

PROBLEM-SOLVING ARTICLE

Non-surgical Management of Acute Nonperforated Appendicitis in Children

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Summary

Acute appendicitis is common condition in the pediatric population. Despite that, there is still actual discussion on most appropriate treatment. In adult population there are evidence that non-surgical treatment in uncomplicated cases is safe and effective, it could avoid unnecessary appendectomies. The experience is very little on pediatric population, but it is known that in certain part of cases conservative management is feasible. Moreover this approach could reduce complication rates associated with surgery.

Key words: Acute appendicitis, non-surgical management, antibacterial therapy

INTRODUCTION

Acute appendicitis (AA) is common condition in the pediatric population and appendectomy is the most common urgent abdominal operation (3;28) Overall risk of AA is 8,7% for boys and 6,7% for girls (3). Since 1889 when *Ch.McBurney* reported his study, early diagnostics and appendectomy was standart treatment (20). Before antibacterial era acute nonperforated appendicitis (NAA) traditionally was treated with urgent early appendectomy because of high risk of diffuse peritonitis and possible lethal outcome. This method significantly reduces mortality, but as any surgical intervention it is related to postoperative complications: dynamic ileus, surgical site infection, intraabdominal abscess and postoperative adhesions may lead to need for repeated operations. (18;31) In last decades, the need for urgent surgical removal of appendix has been challenged, due to developing diagnostic and treatment options. Now more often decision to treat patient without surgical intervention is made. There are reports of high efficiency of non-surgical treatment of AA (12;27). However there are cases when clinical improvement is reached only performing appendectomy. Although there are known several risk factors of non-operative treatment failure, criteria for which group of patients conservative management would be most appropriate is not determined (26;5). There are lack of randomized multicentre trials on pediatric population, therefore algorithms for non-operative treatment of NAA has not been developed yet.

History of non-surgical management

It is thought that non-operative approach to AA treatment have been used much earlier than surgical. In 1910, Smith and Wood Jones described a case of mummy from the Byzantine era where vermiform appendix was found attached to the left pelvic wall suggesting that she had appendiceal rupture with abscess formation. She was cured without no evidence of surgical intervention (6). In 1930 the first treatment algorithm of delayed appendectomy was presented by *Bailey* (8).

First report of successful non-operative management of AA was published in 1945 by *McPherson un Kinmonth* in *British Medical Journal* (23). First larger series was reported by *Coldrey et al.* in 1959. In study 471 patients were included, they all were treated with antibacterial therapy. Only in 48 cases appendectomy was necessary. In 10 cases complications were observed, 9 patients had intraabdominal abscess formation and 1 case lethal outcome (10). In 1977 large study from China was reported, in which 425 patients were included, they all recieved antibacterial treatment in combination with chinese traditional medicine. The recurrence rate 7% was reported in this study (4). In 1990 the study was published where successful broad spectrum antibacterial therapy were used to cure US mariners (2). Also report from Soviet Union of conservative treatment of AA was published (14). In 1995 the first randomized controlled study was published. 40 adult patients divided in two groups were enrolled in this study. Only 5% of cases in group of non-surgical management required appendectomy. Recurrence rate within one year was 37% in this study (11). In 2006 a prospective multicentre randomized controlled trial was reported, comparing antibiotic treatment versus appendectomy (27). The treatment efficiency in non-operative managed patient group was 86% and recurrence rate within 1 year was 14%. The complication rate in surgery group also was 14%. Authors concluded that non-complicated AA can be successfully treated with antibiotic alone and complication risk in surgery group should be compared with risk of recurrence in non-operative group.

Principles of non-surgical management

Algorithms for non-operative treatment of NAA has not been developed yet. Main principles of non-surgical AA management is broad spectrum antibacterial therapy, rehydration and close monitoring of clinical condition in order to avoid complications such as vermiform appendix perforation or peritonitis. The efficiency should be estimated every 4-6 hours. The main indicator of efficiency of therapy is decrease of abdominal pain.

Also dynamics of laboratory tests and radiological findings should be monitored. Appendectomy has been reserved for cases, where non-surgical treatment fails, it should be performed 24 hours after admission.

