

# Conservative therapy for appendicitis in children

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## Abstract

**Question** A 10-year-old girl who was seen in my office last week with acute-onset abdominal pain and fever was referred to an emergency department, was diagnosed with appendicitis, and was treated conservatively with antibiotics, without surgery. Has the paradigm for treating appendicitis changed, and which is the preferred treatment of appendicitis in children: antibiotics or appendectomy?

**Answer** For more than 100 years, surgical management was the principal treatment of acute appendicitis. Potential adverse events associated with appendectomy include bleeding, surgical site infection, and ileus, as well as stress for children and their parents. The option of treating appendicitis with antibiotics has been known for decades, which has led to consideration of antibiotics alone as a therapeutic alternative to surgery for uncomplicated appendicitis. While there is a reasonable body of evidence in support of this practice in adults, the accumulation of evidence of the safety and effectiveness of non-operative management in children is ongoing. Large studies are still needed, and those are being conducted at this time, with results expected in the next few years.

## Traitement conservateur de l'appendicite chez l'enfant

### Résumé

**Question** Une fillette de 10 ans s'est présentée à ma clinique la semaine dernière en raison de l'apparition soudaine de douleurs abdominales et de fièvre. Elle a été référée à l'urgence, où on a diagnostiqué une appendicite et on l'a traitée de manière conservatrice en lui prescrivant des antibiotiques plutôt qu'une opération. Le paradigme du traitement de l'appendicite a-t-il changé et quelle est la prise en charge appropriée de l'appendicite chez les enfants: des antibiotiques ou l'appendicectomie?

**Réponse** Pendant plus de 100 ans, la prise en charge chirurgicale était le principal traitement de l'appendicite aiguë. Au nombre des événements indésirables potentiels associés à l'appendicectomie figurent une hémorragie, une infection au site chirurgical et un iléus, sans compter le stress chez l'enfant et les parents. L'option de traiter l'appendicite avec des antibiotiques est connue depuis des décennies, ce qui a fait en sorte qu'on a envisagé les antibiotiques seuls comme option de rechange thérapeutique à l'intervention chirurgicale pour les cas d'appendicite sans complication. Il existe un ensemble raisonnable de données probantes à l'appui de cette pratique chez les adultes. L'accumulation de données sur la sécurité et l'efficacité de la prise en charge non chirurgicale chez l'enfant se poursuit. D'autres vastes études sont encore nécessaires, qui sont actuellement en cours, et l'on s'attend à en connaître les résultats au cours des prochaines années.

**A**cute appendicitis is the most common surgical emergency in children,<sup>1</sup> with a lifetime risk of 8.6% and 6.7% among male and female populations, respectively. Appendicitis occurs throughout childhood and adulthood; however, the incidence is highest among those between the ages of 10 and 19.<sup>2</sup> While the exact pathogenesis of acute appendicitis is still unclear, several theories relate to mucosal inflammation, lymphoid hyperplasia, or the presence of a fecalith. The latter causes luminal obstruction, distention, and inflammation of the appendix wall, resulting in suppurative transmural inflammation, ischemia, infarction, and perforation of the appendix.<sup>3</sup>

Symptoms often include fever, colicky periumbilical pain, migration of pain to the right iliac region, and anorexia and nausea and vomiting. However, diagnosing appendicitis in preschool children might be difficult

owing to atypical presentation and limited communication skills. Among 120 children from the US (mean age 3.6 years), almost all those younger than 1 year of age had perforated appendicitis at diagnosis, which was primarily attributable to delays in diagnosis.<sup>4</sup> It has been estimated that 7.7% of patients develop appendiceal perforation within 24 hours of the onset of symptoms.<sup>5</sup>

The Pediatric Appendicitis Score (PAS) has been validated in a Canadian centre for the diagnosis of appendicitis.<sup>6</sup> In a systematic review and meta-analysis including 21 studies with 8605 patients aged 21 and younger, presenting to an emergency department (ED) with complaints of undifferentiated abdominal pain or suspected acute appendicitis, cough or hop pain (positive likelihood ratio of 7.6, 95% CI 5.9 to 9.8) and a PAS of 9 or greater (positive likelihood ratio of 5.3, 95% CI

3.34 to 8.3) increased the probability of acute appendicitis in patients with undifferentiated abdominal pain.<sup>7</sup>

It has been more than 130 years since Fitz wrote *Perforating Inflammation of the Vermiform Appendix*,<sup>8</sup> in which he reported the treatment of acute appendicitis as appendectomy. It is a safe, effective, and time-proven operation that has been further refined with the advancement of laparoscopic techniques. Despite improvements in surgical and perioperative care, the risks of general anesthesia and surgery, and the potential for postoperative complications<sup>9</sup> represent a sufficient level of stress and uncertainty for some patients and families<sup>10</sup> to justify the search for an effective alternative to surgery for a child with uncomplicated appendicitis.

