Randomized controlled trial of appendicectomy versus antibiotic therapy for acute appendicitis

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In a prospective controlled study the effect of antibiotics as the only treatment in acute appendicitis was evaluated. Of 40 patients admitted with a duration of abdominal pain of less than 72 h, 20 received antibiotics intravenously for 3 days followed by oral treatment for 8 days and 20 considered as controls were randomized to surgery. All patients treated conservatively were discharged within 2 days, except one who required surgery after 12 h because of peritonitis secondary to perforated appendicitis. Seven patients were readmitted within 1 year as a result of recurrent appendicitis and underwent surgery, when appendicitis was confirmed. The diagnostic accuracy within the operated group was 85 per cent. One patient had perforated appendicitis at operation. Antibiotic treatment in patients with acute appendicitis was as effective as surgery. The patients had less pain and required less analgesia, but the recurrence rate was high.

Over 100 years have passed since McBurney\(^1\) reported his study of eight patients with acute appendicitis with special reference to early appendicectomy.

The idea of conservative treatment with antibiotics is not novel and Coldrey\(^2\) in 1959 treated 471 unselected patients conservatively, with low mortality and morbidity rates. His idea was as controversial then as it is today. Of 500 patients with suspected acute appendicitis 425 were treated conservatively, with use of traditional Chinese medicines and antibiotics in some\(^3\). Only seven of 100 patients at follow-up had recurrent appendicitis. In both studies patients were assessed by history and clinical examination, the treatment differed without standardization and there was no consecutive follow-up. A recent study\(^4\) of 695 children has demonstrated that the administration of preoperative antibiotic treatment can be used as a means of delaying appendicectomy, particularly during twilight hours. The incidence of perforation, complications and hospitalization in children operated on within 6 h was the same as that of those undergoing operation between 6 and 18 h after admission\(^4\).

The appendiceal mass can be treated successfully by conservative management\(^5-10\), but some recommend interval appendicectomy\(^3,11\) in case there is a cecal neoplasm or recurrent appendicitis supervenes.

Conservative treatment of acute appendicitis has been described in American submariners\(^11\) (nine patients) and on board Soviet ships at sea (247)\(^12\). There has been no prospective randomized trial.

The present pilot prospective randomized study compared the results of conservative treatment with antibiotics and surgery in patients with acute appendicitis.

**Patients and methods**

**Patients**

The trial was approved by the local ethical committee. Some 45 adults were admitted with a history and clinical signs of acute appendicitis. The time of onset of abdominal pain was ascertained and patients were examined by the same surgeon before inclusion in the study. Five patients did not agree to be randomized and under-
were discharged after 2 days and received oral treatment with ofloxacin (Tarivid; Hoechst) 200 mg twice daily and tinidazole 500 mg twice daily for 8 days.

Surgery

Patients who underwent surgery were treated with antibiotics only in the event of perforation or for 24 h in cases of abdominal spillage. Operated patients were discharged when conditions were satisfactory and they wished to return home. Visual analogue scale scores were registered every 6 h and oral temperature was measured twice daily. All excised appendices were sent for histological examination.

Follow-up

All patients were seen at 6, 10 and 30 days after admission and blood was taken for determination of WBC and CRP levels, pain registered as visual analogue scale scores and oral temperature measured. Abdominal and rectal examinations were carried out on days 6 and 10. Stools were examined for Clostridium difficile toxin at day 30 to exclude pseudomembranous colitis. Ultrasonography was performed on days 10 and 30; results have been presented elsewhere. All conservatively treated patients with suspected recurrent appendicitis underwent surgery.

Methods

Ultrasonography was applied by using the compressive technique described by Puyhaubert. Positive findings for acute appendicitis included a diameter greater than 6 mm and a non-compressible appendix. An invisible appendix was considered as negative.

CRP levels were quantified by a turbidimetric assay on a Paramax instrument (Baxter, Irvine, CA, USA) using antibodies (Dako, Copenhagen, Denmark). The upper limits of the reference intervals used were 9.0 x 10^9/l for WBC and 10 mg/l for CRP.

Pain was registered by patients using a visual analogue scale every 6 h during hospital stay. Pain was also checked daily by the same surgeon (S.E.) with a visual analogue scale score and at follow-up. The score ranged from no pain (0 mm) to unbearable pain (100 mm). Pain was treated with morphine delivered intramuscularly or intravenously during hospitalization, which was noted. Patients wanting analgesia at home were prescribed paracetamol (Alvedon, Astra, Sodertalje, Sweden) and dextropropoxyphene (Doloxene; Lilly, Stockholm, Sweden).

Statistical analysis

Statistical comparisons between groups were made using Student’s t test for uncorrelated means and within groups by use of the pairwise Student’s t test for correlated means. Descriptive statistics and graphical methods were employed to characterize the data. All analyses were carried out using the Statistical Analysis System (SAS Institute, Cary, North Carolina, USA). P < 0.05 was considered significant.

