



Research Paper

Antibiotics versus a emergency open appendectomy conservative management- A primary treatment of uncomplicated acute appendicitis: A randomized controlled trial

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Abstract

Background: Although appendectomy is the gold standard treatment of acute appendicitis. The main motive of this randomized controlled study is to determine the role of antibiotics in management of uncomplicated acute appendicitis and to ensure that appendectomy is still gold standard or not.

Method: After randomization between 100 consecutive suspected acute appendicitis, patients were screened by clinical examination and modified alvarado score. All randomly selected patients were allocated equally in conservative or antibiotic (AG) and surgical group (SG). Follow up was done till 6 months.

Result: In this randomized study 90% patients have responded to conservative management. 6% patients have treatment failure and undergone emergency appendectomy in primary hospital stay. 4% patients in subsequent follow up period of 6 months developed recurrent appendicitis and were operated at some other institute. Hence, the recurrence rate in conservative group is 4%. The success rate of appendectomy group is 100% by definition, but surgery related complications, wound related complication and prolonged hospital stay is much higher in comparative to conservative group.

Conclusion: By our study we can infer that conservative management had many advantage like high success rate, lower recurrence rate and shorter hospitalization stay with reduced mortality and morbidity, hence should be offered to young patients of uncomplicated acute appendicitis as a first line treatment by choice.

Introduction

It goes without saying that the abdomen is a magic box and poses new surprises to surgeon every time. Acute appendicitis still ranks as one of the most common surgical emergency.¹

Despite these extraordinary advances in modern radiographic imaging and laboratory investigation, the accurate diagnosis of acute appendicitis still remains an enigmatic challenge.^{1,2}

Acute appendicitis is inflammation of vermiform appendix and remains the most common acute

surgical condition of abdomen in all ages and common disease in surgical practice which comprises 10% of all surgical cases in emergency department.^{1,2,3}

Appendectomy has not been challenged till recent time as the best treatment because of age, old concern of prognosis of acute appendicitis to appendicular perforation.^{4,5} However multiple studies in recent years have suggested that conservative management by antibiotic therapy can be useful in treating acute appendicitis.^{6,7,8,9,10} Studies have also suggested that immediate appendectomy can be avoided at least for 24 hours without increasing morbidity and mortality if antibiotics are given.^{11,12} Appendectomy may not be necessary for most of the cases for acute uncomplicated appendicitis as the disease may resolve spontaneously without any need of surgical approach or the rest cases be treated with antibiotics alone.¹³

This conservative management approach has many advantages including high success rate, lower recurrence rate, shorter hospitalization, reduced morbidity & mortality along with reduced cost of treatment.¹⁴

Consequently, the aim of this review was to evaluate the current literature on the role of antibiotics versus appendectomy in the management of acute uncomplicated appendicitis and to assess if appendectomy remains the gold standard treatment of care.

Material and Methods

Study Population: Our study was a prospective randomized controlled study which was conducted on 100 patients of acute uncomplicated appendicitis admitted in the Department of Surgery, J.A. Group of Hospitals, Gajra Raja Medical College, Gwalior during January 2017 to March 2018 after getting written informed consent from the patients.

A total number of 100 patients were enrolled in the study based on inclusion criteria (all the patients > 12 years of both sexes with history of right iliac fossa pain for less than 48 hours and

having modified Alvarado score more than 7) and exclusion criteria (USG or clinical findings suggestive of right iliac fossa pain having duration more than 48 hour, appendicular lump, appendicular perforation, recurrent appendicitis or co-morbid diseases like diabetes mellitus, hypertension, HIV, pregnancy and antibiotic allergy).

Modified Alvarado Scoring System was applied and patient with score ≥ 7 were included in this study. Adequate physical examination, total leucocyte count and USG abdomen along with urine analysis and Xray KUB region were done for making clinical diagnosis of acute uncomplicated appendicitis.

Randomization: After confirming the diagnosis of acute uncomplicated appendicitis by Modified Alvarado Score, all 100 clinical participants were randomized, each patient was randomly assigned a number between 1 to 100 by the independent senior resident surgeon.

Thus the odd number patient remained under antibiotic group (AG) and even number of patients received surgical treatment after randomization of the patients.

Management

Surgical Management (SG): After randomization of patient receiving surgical option, open appendectomy was performed by standard technique using grid iron incision with prophylactic antibiotic as a single dose of intravenous injection Ceftriaxone 1 gm and 500 mg of Metronidazole I/V was administered prophylactically.

Success in the surgical group is defined as successful appendectomy, evaluated as 100%.

Conservative Management (AG): After randomization, antibiotic group patients received intravenous Ceftriaxone 1 gm 12 hourly and Metronidazole 500 mg 8 hourly for 2 days.

The clinical status of antibiotic group patient were re-evaluated within 24 hours and 48 hours after admission. If the condition of the patient deteriorated or worsened due to progressive infection, perforated appendix or peritonitis, the

patient was subjected to emergency appendectomy. The two days intravenous antibiotic treatment, if led to improvement of pain and general condition, the patient were kept on oral antibiotic therapy with Tab. Cefexime 200 mg 12 hourly, Tab. Metronidazole 400 mg 8 hourly and was subsequently discharged once he was relieved of pain and fever.

