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Original Research Article

Non-operative treatment of acute appendicitis in selected patients

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ABSTRACT

Background: Surgical approach for acute appendicitis (AA) is a standard live saving treatment method. The purpose of this study was to assess the feasibility, initial safety and success rate of non-operative treatment of AA in selected patients.
Methods: Selected AA patients were enrolled in this prospective study (non-operative treatment). This was based on IV antibiotic therapy and followed up with oral antibiotic. Patients who declined to participate or excluded were managed with appendectomy and considered as controls. The primary goal of the study was to determine the feasibility, initial safety, early and late success rates of non-operative management. Secondary outcomes include hospital length of stay and charge, days of missed works and return to normal activity at home of patients treated non-operatively in comparison to appendectomy group.
Results: In non-operative group (36 patients), 7 patients failed to response and managed by appendectomy with early success rate of 80.5%. Three patients experienced recurrent attacks of AA were managed with appendectomy. Late success rate was 72.2%. In appendectomy group (53 patients) one patient with adenocarcinoma of the colon detected during surgery and in ten patients the appendix was perforated. One patient died due to generalized peritonitis. In non-operative group length of stay and hospital charge were lower but only days to resume home activities and days of missed work were shorter and statistically significant as compared to appendectomy group.
Conclusions: This study confirms the feasibility, safety and optimum success rate of non-operative treatment of early AA in selected patients.

Keywords: Non-operative treatment, Uncomplicated acute appendicitis

INTRODUCTION

Recent advances have permitted surgeons to re-evaluate every step of their traditional surgical practice aiming to treat patients with more conservative methods that established its place in certain conditions such as peptic ulcer diathesis, anal fissure and low-moderate grades of solid intra-abdominal organs injuries.[1,2] Surgical treatment of acute appendicitis (AA) was golden standard since MacBurney's description of this condition. This surgical approach was valid, successful and life saving for more than 125 years. However, this approach has its morbidities such as wound complications, intra-abdominal adhesions resulting in imminent intestinal obstruction and up to 10% of normal appendectomies. On other hand, immunological function of the appendix is well documented as permanent loss of this organ is linked with increased incidence of colon, lymphoid tissue and breast cancers in appendectomized patients.[3,4] Therefore, the logical question rises why we not try to preserve this important organ? Nowadays there is general consensus that AA is of wide spectrum severity. It might be simple catarrhal inflammation form that might respond to conservative non-operative treatment or more aggressive gangrenous form with impending perforation particularly in two extremities of life where surgical treatment should be considered seriously. In modern surgery, there are good reasons to change our routine practice in this specific field.

Therefore, non-operative treatment of uncomplicated AA emerges as a possible alternative management that will provide safe recovery with an intact appendix.[5-11] In this study we evaluated the feasibility, initial safety and success rate of non-operative treatment of uncomplicated AA in selected patients.

METHODS

This prospective study was performed with patients presented to our Department of General Surgery, Faculty of Medicine, Karadeniz Technical University between June 2011 and March 2016 with abdominal pain complain who were diagnosed with AA on the basis of physical examination, laboratory findings, ultrasonography and/or computerized tomography (USG/CT). Patients with uncomplicated AA who met inclusion criteria were offered to enroll in the study (non-operative treatment of appendicitis) and criteria of selecting patients to this option were based on clinical and laboratorial findings such as; early presentation of the patient (<48 hours of abdominal pain), physical findings localized to lower abdomen, mild fever (<38 C), leucocytes <18000 and on USG/CT findings with appendix diameter <1.1 cm, no faecolith and no signs of perforated appendicitis (no phlegmon, abscess or fluid collection).

This non-operative treatment was based on nothing by mouth, intravenous (IV) fluid replacement, IV antibiotic therapy (Cefitriaxone 1000 mg b.i.d and Metronidazole 500 mg t.i.d) for minimum of 24-48 hours and when the oral fluid is tolerated, the patient is discharged with oral antibiotic (Ciprofloxacin 500 mg b.i.d and Metronidazole 500 mg t.i.d) continued for 10 days.

