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Research Article

**EVALUATION THE USE OF ANTIBIOTICS FOR
MANAGEMENT OF ACUTE NON- PERFORATED
APPENDICITIS**

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Abstract:**Background:**

Appendicitis is one of the common medical intra- abdominal emergencies which require an emergent surgery. In the recent years a lot of literatures published in regard to the use of antibiotics in the management of acute non-perforated appendicitis.

Objective:

In our review we aim to evaluate the role of antibiotics in compare to early appendectomy in the management of acute non- perforated appendicitis

Methods:

PubMed database were used for articles selection. All relevant articles related to our review were chosen to cover the following topics: Appendicitis, Management, Appendectomy and Antibiotics. We excluded other articles, which are not related to our objectives. The data have been extracted according to specific form to be reviewed by the authors

Conclusion:

In this review we compared non- operative treatment with antibiotics to surgery for acute uncomplicated appendicitis, we have found that non- operative treatment is feasible, safe and cost effective.

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INTRODUCTION:

Over 200 million of surgical procedures performed annually around the world [1], appendectomy remain the most common intra-abdominal procedure worldwide [2,3]. In the United States, the annual incidence of AA is approximately 9.4 per 10,000 population, [4] with a mortality of 0.2-0.8% [5].

132 years ago, Reginald Heber Fitz establish the term "appendicitis" to describe inflammation of the vermiform appendix [6]. Fitz also found the clinical course of appendicitis is variable from spontaneously resolved to perforation and peritonitis. It was the awareness of the possible progression of appendiceal perforation to generalized peritonitis, with almost invariably fatal outcomes that may happen. After three years of Reginald Fitz description to appendicitis and his recommendation to find operation to limit the appendiceal perforation, Dr. Charles McBurney advocated the early appendectomy when he published his classical paper "Experience with early operative interference in cases of disease of the vermiform appendix" in 1938

METHODOLOGY:

Sample

PubMed was chosen as the search database for the articles selection, because it is one of the major research databases within the suite of resources that have been developed by the National Center for Biotechnology Information (NCBI). The following topics were used: ("acute appendicitis management"[MeSH Terms] AND ("appendectomy"[MeSH Terms] AND "antibiotics"[MeSH Terms] AND (Clinical Study[ptyp] AND "2013/12/12"[PDat]: "2018/12/10"[PDat] AND "humans"[MeSH Terms] AND English[lang]). A 35 articles were shown. The chosen articles were screened by titles, and reviewing the abstracts yielded 6 articles which were enrolled.

Inclusion criteria: The articles were selected based on the relevance to the research project which should include one of the following topics {acute

[7]. Dr. McBurney also described the early clinical course of the disease, including tenderness at a point "almost exactly two inches from the anterior iliac spine, on a line drawn from the process through the umbilicus, which later on this sign named after him.

The clinical diagnostic scoring system for acute appendicitis is combination between history, physical examination, laboratory and radiological studies, the Alvarado score, has the reported sensitivity [with corresponding 95% confidence interval (CI)] of 82% (95% CI 76–95%) and specificity 81% (95% CI 76–85%) [8]. Ultrasonography is the initial radiological investigation for diagnosis of appendicitis, although computed tomography (CT) is the most accurate test [9].

In the recent time, there are a lot of publications discussed the possibility of antibiotics use in treatment of acute non-perforated appendicitis. Therefore, in our review we aim to evaluate the role of antibiotics in the management of acute non-perforated appendicitis in compare to early appendectomy.

appendicitis, appendectomy, antibiotics}. **Exclusion criteria:** All other articles which did not suit with these topics as their primary end, or repeated studies, and reviews studies.

Analysis

No software was used, The data extracted based on specific form that contain (name of the author and publication year, study design, Objective, and Outcomes), these data were reviewed by the authors to compare management plans of acute appendicitis.

RESULTS:

We enrolled a total of 5 studies according to our inclusion, and exclusion criteria described above. 1 of them was a prospective cohort study, and the 4 were a randomized clinical trial. All of the included studies compared the antibiotic therapy to appendectomy in management of acute appendicitis Table 1.

Table (1): Included studies details.

