intravenous antibiotics for

one to three days and discharged with oral antibiotics (for up to 10 days) upon clinical improvement [5].

Comparative evidence for the management of uncomplicated appendicitis

At present, there are six randomized trials, that have specifically evaluated the use of antibiotic therapy versus an appendectomy for uncomplicated appendicitis in adults [6-11]. Most patients who are treated solely with antibiotics do respond with a reduction in white blood cell count [8], symptom improvement [7,9,10] and ultimately do not progress to peritonitis [8]. Also, these patients have lower or similar pain scores [6-8], require fewer doses of narcotics [8], have a quicker return to work [7,8], and do not have a higher perforation rate as opposed to those who underwent an appendectomy. Within the first year of being treated with antibiotics for appendicitis approximately 70 percent of patients were able to avoid surgery. However, the remaining thirty percent of patients experienced recurrent appendicitis or symptoms of abdominal pain with a mean time to appendectomy of 4.2 to 7 months [6,8,9].

Short-term results do support antibiotics as an alternative to surgery for treating uncomplicated acute appendicitis, however data indicating benefit in the long-term (beyond the first year) is largely unexplored. Just recently, in October 2018, a five-year observational follow-up study determining the late recurrence rate of appendicitis after antibiotic therapy for the treatment of uncomplicated acute appendicitis has been released [12]. In 257 patients initially treated with antibiotics for uncomplicated acute appendicitis, the cumulative incidence of recurrent appendicitis was 27.3 percent at 1 year, 34.0 percent at 2 years, 35.2 percent at 3 years, 37.1 percent at 4 years, and 39.1 percent at 5 years [12]. No patients suffered a major complication. Compared with the antibiotic group, the appendectomy group had a higher five-year overall complication rate (24.4 versus 6.5 percent), required a longer sick leave, and there was no difference in the length of hospital stay [12]. However, one must keep in mind that the appendectomy group consisted of both laparoscopic and open appendectomy patients which may account for the difference.

Although there is a substantial amount of evidence regarding the use of antibiotics alone for uncomplicated appendicitis, reliable patient selection is not fully elucidated. Antibiotic therapy is indicated only for patients with non-perforated appendicitis. This is an issue because pre-operative CT imaging does not always reliably discern uncomplicated appendicitis from complicated/perforated appendicitis. Also, patients with non-perforated appendicitis with fecaliths on imaging have a high rate of progressing to complicated appendicitis (up to 40 percent) [13]. Thus, non-operative management would not be recommended for those patients [6,13].

Furthermore, patients that are immunocompromised, older or have multiple medical comorbidities may be at greater risk for the severity of their disease being underestimated with non-operative management. For example, the risk of unexpected lesions in the appendix such as a carcinoid or

carcinoma can be higher in these populations and can go undetected without an appendectomy [14,15]. On the other hand, these high risk patients may benefit from a conservative management approach but they are generally excluded from the trials. As a consequence, the outcomes of an antibiotics first approach in this population is still unknown.

For some patients who have a history of surgical complications or are apprehensive to appendectomy, a non-operative approach could be offered as an alternative to immediate surgery. However, these patients should be clearly counselled on the risks and benefits of their choice and be made aware that there is a recurrence rate of 15 to 25 percent but may be up to 38 percent [6,16].

In 2016, a collaborative international study including more than 4000 patients from 44 countries confirms that the dominant strategy for uncomplicated appendicitis remains operative, (either open/laparoscopic). In this study, 95.7 percent underwent surgery (42.2 percent open appendectomy, 51.7 percent laparoscopic appendectomy, 1.8 percent other procedures) and only 4.3 percent were managed non-operatively with antibiotics alone [17]. The overall mortality rate was 0.28 percent and mostly correlated with disease severity and comorbidities [17]. The study concluded that appendectomy is the most effective treatment worldwide due to the low mortality rate.

Conclusion

In summary, non-operative management of appendicitis is still controversial and should not be implemented as standard of care despite mounting evidence that use of antibiotics first may be sufficient for managing the initial presentation of appendicitis. This is consistent with treatment guidelines from the American College of Surgeons, World Society of Emergency Surgery, Society for Surgery of the Alimentary Tract, European Association of Endoscopic Surgery and Society of American Gastrointestinal and Endoscopic Surgeons and, all of which recommend appendectomy as the treatment of choice for adult patients with non-perforated appendicitis. Implementing the use of antibiotics first in uncomplicated appendicitis as standard of care is yet premature because a significant proportion of patients initially treated with antibiotics alone may eventually require surgery due to recurrent appendicitis; and there is no reliable method of identifying these patients beforehand. It is also uncertain if avoiding immediate surgery justifies the fear and burden of potential recurrence or missed neoplasm (especially in older adults). In conclusion, some patients with acute uncomplicated appendicitis may benefit from initial antibiotic therapy as a feasible alternative; but overall, operative management should be considered first line.

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