Clinical worsening such as increased pain, tenderness, progressive systemic sign of sepsis, no resolution of fever and continued nausea and vomiting within 24 hours of antibiotics are considered as evidences of failure and surgical option was considered. Patients who declined to participate in non-operative treatment or excluded were managed with standard open appendectomy and considered as controls. Exclusion criteria included symptoms greater than 48 hours, presence or suspicion of abscess on imaging and clinical suspicion of perforated appendicitis, or presence of co-morbidities. Colonoscopic examination was recommended after 3 months of resolution of AA for patients with age >45 responded to non-operative treatment.

The primary goal of the study was to assess the feasibility, initial safety and early success rate of non-operative treatment of AA defined as the percent of patients treated by antibiotic therapy without any surgical intervention. To determine late success rate of this management the patients were followed up at least for one year. Secondary outcomes include hospital length of stay, total hospital charge, days of missed works and return to normal activity at home of patients treated non-operatively in comparison to appendectomy group. Approval for this study was obtained from institutional review board of the Faculty of Medicine, Karadeniz Technical University.

Statistical analysis

Variables were described with means and standard deviations or medians and compared between treatment groups using t-tests or Mann-Whitney U tests. The chi-square test was used for analyzing nominal parameters. P value <0.05 was considered significant. Data were analyzed using SPSS Statistics version 23.

RESULTS

Diagnosis of the AA was based primarily on clinical examination and confirmed radiologically. Abdominal USG examination was performed in 61 out of 89 patients and diagnosis of AA was established in 52 patients (85.2%); in 40 patients with USG alone, in 11 patients combined with CT and in one patient where CT was negative. Abdominal CT examination was required for additional information about appendix in 48 out of 89 patients and diagnosis of AA was confirmed in 45 patients (93.7%); in 27 patients with CT alone, in 11 patients combined with USG and in 7 patients that were negative for AA by USG examination (Table 1). In 2 patients both USG and CT examination were non-diagnostic for AA. In 3 pregnant patients AA was confirmed by USG in 2 patients and with abdominal MR in one patient.

In non-operative group (36 patients) there were 19 males (72.5%) and 17 females (27.5%) patients. The age of the patients ranged from 18 to 73 years with median of 33.06 years. 18-49 years age group accounted for majority of the patients (n = 28.68.6%). The most frequent symptom of the patients was acute abdominal pain (n = 36, 100%) followed by nausea and vomiting (n = 7, 21.5%). The interval between onset of pain and admission ranged from 4 hours to 36 hours with mean of 17.19 hours. Most frequent physical examination finding was right iliac fossa tenderness (n = 36, 100%) followed by muscular rigidity (n = 24, 66.7%) and rebound tenderness (n = 6, 16.7%). Laboratory examination revealed blood leucocyte cells ranged from 2200 µ/L to 18000 µ/L with mean of 11,290 µ/L and C reactive protein (CRP) value which is available in 33 patients ranged from 0.1 to 12 mg/dL with mean of 2.003 mg/dL. On radiological examination the appendix diameter ranged from 6.1 mm to 11 mm with mean of 8.53 mm (Table 1).

29 out of 36 patients with uncomplicated AA were successfully treated with antibiotics alone including two pregnant patients. 7 patients failed to response to this treatment and managed by appendectomy with one postoperative wound infection (Figure 1). Histopathological examination of the appendix revealed AA in all patients and a perforated appendix in one patient (2.77%). Early success rate (30 days) was 80.5% (Table 2). The mean follow-up period was 21.24 months (range 12-62 months). Two out of 29 patients previously treated

successfully with antibiotics alone experienced recurrent symptoms after the initial attack and the duration between the two attacks were 2 and 18 months. These two patients offered same treatment protocol and discharged with good condition with follow up to 35 and 12 months respectively. Another three out of 29 patients previously treated successfully with antibiotics experienced recurrent symptoms after the initial attack and the duration between the two attacks were 3, 4, 7 months with mean of 4.6 months. These 3 patients were managed straight forward with appendectomy by another surgical team unaware of this study and histopathological examination proved AA in two patients while third one was reported as normal appendix.

Table 1: Demographic and clinical characteristics.