Perioperative complications after uncomplicated appendectomy occur in 8% to 11% of cases, depending if it laparoscopic or conventional (35). Effective non-surgical AA management decreases the number of performed appendectomies (22). In the certain part of cases patients could avoid possible complication risks of general anesthesia and surgery.

Safety and efficiency

Non-operative management of NAA has become one of the standart treatment options in several European countries and USA (16). Nevertheless some authors considers that non-surgical management is inferior comparing with surgical management. *Vons et al* performed prospective randomised trial comparing patient groups of non-surgigal and surgical management. Authors concluded that higher risk of peritonitis has patient who are treated with antibiotic therapy alone, than in surgical management group, 8% and 2% of patients respectively. Although athors reveald that recurrence rate in non-surgical group is 26% (32). The protocol of this study provided antibacterial therapy with Amoxicillin/Clavulanic acid. However this was study on adult population. There is small evidence of safety using antibacterial therapy alone in treatment of NAA in pediatric population, because of the lack of wide multicentre randomized trials. In 2006 *Abes et al* first reported their retrospective study with small cohort of pediatric patients. Overall 16 patients with abdominal pain less than 24 hours and radiologically confirmed diagnosis of AA were enrolled in conservative treatment group. In 15 cases the non-surgical approach was sucessful (1). A pilot randomized controlled trial comparing antibacterial versus surgical treatment of NAA by *Svensson et al* was reported in 2014. Overall 50 patients with NAA were enrolled in this study, 26 were included in surgery group and 24 in non-surgical group. Meropenem and Metronidazole were prescribed in non-surgical group. Patients in surgery group received preoperative prophylaxis with Metronidazole. In 92% of patients treated conservatively had initial resolution of symptoms. Only 1 patient or 5% of cases had recurrence of AA during 1 year follow-up and appendectomy was performed. Another 6 appendectomies were performed due to recurrent abdominal pain and parental wish (1 case). Authors concluded that non-operative treatment is feasible and safe in case of NAA (30). There are some reports from single centre studies. Study from USA, have been reported, wich purpouse was to determine if uncomplicated AA can be safely and effectively managed with non-surgical treatment. In this study the patients who had right lower quadrant abdominal pain less than 48 hours and typical radiological findings of AA- appendix with thick wall, uncompressible without appendicolith in lumen were selected. Patients were divided in 2 groups 12 patients in each. Ciprofloxacin

and Metronidasole or Ampicillin, Gentamycin and Metronidasole were prescribed during hospital stay. Amoxicillin/Clavulanic acid was prescribed after discharge. In non-surgical group therapy failed in 2 patiens or 16,7% . Reccurent AA during 7 month follow-up had 1 patien or 8,3 % of cases. From these patients there were no evidence of perforation or peritonitis during appendectomy. Authors reveald that 75% of patient were cured without necesstety of surgical intervention (7). Another study by *Minnecci et al* comparing patient groups with non-surgical and surgical aproach showed the non-surgical efficiency in 90% of patients. Inclusion criteria for this study were age 7 to 17 years, abdominal pain less than 48 hours, white blood cell count <18,000 cells/ μ /l, nonruptured acute appendicitis on either ultrasound or CT with an appendiceal diameter <1.1 cm without phlegmon, abscess, or appendicolith. Antibacterial therapy consisted of Piperacillin-Tazobactam or Ciprofloxacin/Metronidazole. There were 30 patients in non-surgical group included and 3 of them antibacterial treatment failed. They all had laparoscopic appendectomy. During surgery there were no evidence of appendix perforation or peritonitis (22). Non-surgical managment seems to be safe and effective in selected cases, also it doesn't increases the risk of perforation and peritonitis (7;22;19). However all these studies enrolled small count of patients, so these data should be confirmed in randomized controlled trials (table1). It should be taken into account that careful follow-up is necessary after non-operative AA treatment. Patients and their parents should be informed of possible recurrence of disease.

Table 1. Studies on pediatric population.