Results

In all patients there was a significant increase in CRP levels from admission to randomization (Fig. 1), and a significant decrease in WBC (Fig. 2).

Conservative treatment

There was a significant decrease in morphine consumption in patients managed with antibiotics (P < 0.001) (Table 1) and significantly less pain was recorded after 12 h conservative treatment (P < 0.001) (Fig. 3). Significantly lower pain scores were also noted by the surgeon (Fig. 4). The WBC declined significantly faster in patients treated with antibiotics (Fig 2) and mean temperature was significantly lower on days 1 and 2 (P < 0.05), with not more than

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Fig. 1 Mean (s.e.m.) concentration of C-reactive protein (CRP) in patients with acute appendicitis treated with antibiotics (■) or surgery (○) during hospitalization and at 30 days of follow-up. *P < 0.001 (admission versus randomization, Student’s t test)

Fig. 2 Mean (s.e.m.) total white blood cell count (WBC) in patients with acute appendicitis treated with antibiotics (■) or surgery (○) during hospitalization and at 30 days of follow-up. *P < 0.001 (admission versus randomization); §P < 0.05, ¶P < 0.01, §§P < 0.001 (surgery versus antibiotics, Student’s t test)

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patients treated with antibiotics before surgery. None of the positive findings (one surgical patient was not analysed). Postoperative infection was noted in the three surgical patients with phlegmonous appendicitis was readmitted on day 6 after appendicectomy because of a wound infection without abscess formation and treated with antibiotics for 4 days (cefotaxime and tinidazole intravenously) (Table 1). No postoperative infection was noted in the three surgical patients treated with antibiotics before surgery. None of the 39 patients having stools checked for C. difficile toxin had positive findings (one surgical patient was not analysed).

0°C difference. The pattern of CRP levels in both groups was the same (Fig. 1).

Surgery

Of patients who underwent surgery 17 had proven appendicitis at histological examination (Table 2). Three patients were treated with antibiotics during or directly after operation.

Follow-up

There was a significant decrease in pain on days 6 and 10 in patients treated with antibiotics \( (P < 0.01) \) (Fig. 4). The WBC also continued to decrease in this group on day 6 (Fig. 2). There were no differences in CRP levels and mean temperature between the two groups at these visits (Table 2). One patient with campylobacter enteritis who underwent surgery returned at day 4 with diarrhoea and was treated with erythromycin for 1 week. One patient with phlegmonous appendicitis was readmitted on day 6 after appendicectomy because of a wound infection without abscess formation and treated with antibiotics for 4 days (cefotaxime and tinidazole intravenously) (Table 1). No postoperative infection was noted in the three surgical patients treated with antibiotics before surgery. None of the 39 patients having stools checked for C. difficile toxin had positive findings (one surgical patient was not analysed).

Seven patients given antibiotic treatment were readmitted with recurrent appendicitis: six had phlegmonous appendicitis and one a perforated appendicitis after 15 h of pain before hospitalization. Surgery occurred after a mean of 7 (range 3–12) months after conservative management. No chronic findings were noted at histopathological examination.

Discussion

High diagnostic accuracy is required in patients with suspected acute appendicitis as negative appendicectomy carries significant morbidity from wound sepsis, intestinal obstruction, pneumonia and infertility from fimbrial damage. There is a greater risk for abdominal adhesions after laparotomy for healthy appendices compared with that for acute appendicitis. The appendix can be a useful conduit for reconstructive surgery (e.g. heipaticoporto-"appendicostomy or ureteroplasty).

Measurement of WBC and CRP levels, and ultrasonography, may help achieve a more accurate diagnosis. The WBC was significantly decreased in both groups between the level found on admission and at randomization as previously reported. During this period the level of CRP significantly increased, emphasizing the importance of repetitive analyses in patients with suspected acute appendicitis.

Clinical follow-up at day 30 after antibiotic treatment is probably sufficient. The present study demonstrates that 10-day antibiotic treatment is sufficient in patients treated conservatively. This is a shorter period than that described by others. Conservative treatment started within 6 h of abdominal pain was not less effective as reported by others.

All patients were followed after conservative treatment until normal findings were found at ultrasonography or surgery, and results, have been reported elsewhere. A mucocoele can be recognized by ultrasonography. Carcinoid, the most common tumour of the appendix, might not have normal findings at ultrasonographic follow-up, as it is a firm solid lesion most often located in the tip of the appendix. The incidence of carcinoid is three to seven per 1000 appendicectomies; the tumour occurs more frequently in women (2–4:1) and is often asymptomatic.

Recurrence in the present study was high (seven patients at 17–2 months) and could increase with time. This value was higher than that reported in earlier studies of patients with appendicitis treated with antibiotics and in those with appendicular absceses, but inclusion criteria were more liberal and follow-up periods short. Recurrence of appendicular abscess after 3 months is rare. Larger studies are needed to establish the superiority of antibiotic treatment over surgery in a larger population.

The study indicates patients’ interest in conservative treatment as 40 of 45 agreed to participate in the study despite being informed about the risk for recurrence.

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