	Non-operative treatment n (%)	Appendectomy n (%)	P value
Age (years)	33,06±15.55	33.25±16.93	0.955
Male/female n	19/17*	32/21*	0.037
Duration of pain (h) median	17.19±8.36	23.72±18.91	0.126
Vomiting n (%)	7 (19.4%)	20 (37.7%)	0.108
Leucocyte cells µ/L median	11.290±3658*	15,101±3003*	0.001
USG n (positive %)	20/23 (87%)	32/38 (%85)	1.000
CT scan n (positive %)	21/21 (100%)	24/27 (%89)	0.246
CRP median	2.003±3.16*	5.20±8.71**	0.037
Appendix diameter (mm)	8.53±1.52*	10.53±3.06**	0.002
Perforated n (%) appendicitis	1/36 (2.77%)	10/53 (18.86%)	0.530

(*) signify that the difference between related means were statistically significant.

Table 2: Comparison of primary and secondary outcomes.

	Non-operative treatment n (%)	Appendectomy n (%)	P value
Early success rate (30 days)	29/36 (80.5%)	NA	
Late success rate (one year)	26/36 (72.2%).	NA	
Length of stay in hospital (hours) median	60.81±27.33	69.85±41.33	0.253
Days to resume normal activities median (days)	3.50±1.18*	4,62±1.67**	0.001
Days of missed work median (days)	9.67±3.69*	12.65±5.88**	0.008
Duration of follow- up months, range mean	(12-62) 21.24±25.08 months	NA	
Total hospital charge TL, range, mean	(149-1606) 547.8±350.88	(440-1503) 601.9±265.05	0.41

(*) signify that the difference between related means were statistically significant.

The follow-up data was complete for >12, >18 and >24 months periods for 26, 13 and 7 patients respectively with no recurrence of AA. Late Success rate (one year) was 72,2%. Patient's age, sex, leucocyte 15000-18000 cells µ/L, CRP >5 mg/dL and appendix diameter 8.2-10.1 mm were tested as predictive factors for recurrence or treatment failure on multivariable regression analysis. However number of the patients was too small for this analysis.

In non-operative group; length of stay in hospital was of median 60.81 hours, total hospital charge of mean 547.8 Turkish lire (TL), days to resume normal activities at home of median 3.50 days and days of missed work of median 9.67 days (Table 2). In this group, there were 4 patients aged >45 years and colonoscopic examination was recommended after 3 months of resolution of the AA but no patient accept and attend for this evaluation. In appendectomy group (53 patients) there were 32 males (72.5%) and 21 female patients (27.5%). The age of the patients ranged from 18 to 83 years with median of 33.25 years. 18-29 years age group accounted for majority of the patients (n = 34, 68.6%). The most frequent symptom of the patients was acute abdominal pain (n = 89, 100%) followed by nausea and vomiting (n = 20, 37.7%). The interval between onset of pain and admission ranged from 7 hours to 96 hours with mean of 23.72 hours. The most frequent physical examination finding was right iliac fossa tenderness (n = 53, 100%) followed by muscular rigidity (n = 52, 98.1%) and rebound tenderness (n = 36, 67.9%). Laboratory examination revealed leucocyte cells ranging from 6200 µ/L to 20700 µ/L with mean of 15.101 µ/L and

CRP value which is available in 39 patients ranged from 0.1 to 43 mg/dL with mean of 5.20 mg/dL. On radiological examination, the appendix diameter ranged from 6.1 mm to 20 mm with mean of 10.53 mm. Blood leucocyte, CRP and appendix diameter values in this group were higher and statistically significant as compared to non-operative group (P values = 0.001, 0.037 and 0.002 respectively) (Table 1).