### Non-operative therapy

The surgical dogma dictating emergent appendectomy has seen a paradigm shift to a non-operative approach.<sup>11</sup> In a meta-analysis of randomized controlled trials including 5 studies and 1430 adult patients with uncomplicated acute appendicitis, the success rate of antibiotic treatment during the initial hospitalization was 84%. Readmission for recurrent appendicitis requiring treatment occurred in another 21% of patients during the subsequent year of follow-up. Overall, treatment with antibiotics was associated with a 39% risk reduction in complications compared with those undergoing appendectomy.<sup>11</sup>

Similar observations have been emerging in children.<sup>10,12,13</sup> In 1956, Coldrey reported successful conservative treatment, with a combination of ampicillin with sulbactam until abdominal pain resolved, and among 137 patients 1 died.<sup>14</sup> In 2007, Abeş and colleagues performed an observational study in which 16 of 136 children aged 5 to 13 were selected for non-operative treatment, and successful resolution of abdominal tenderness was reported in 15 of them (93.7%).<sup>13</sup>

In a randomized controlled trial from Sweden, aiming to evaluate the feasibility and safety of non-operative treatment of acute nonperforated appendicitis with antibiotics,<sup>15</sup> 50 children (mean age was 11.2 years) were assigned to have surgery with 1 dose of preoperative antibiotic prophylaxis (metronidazole) or intravenous antibiotics (meropenem and metronidazole) for at least 48 hours. While the study was underpowered to detect differences between groups, the findings showed that most (92%) patients treated with antibiotics achieved initial resolution of symptoms, and only 1 patient (5%) had recurrence of histologically proven acute appendicitis during the 1-year follow-up.

Recently, 3 systematic reviews and meta-analyses<sup>16-18</sup> provided further evidence for the use of conservative treatment of children with appendicitis. A report from Switzerland<sup>18</sup> with 3 prospective cohort studies, 1 retrospective cohort study, and 1 randomized study included 442 patients (189 received conservative treatment and 253 underwent surgical intervention) and defined

efficacy of appendectomy as the absence of postoperative complications, including readmission. Non-operative treatment was considered successful if no serious posttherapeutic complications developed, including the absence of the following: failure of antibiotic treatment or recurrence of appendicitis requiring appendectomy, or development of serious posttherapeutic, postoperative complication including readmission. Conservative therapy was associated with reduced efficacy (relative risk [RR] of 0.77, 95% CI 0.71 to 0.84;  $P < .001$ ), increased readmission rate (RR=6.98, 95% CI 2.07 to 23.6;  $P < .001$ ), and a comparable rate of complications (RR=1.07, 95% CI 0.26 to 4.46). In Kessler and colleagues' analysis, 7 children had complications (3 of 189 who received conservative treatment vs 4 of 253 who underwent appendectomy). Even after excluding appendicitis with fecalith, evidence of lower treatment efficacy (RR=0.8, 95% CI 0.73 to 0.88;  $P < .001$ ) and a higher readmission rate (RR=6.3, 95% CI 1.44 to 27.5;  $P < .05$ ) remained. Based on limited efficacy of conservative treatment and the higher readmission rate, the authors suggested appendectomy as the treatment of choice for the management of uncomplicated appendicitis in children.<sup>18</sup>

In another systematic meta-analysis<sup>16</sup> with 10 studies, conservative management was unsuccessful as initial treatment in 17 of 413 children (it was successful in 97% of children [95% CI 96% to 99%]) and resulted in appendectomy. Children treated with appendectomy had a shorter initial length of stay in the hospital compared with children with conservative management (mean difference 0.5 days; 95% CI 0.2 to 0.8). There were no serious adverse events related to conservative management. After 8-week to 4-year follow-up, conservative management remained effective in 82% of children (95% CI 77% to 87%). Conservative management as a first-line therapy was safe, but follow-up was relatively short and methodology included mostly retrospective cohort designs with only 1 randomized controlled study.<sup>15</sup>

Similarly, Hung and colleagues reported in their meta-analysis<sup>17</sup> 5 studies with 442 children for whom non-operative treatment had a lower treatment efficacy (RR=0.77, 95% CI 0.71 to 0.84;  $P < .001$ ) and increased readmission rate (RR=6.98, 95% CI 2.07 to 23.6;  $P < .001$ ) over 1 to 4 years of follow-up.<sup>17</sup>

### Conclusion

Non-operative treatment provides parents and children with an additional option of therapy for uncomplicated appendicitis. However, current findings suggest lower efficacy, prolonged length of hospital stay, and increased readmission rates compared with surgical appendectomy. Prospective research is needed in order to definitively determine the safety and efficacy of antibiotics alone, as an alternative to appendectomy. Three such studies are ongoing: the APPY study<sup>19</sup> (a multicentre, randomized controlled trial comparing non-operative

treatment [antibiotics] with surgery [appendectomy] in children aged 5 to 16), the CONTRACT (CONservative TRreatment of Appendicitis in Children) study<sup>20</sup> (a randomized controlled trial of children aged 4 to 15), and APRES<sup>21</sup> (a prospective randomized controlled noninferiority study to evaluate the effectiveness and safety of non-operative management for appendicitis in children aged 5 to 15 with acute uncomplicated appendicitis), which will include qualitative components. These studies are conducted with a multicentre, randomized methodology comparing conservative treatment to appendectomy for acute uncomplicated appendicitis in children. These prospective trials will hopefully provide families with the data they need to make a choice on how to treat their children with appendicitis. For some, avoidance of anesthesia, surgery, and potential complications will be important factors, while for others, a definitive, durable treatment will be more important. 🌿

#### Competing interests

None declared

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