Success in antibiotic therapy was defined as resolution of pain, tenderness and fever resulting in discharge from the hospital without the need for surgical treatment.

Results

In this randomized controlled study, 100 patients of acute appendicitis were enrolled after admission in surgery department of G.R. Medical College and J.A. Group of Hospitals, Gwalior during the period of January 2017 to March 2018.

The study group consisted of 53 male & 47 female ranging from 12 to 70 years. A peak in incidence of acute appendicitis was noted in age group of 21 to 30yrs of both sexes.

The incidence gradually declined after 3rd decade. The ratio of female to male having acute appendicitis was 1:1.17.

Table 1: Age wise distribution of participant in conservative and surgical group

Age group (years)	Conservative group		Surgical group		p value
	Frequency	%	Frequency	%	
12-20	6	12	11	22	0.5842
21-30	23	46	18	36	
31-40	11	22	8	16	
41-50	6	12	9	18	
51-60	2	4	2	4	
> 60	2	4	2	4	

71% of patients were admitted with feature of acute appendicitis in surgical ward with duration of symptom less than 24 hours. 29% patients presented with symptoms presenting for more than 24 hours but less than 48 hours.

Table 2: Time duration of symptoms in study sample

Time duration	No. Of patients	Percent
< 24 hrs	71	71
24-48 hrs	29	29
Total	100	100

When we categorized the whole study population as per modified Alvarado score, 91% of the patients had abdominal pain as their primary most common and consistent symptom. Migratory right iliac fossa pain was the first complaint to begin with, starting in periumbilical region but shifting to right iliac fossa with in 8-16 hours of duration. Leukocytosis is second most common (89%) feature as per modified Alvarado score, found in the study group. 80% of patients were suffering from fever at the time of admission.

Table 3: Frequency percent of components of Modified Alvarado Score system

Symptoms/Clinical Findings	Present	Absent	Percent
Migratory RIF Pain	91	09	91
Anorexia	66	34	66
Nausea and Vomiting	79	21	79
Tenderness in RIF	84	16	84
Elevated Temperature 99°F (37°C)	80	20	80
Leukocytosis	89	11	89

Table 4: Outcome of conservative treatment

Time duration	No. of patients	Percentage
Successful	45	90
Treatment failure	3	6
Recurrence	2	4
Total	50	100

Total 50% of study population underwent conservative treatment. Among these 45 (90%) patients had recovered successfully.

One patient had persistent tenderness with tachycardia, not resolving to I/V antibiotics given for 2 days. The patient was subsequently operated on 3rd day and had perforated appendix in intra operative finding. The other two patients had persistent high grade fever with tachycardia. They were also operated on 4th post admission day and were found to have intraoperatively appendicular abscess. In antibiotic group, thus 3 patients (6%) failed to respond to conservative treatment.

4% (2) cases of patients after conservative treatment had recurrence within a period of 6 months. They were operated within the follow up period of 6 months at some other institute.

Table 5: Complications of surgical group

Disease	No. of patients	Percentage
Incisional hernia	1	2
Subacute intestinal obstruction	2	4
Wound related complications	8	16

In surgery group, 8 patients (16%) developed wound infection, of which 3 patients required secondary suturing due to wound dehiscence. 1 patient of these 3 patients later on developed incisional hernia after 4 months. The other 5 patients had seroma formation resulting in skin gape which healed by secondary intention. 2 patients developed features of subacute intestinal obstructions after 4 and 5 months of primary attack of acute appendicitis and were managed successfully by conservative approach.

Table 6: Mean duration of hospital stay

Group	Mean duration
Conservative group	3.96 days
Operative group	4.22 days

Mean duration of hospital stay in conservative group was 3.96 days while in operative group was 4.22 days. Those patients of conservative/antibiotic group who were operated in primary stay had median stay of 7 days. Hence there is significance difference in hospital stay in surgical group patients and those who underwent appendectomy due to development of localized peritonitis after conservative management with antibiotics.

Table 7: Return to normal activity

Group	Mean duration
Conservative group	7.4 day
Operative group	10.8 day

The patients who were subjected to conservative treatment by antibiotics returned to normal activity with a mean duration of 7.4 day, while the mean duration of return to normal activity for surgical group was 10.8 days. In patients who failed conservative management and were

operated, had mean duration of 12.12 days for returning to normal activity.

Discussion

Acute appendicitis is one of the most common causes of pain in abdomen. Traditionally, any patient presenting with features of acute uncomplicated appendicitis is referred for urgent surgery. Although, appendectomy has been considered as gold standard, conservative management with antibiotic is gaining more and more acceptance. The greatest advantage is of newer generation of highly effective broad spectrum antibiotics has allowed for more conservative approach in such cases.¹⁵ Antibiotics can give better results in those areas of particularly developing countries where resources for surgical treatment are not readily available. Conservative treatment is associated with more cost effectiveness in comparison to surgical approach.

In our study of 100 patients, most number of patients was of 3rd decade (41%). The males outnumbered the females in the ratio of 1.17:1. The rate of acute uncomplicated appendicitis started decreasing after the 3rd decade.