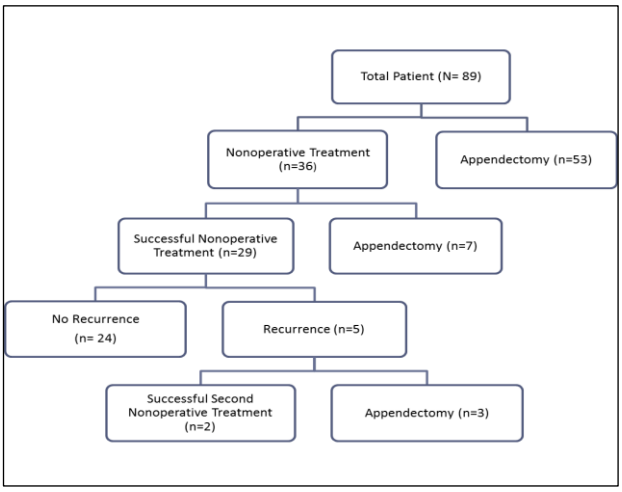

Figure 1: Flow diagram of stratified approach and follow up of patients with uncomplicated acute appendicitis.

In appendectomy group, almost all were managed successfully surgically including one pregnant patient. In one patient aged 65 years presented with AA, a hard mass was detected at the caecum during surgery and right hemicolectomy performed which revealed adenocarcinoma of the colon histopathologically. Two patients developed postoperative wound infection and one patient already diagnosed with brain tumor, while on chemotherapy developed perforated appendicitis and refereed to our surgical unit in late stage with generalized peritonitis sand sepsis. He was on mechanic ventilation postoperatively and died at 5th postoperative day in the ICU. Histopathological examination of the appendix in this group revealed perforated appendix in ten patients (18.86%) and normal appendix in two patients (3.7%).

Incidence of perforated appendicitis in appendectomy group was higher as compared to patients that failed to response to non-operative treatment but the difference between two groups was not significant statistically (P = 0,530). In this group length of stay in hospital was of median 69.85 hours, total hospital charge of mean 601.9 TL, days to resume normal activities at home of median 4.62 days and days of missed work of median 12.65 days. Length of stay in hospital and total hospital charge in appendectomy group were higher but not significant as compared to non-operative group. However, days to resume normal activities at home and days of missed work in appendectomy group were longer and statistically significant as compared to non-operative group (P values = 0.001 and 0.008 respectively) (Table 2).

DISCUSSION

Ongoing advances in surgical science have paved the way to better understanding of pathogenesis of various conditions and availability of modern diagnostic tools enabled physicians not only in the diagnosis but further to select which patient might be best candidate for non-operative or surgical treatments. For instance, in uncomplicated acute diverticulitis, antibiotic treatment is successful in reversing inflammatory process most of the time with intact colon and still we warn the patient with possibility of failure and recurrence of the disease. However, complicated acute diverticulitis with perforation is urgently treated surgically.[12,13] Acute inflammation of the appendix is of a wide spectrum in severity and its outcome varies according to many risk factors such as age, luminal obstruction and immune defense mechanism of the patient. Although appendectomy is curative but carries up to 10% perioperative complications. Various studies have shown that non-operative treatment of uncomplicated cases of AA is a good alternative in management of considerable portion of patients.[5-14]

Additionally, other studies have shown that presence of fecalith and appendix diameter >1.1 cm are main predictive factors that might be associated with higher failure rate of this non-operative treatment.[15,16] Therefore, stratification of the patients with AA based on clinical, laboratory and radiological findings allow for the identification of patients with uncomplicated appendicitis which can be managed by antibiotics alone with higher success rate and lower recurrence rate. In this study criteria of selecting patients to this option were; early presentation of the patient (< 48 hours of abdominal pain), physical findings localized to lower abdomen, mild fever (<38 C), leucocytes <18000, appendix diameter <1.1cm, no faecolith and no signs of perforated appendicitis. Reflection of this selective approach is obvious from the values of blood leucocyte, CRP and appendix diameter which were lower and statistically significant in non-operative group as compared to appendectomy group (P values = 0.001, 0.037 and 0.002 respectively).