	<i>Abes et al.</i> 2006	<i>Armstrong et al.</i> 2014	<i>Minnecci et al.</i> 2014	<i>Svensson et al.</i> 2014.
Number of patients	16	12	30	24
Type of study	Retro-spective	Retro-spective	Prospective nonrandomized	Prospective Randomized controlled
Duration of symptoms	<24	<48 h	<48 h	-
Length antibacterial therapy	5 days i/v	24 hours i/v 7 days p/o	24 hours i/v 9 days p/o	48 hours i/v 8 days p/o
Follow-up (month)	12	6	12 (planned)	12
Efficiency %	93,7	83,3	90	92
Recurrence %	13,3	8,3	-	5

i/v- intravenously, p/o- orally

Predictive factors for negative outcome

Overall the efficiency of non-surgical management is thought to be 90%, and possibility of recurrent AA is up to 17% in selected cases (29). The fail of non-surgical management can be much higher in unselected patient groups. *Shindoh et al* in 2010 reported his study were 224 patients were included. The non-surgical treatment was not effective in 40,6% of cases. Appendicolith was identified as significant predictive risk factor for treatment failure. In the same time authors reveal that appendicolith doesn't increase morbidity. To predictive negative outcome risk factors also belongs intraluminal fluid collection in vermiform appendix detected in US or CT (19). In the study were 125 patients after successful nonsurgical AA treatment were enrolled during 30 month of follow-up recurrent AA was found in 19% of cases. Authors concluded that statistically significant risk factor is intraluminal fluid detected previously in first episode. Nearly 46% of these patients had recurrent disease, whereas in patients without intraluminal fluid on first episode recurrent disease were detected in 8% of cases. Also this study showed that diameter of appendix >9mm was associated with higher possibility of recurrence. Further research is necessary to determine which group of patients is more likely have recurrent disease.

Diagnostic accuracy

Ultrasonography (US) is the most frequently used radiological diagnostic method for children with acute abdominal pain. It has several benefits, it is available, relatively cheap and with high diagnostic value. Published reports shows very high sensitivity 98,7% and specificity 95,4% (13). Although there are reports which shows much more lower specificity. *Schuh S et al.* reported study with 263 patients included, and only in 68% US examination was accurate. Increased body mass index (BMI) was identified as the most significant factor decreasing value of examination. Another factor which leads to incorrect diagnosis is inaccurately performed examination (33). This shows that value of US examination depends not only on objective, but also on subjective factors and qualification of examination performer.

Second most frequently used radiological examination is computer tomography (CT). *Sodickson AD* in his 18 year retrospective study, including 971 adult patients, concluded that negative appendectomy rate decrease from 23% to 1,7% using preoperative CT scanning (24). The use of CT in pediatrics limits the impact of radiation. Although some authors recommend CT if there is clinically suspicions of AA (34). The CT is radiological examination method with very high sensitivity and specificity, it should be used only in indistinct cases. Magnetic resonance (MRI) has high resolution visualization and it doesn't cause radiation. The reported accuracy levels reach 99-100% (9,17). The use of MRI as routine examination method is limited by reduced availability, relatively long examination time, necessity of sedation for younger children and high costs.

Hospital stay and costs

It is believed that the length of hospital stay (HS) for patients treated non-operatively is shorter. Previous studies on adult patients have shown that non-surgical approach is associated with decreased intensity and duration of abdominal pain (27). *Hansson et al* concluded that non-operatively managed patients have shorter duration of pain after discharge compared with patients managed surgically (15). However in recent reported pilot randomized trial, mentioned above, time to discharge was significantly shorter in surgery group 34,5 hours and 51,5 hours respectively (30). It is explained with the trial protocol, in which parenteral administration of antibiotics was provided for 48 hours. Also other authors found that HS is longer in non-operative treatment group median 38 hours versus median 20 hours in surgical group. In the same time they concluded that patients in non-surgical group faster returned to normal activities and had fewer disability days compared with surgery group (22). *Sakrofas et al* in their review concluded that there is reduced cost and morbidity associated with non-surgical treatment (25). Also there are reports where is no significant cost difference between surgical and non-surgical groups (21). However there are no multivariate cost analysis in pediatric population.

CONCLUSIONS

Non-surgical management of NAA is effective for certain part of patients. Specially for those who have no risk factors of treatment failure. There is no evidence of higher possibility of perforation of appendix and possible risks of peritonitis for patients treated non-surgically. Clinical signs, laboratory and radiological examination findings allow to identify AA with high accuracy. Failure of conservative treatment is not associated with higher morbidity. Due to small number of randomized controlled trials on pediatric population, further studies are needed.

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