Author (year)	Study design	Objective	Outcomes	Ref.
Salminen et al. (2015)	randomized clinical trial	To compare antibiotic therapy with appendectomy in the treatment of uncomplicated acute appendicitis confirmed by computed tomography (CT).	Antibiotics therapy is not inferior to appendectomy. Most of the patients who were treated with antibiotics didn't required appendectomy during 1 year follow-up period, and the one who required appendectomy didn't had significant complication.	10
Park HC et al. (2014)	prospective cohort study	To compare the outcomes between antibiotics therapy and appendectomy in appendicitis and appendiceal diameters ≤ 10 mm.	Antibiotic therapy without surgery may be a safe treatment for uncomplicated appendicitis in select patients with appendiceal diameters ≤ 10 mm.	11
Svensson et al. (2015)	Randomized Controlled Trial	to evaluate the feasibility and safety of nonoperative treatment of acute nonperforated appendicitis with antibiotics in children.	1) the cost-effective was overall similar between two groups, but the cost of the initial inpatient treatment was significantly higher in the surgery group. 2)nonperforated acute appendicitis in children may be safely treated with antibiotics	12
Talan et al (2017)	Randomized Controlled Trial	To assess feasibility of a multicenter US study comparing antibiotics-first, including outpatient management, with appendectomy.	A multicenter US trial comparing antibiotics-first to appendectomy, including outpatient management, is feasible to evaluate efficacy and safety.	13
S. Sippola et al. (2017)	randomized clinical trial	to compare the costs of antibiotics alone <i>versus</i> appendectomy in treating uncomplicated acute appendicitis within the randomized controlled trial.	Patients receiving antibiotic therapy for uncomplicated appendicitis incurred lower costs than those who had surgery.	14

DISCUSSION:

Appendectomy is considered as the most common intra-abdominal surgical procedure worldwide. In addition, it's one of the most emergent operation that require urgent intervention to prevent appendicitis

burst and then peritonitis. Early appendectomy has been advocated, especially since R. Fitz in 1886 published a classic paper on 247 patients with perforated appendicitis [6]. Recently, multiple literatures were published in order to evaluate the role

of antibiotics in management of acute appendicitis. In our review, we aim to evaluate the recent articles published in this field in order to understand the antibiotics role and its effectiveness.

Salminen et al. (2015) [10], aimed to compare antibiotics treatment to open appendectomy in management of acute non-perforated appendicitis. He conducted randomized clinical trial in a period between November 2009 to June 2012, which he enrolled 530 patients with acute non-complicated appendicitis in which the diagnosis was confirmed by computed tomography (CT). Of 272 patients in surgical group had successful open appendectomy, resulting in success rate of 99.6% (95% CI, 98.0% to 100.0%), and in antibiotic group, 70 patients (27.3%; 95% CI, 22.0% to 33.2%) underwent appendectomy within 1 year of initial presentation for appendicitis. Of the 256 patients available for follow-up in the antibiotic group, 186 (72.7%; 95% CI, 66.8% to 78.0%) did not require surgery. Most important, there were no intra-abdominal abscesses or other major complications associated with delayed appendectomy in patients randomized to antibiotic treatment. Salminen et al. found that most of patients randomized to antibiotics treatment for uncomplicated appendicitis did not require appendectomy during the 1-year follow-up, and the patients who required appendectomy didn't experience any serious complication. Park HC et al. (2014) [11] compared the outcomes between antibiotics therapy and appendectomy in appendicitis and appendiceal diameters ≤ 10 mm. They enrolled 119 patients who initially received antibiotics therapy over two years. They defined the failure of antibiotics treatment as the need of appendectomy or true appendicitis. Peritonitis was defined as either complicated appendicitis or intra-abdominal abscess postoperatively. Park HC et al. found Nine patients (7.6%) failed to respond to initial antibiotic therapy, and 6 had true appendicitis after subsequent surgery. Two patients had complicated appendicitis (peritonitis), but no patient displayed intra-abdominal abscess. During 14 months follow-up period, 14 patients (12.7%) experienced recurrence. They found that antibiotic treatment with second-generation cephalosporin and metronidazole alone for uncomplicated appendicitis in selected patients with appendiceal mass ≤ 10 mm is safe. Svensson et al. (2015) [12], evaluated the feasibility and safety of nonoperative treatment of acute nonperforated appendicitis with antibiotics in children. They randomized fifty patients after imaging-confirmed acute nonperforated appendicitis to treatment to either antibiotics or to surgery. Follow-up was for 1-