There are certain arguments against non-operative treatment of AA. One of these is possibility of the failure of this treatment and recurrence of the disease which is reported as up to 30%.[5,8-10,17,18] In this study 29 out of 36 patients with uncomplicated AA were successfully treated with antibiotics alone. 7 out of 36 (19.5%) patients failed to response to this treatment and managed by uneventful appendectomy with one postoperative wound infection. Histopathological examination of the appendix revealed AA in all patients and a perforated appendix in one patient. Two out of 29 patients previously treated successfully with antibiotics alone experienced recurrent attack of AA after 2 and 18 months. These patients offered same treatment protocol and discharged with good condition with follow

up 35 and 12 months respectively. Another three out of 29 patients previously treated successfully with antibiotics experienced recurrent attacks of AA after 3, 4, 7 months. These patients were managed straight forward with appendectomy by another surgical team not aware of this study. Histopathological examination of the appendix proved AA in two patients while third one was reported as normal appendix. The follow-up data was complete for >12, >18 and >24 months periods for 26, 13 and 7 patients respectively with no recurrence of AA. Present results of early and late success rate with non-operative treatment were 80.5% and 72.2% respectively which are comparable to other studies.[5,8-10,17,18]

Many studies have shown that non-operative treatment of early uncomplicated AA could, if successful, avoid many emergency surgical interventions, help reduce healthcare costs and patients would have quicker recovery, early return to work and resume to normal home activity and have improved quality of life scores.[5,9,18] In this study shorter duration of stay in hospital (60.81 hours) and lower total hospital charge (547.8 TL) of non-operative group were not significant statistically as compared to appendectomy group (69.85 hours and 601,9 TL respectively). However, days to resume normal activities at home (mean 3.50) and days of missed work in non-operative group (mean 9.67) were shorter and significant statistically as compared to appendectomy group (mean 4.62 and 12.65 days, P = 0.001 and 0.008 respectively).

Surgeons and public concern about risk of perforation can be alleviated by studies which shows that this risk is extremely rare event and perforated and non-perforated appendicitis are pathologically distinct entities.[5,19] In non-operative group, 7 out of 36 patients who failed to response to antibiotic treatment and eventually managed by appendectomy, a perforated appendix was reported only in one patient (2.77%) with uneventful postoperative course. However, in appendectomy group, perforated appendix was higher and reported in 10 patients (18.86%). Incidence of perforated appendicitis between two groups was not significant statistically (P = 0.530). This difference might be attributed to selectivity at inclusion of the patients to each group with condensation of more sever attacks of AA in appendectomy group as indicated by values of blood leucocyte, CRP and appendix diameter which were higher and statistically significant as compared to non-operative group (P values = 0.001, 0.037 and 0.002 respectively) or might be due to the fact that perforated and non-perforated appendicitis are really distinct entities as suggested before that require a stratified approach at initial assessment of the patients and different outcome should be anticipated during the clinical course of this disease. The only mortality in appendectomy was a patient with brain tumor on chemotherapy diagnosed with a perforated appendicitis refereed to our surgical unit in late stage with generalized peritonitis and sepsis. Another concern is occult tumors of appendix and colon that may present occasionally as AA. In appendectomy group one patient aged 65 years presented with AA, where a hard mass was detected in the caecum during surgery and right hemicolectomy performed which revealed adenocarcinoma of the colon histopathologically. Therefore, every patient treated non-operatively with age >45 years should be evaluated with clinical and colonoscopic examinations after resolution of the AA. In the present study, there were 4 patients aged >45 years in non-operative group but no patient accepted and attended for this evaluation.

One limitation of this study is the small number of patients which is attributed to being of single personal experience, strict criteria of inclusion of selected patients and current public perception of appendicitis famed with possibility of perforation and its grave historical sequels. Generalization of this non-operative approach might be inappropriate at present time and further studies might be required. Meanwhile, in our opinion the best approach is to be selective and to stratify the patients based on clinical, laboratory and modern radiological facilities taking in to consideration risk factors of each particular patient and health care facilities of each region independently. Well awareness of the patients about this disease, easy access to health care organizations, early presentation of the patients, availability of diagnostic facilities (USG/CT) and treatment with effective antibiotics are encouraging factors for application and high success rate of this conservative non-operative approach for AA especially in developed countries.

CONCLUSION

This study confirms the feasibility, safety and optimum success rate of non-operative treatment of early uncomplicated AA in selected patients with shorter days to resume normal home activities and days of missed work as compared to appendectomy group. Furthermore, it avoids many surgical emergency operations and its sequels. This option can be offered to the patients with AA and warned at same time about possibility of the failure and chance of recurrence at future.

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