11% of the patient presented with most common symptoms of migratory pain in right iliac fossa, anorexia, nausea and vomiting within 24 hours of onset of symptoms, 89% of the patients revealed leukocytosis in their blood examination report.

In antibiotic group, 3 patient developed complications and had undergone appendectomy in primary hospital stay. One patient was operated on 3rd post admission day and intra-operative finding was of a perforated appendix. The other two patients had appendicular abscess who were subjected to appendectomy after failed conservative treatment.

The primary recovery rate in antibiotic group was 94%. Two patients in subsequent follow up period of 6 months developed recurrent appendicitis and were operated at some other institute. Hence, the recurrence rate was 4% in antibiotic group.

In surgery group, during follow up period, 2 patients (4%) later presented with recurrent subacute intestinal obstructions and were improved by conservative treatment. One patient developed incisional hernia later on after 4 months and was advised surgery. The patient did not turn up for surgery. In the primary hospital stay, 8 patients (16%) developed wound related complications like wound gaping and dehiscence increasing the duration up primary stay and financial constraints. This led to the over utilization of hospital beds, resources and manpower. Mean duration of hospital stay in conservative antibiotics groups was 3.96 days in comparison to 4.22 day of operative appendectomy group.

In this RCT, according to definition of success, treatment efficacy in antibiotic group was 94% as compared to surgery group where it is 100%. But rate of early complication in appendectomy group was 16% (wound related complications).

Also the patients of conservative antibiotics group returned to normal activity within 7.4 days which is significant in comparison to patients of surgery group who returned to normal activity within 10.8 days.

A study done by Styrud et al.¹⁶ had 252 male patients between 18-50 years old with clinically assumed non perforated appendicitis suggested 88% recovery rate in antibiotic group with 14% recurrence rate in 1 year. In the study done by Styrud et al. 2007, after one year of previous surgery with same antibiotic regimen showed a recurrence rate of 24% after 5 year follow up. Several other studies, meta-analysis and systematic reviews have showed approximately 90% recovery rates with antibiotic group and 10-15% recurrence rates within one year follow up period.^{16,17,18,19}

Our randomized study also had 90% success rate with 4% recurrence in 6 month follow up which was in compliance to above studies.

Our study showed a recurrence rate of 4%. The patient who had recurrence were operated for appendectomy in follow up period. First year

recurrence rate of acute appendicitis treated successfully conservatively ranges between 10-15% in other randomized trial. Our RCT results are comparable to other RCT. Higher percentages have been reported in the previous study of Eriksson et al.¹⁷ and in a prospective study by Vons et al¹⁹ (36-8% and 26% respectively).

We did not analyze the hospital costs in between 2 groups but there was significant difference as reported by Hansson et. al²⁰ with a reduction in expenses of 25-50% in the antibiotic group compared to surgery. Even, studies of patients on ships suffering from acute appendicitis have reported a recovery rate of 84.1% with use of antibiotic only.

Many meta-analysis and Cochrane report^{21,22,23} comparing antibiotics with surgery published in recent years had not found any consensus or unanimous reviews over the conclusive decision of superiority of any of the regimen. Some authors preferred antibiotics due to its safety and over all reduced complication rate while others considered that appendectomy should remain the gold standard treatment.

The American College of Surgeons²⁴ and the World Wide Society of Emergency Surgery²⁵ had considered appendectomy (either open or laparoscopic) as treatment of choice for appendicitis. Regarding antibiotics first strategy they suggested that it can be effective but there is a higher chance of recurrence.²⁶ The World Wide Society of Emergency Surgery²⁵ states that "this conservative approach features high rate of recurrence and is therefore inferior to traditional appendectomy. Non operative antibiotic treatment may be used as an alternative treatment for specific patients for whom surgery is contraindicated". Europeans also have suggested that almost half of the patients treated as antibiotic first strategy will have treatment failures and all of them will suffer from risk of recurrent appendicitis that may ultimately require appendectomy.²⁷

It is recommended that although conservative management by antibiotic remains the favoured

treatment for appendicitis but surgeons should inform the patient about the pros and cons of the antibiotics first strategy as well as the future outcomes or uncertainties.

However still the question of superiority of antibiotics over surgery is highly debated.

By our study, we can infer that conservative antibiotic management approach had many advantages like high success rate, lower recurrence, shorter hospitalization stay and reduced morbidity and mortality, hence should be offered to young patients of acute uncomplicated appendicitis as first treatment choice.

Conclusion

Appendectomy is considered as the gold standard for treating uncomplicated acute appendicitis and is universally considered as a "mile stone" in modern medicine. The comparison of surgery versus antibiotic therapy is still an ongoing debate. The comparison of antibiotic and surgery needs a homogeneous and more objective patients selection and guidelines. Some advantages and disadvantages are inherent in both the groups that cannot be compared.

Nevertheless for a selected subgroup of patients with no risk factors for complicated appendicitis and/or high surgical risk, conservative therapy with antibiotic can be safe and effective. The decision to treat patients of acute uncomplicated appendicitis must be customized individually and then should be followed closely.

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