year. Two of 24 patients in the nonoperative treatment group had appendectomy within the time of primary antibiotic treatment and 1 patient after 9 months for recurrent acute appendicitis. Another 6 patients have had an appendectomy due to recurrent abdominal pain ($n = 5$) or parental wish ($n = 1$) during the follow-up period; none of these 6 patients had evidence of appendicitis on histopathological examination. Twenty-two of 24 patients (92%) treated with antibiotics had initial resolution of symptoms. Of these 22, only 1 patient (5%) had recurrence of acute appendicitis during follow-up. Overall, 62% of patients have not had an appendectomy during the follow-up period. This trial suggests that nonoperative treatment of acute appendicitis in children is feasible, safe and the cost-effective. Talan et al (2017) [13], assessed feasibility of a multicenter US study comparing antibiotics-first, including outpatient management, with appendectomy. They enrolled patients aged 5 and older with uncomplicated appendicitis. These 30 consented patients were randomized to 14 (46.7%) patients who had appendectomy and 16 (53.3%) patients had intravenous antibiotics. The patients were selected based on specific inclusions and exclusions criteria. Of 15 antibiotic-treated adults, 14 (93.3%) were discharged from the ED and all had symptom resolution. At 1 month, major complications occurred in 2 appendectomy participants (14.3%; 95% confidence interval [CI] 1.8% to 42.8%) and 1 antibiotics-first participant (6.3%; 95% CI 0.2% to 30.2%). Antibiotics-first participants had less total hospital time than appendectomy participants, 16.2 versus 42.1 hours, respectively. During median 12-month follow-up, 2 of 15 antibiotics-first-treated participants (13.3%; 95% CI 3.7% to 37.9%) developed appendicitis and 1 was treated successfully with antibiotics; 1 had appendectomy. No more major complications occurred in either group. Talan et al. has led us to conclude that a multicenter US trial comparing antibiotics-first to appendectomy, including outpatient management, is feasible to evaluate efficacy and safety. S. Sippola et al. (2017) [14] compared the costs of antibiotics alone versus appendectomy in treating uncomplicated acute appendicitis within the randomized controlled trial from November 2009 until June 2012. 273 patients were assigned to the appendectomy group and 257 to antibiotic treatment after CT-conformed uncomplicated acute appendicitis. All costs were recorded, whether generated by the initial visit and subsequent treatment or possible recurrent appendicitis during the 1-year follow-up. They found that patients who had appendectomy have 1.6 times higher costs than the patients who had antibiotics

treatment.

Despite the revolution at field of medicine, the approach of acute appendicitis has not change since Fitz's observation [6] that led to choose the appendectomy as a definitive treatment [15]. This practice came from assumption of progression of non-perforated appendicitis to perforated with intraluminal obstruction as leading cause. The theory of intraluminal obstruction was based on the observational studies in early part of the 20th century discussed that fecalith was frequently found in removed inflamed appendix. However, luminal obstruction as the instigating event in appendicitis was never proven, because many patients with appendicitis do not exhibit any obstruction. In the early 20th century, Wangenstein and Bowers [16] found an infectious cause for appendicitis as a contributing factor; nonetheless, the obstruction theory took root and was not challenged until 1984 when Arnbjornsson and Bengmark [17] measured intraluminal pressure in human subjects with acute appendicitis. Arnbjornsson and Bengmark suggested that obstruction was of minor importance in the development of acute appendicitis, although it could be one of the contributing factors for perforation, whereas enteric bacteria probably played a more important role in the pathogenesis of a cute appendicitis [17].

It has been found since the era of Fitz that acute appendicitis could have many different clinical courses, including: spontaneous resolution, persistent non-perforated appendicitis and perforated appendicitis. Therefore, there should be different management options according to clinical course of acute appendicitis after ultrasonography and CT confirmation.

An initial nonsurgical approach for acute appendicitis has been relatively widely accepted [18]. One of the reasons why this approach is accepted is the relatively low of surgical complications, operative mortality and cost-effective.

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