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REVIEW

Optimal Antibiotic Selection for the Treatment of Pouchitis After Ileal Pouch-Anal Anastomosis

Sérgio Bronze[1,2], Maia Kayal[3]

[1]Gastroenterology and Hepatology Department, Unidade Local de Saúde de Santa Maria, Lisbon, Portugal; [2]Faculdade de Medicina de Lisboa, Universidade de Lisboa, Lisboa, Portugal; [3]Division of Gastroenterology, Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, NY, USA

Correspondence: Maia Kayal, Icahn School of Medicine at Mount Sinai, One L. Gustave Place Box 1069, New York, NY, 10029, USA, Email maia.kayal@mountsinai.org

Background: Pouchitis is the most common complication following ileal pouch–anal anastomosis for ulcerative colitis. Antibiotics remain the cornerstone of therapy for acute and chronic antibiotic dependent pouchitis, though evidence guiding their optimal use is limited.

Material and Methods: A comprehensive literature search of PubMed, MEDLINE, Embase, and Google Scholar was conducted from database inception through October 2025 to identify studies evaluating antibiotic therapy for acute pouchitis. Eligible studies included randomized controlled trials, cohort studies, and observational series reporting clinical, endoscopic, or histologic outcomes. Data were extracted from 10 studies on study design, antibiotic regimen, efficacy, safety, and recurrence.

Results: Data on the optimal selection of antibiotics for pouchitis is limited. Ciprofloxacin and metronidazole are the most extensively studied and commonly prescribed antibiotics. In a randomized clinical trial, ciprofloxacin demonstrated superior efficacy and tolerability compared with metronidazole. Rifaximin and vancomycin show potential benefit in selected cases.

Conclusion: Antibiotic therapy provides rapid and effective symptom control in most patients with acute pouchitis. Ciprofloxacin should be considered first-line, with metronidazole or combination therapy reserved for non-responders.

Keywords: acute pouchitis, antibiotics, ulcerative colitis, ciprofloxacin, metronidazole

Introduction

Despite significant advances in medical therapy, approximately 10–15% of patients with ulcerative colitis (UC) ultimately require surgical intervention. Restorative proctocolectomy (RPC) with ileal pouch–anal anastomosis (IPAA) remains the gold-standard surgical procedure for these patients, as it preserves gastrointestinal continuity and avoids the need for a permanent stoma.[1] Pouchitis is the most common and extensively studied complication following IPAA, affecting up to 55% of patients within the first two years after surgery.[2,3] The incidence of pouchitis has increased over recent decades, rising from 40% in 1996–2000 to 55% in 2015–2018, with substantial consequences for patient quality of life and healthcare resource utilization.[4]

Pouchitis is broadly categorized into intermittent, chronic antibiotic-dependent, or chronic antibiotic-refractory. Intermittent pouchitis is characterized by infrequent, self-limiting episodes of increased stool frequency, urgency, abdominal cramping, and loose bowel movements that resolve spontaneously or with short courses of antibiotics, with long symptom-free intervals in between.[5] Chronic antibiotic-dependent pouchitis is characterized by recurrent symptoms that respond to antibiotic therapy but relapse shortly after discontinuation, often requiring repeated or continuous antibiotic use to maintain remission.[5] In contrast, chronic antibiotic-refractory pouchitis is characterized by persistent or relapsing symptoms that fail to respond adequately to standard antibiotic regimens, frequently necessitating escalation to advanced therapies such as biologics or small molecules.[5]

The development of pouchitis is multifactorial, arising from the complex interplay between host, microbial, and surgical factors. Anatomical changes following pouch construction promote fecal stasis, bacterial overgrowth, and

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dysbiosis, and lead to disruptions in innate and adaptive immune responses. Additional contributors include ischemia, tissue hypoxia, mesenteric tension, and oxidative stress, all of which may impair mucosal integrity and healing.[6] These factors collectively create a pro-inflammatory environment that predisposes to pouchitis.

Antibiotic therapy is the mainstay of treatment for acute and chronic antibiotic dependent pouchitis. This study aims to review and clarify the optimal antibiotic management strategies for acute and chronic antibiotic dependent pouchitis.

Materials and Methods

Search Strategy

A comprehensive literature search was performed to identify studies assessing the use of antibiotics for treating acute pouchitis. The electronic databases PubMed, MEDLINE, Embase, and Google Scholar were searched from their starting points through October 2025. The search combined Medical Subject Headings (MeSH) and free-text terms related to pouchitis and antibiotic treatment, including "pouchitis", "ileal pouch", "antibiotic", "ciprofloxacin", "metronidazole", "rifaximin", "vancomycin", "tinidazole", "amoxicillin", and "antimicrobial therapy". Boolean operators ("AND", "OR") were used to refine the results. Reference lists from relevant articles and reviews were also manually screened to find additional studies.

Eligibility Criteria

Studies were eligible for inclusion if they evaluated antibiotic therapy for acute pouchitis, defined as symptom onset within four weeks following IPAA or recurrent self-limiting episodes responsive to short antibiotic courses. Only original research articles published in English were included, encompassing randomized controlled trials, cohort studies, and observational series that reported clinical, endoscopic, or histologic outcomes. Studies focusing exclusively on chronic antibiotic refractory pouchitis, Crohn's-like disease of the pouch, cuffitis, or prophylactic strategies unrelated to acute episodes were excluded, unless they provided data relevant to acute management. Case reports, conference abstracts without available full texts, and non-English publications were also excluded.

Study Selection and Data Extraction

Two reviewers independently screened titles and abstracts for eligibility, followed by full-text review. Discrepancies were resolved by consensus. Extracted data included study design, sample size, diagnostic criteria (including Pouchitis Disease Activity Index [PDAI] where available), antibiotic regimen (agent, dose, duration), comparator group (if applicable), clinical and endoscopic outcomes, and adverse events. Where available, effect measures such as remission rates, mean change in PDAI, and recurrence rates were recorded. Observational data were summarized descriptively to complement findings from randomized controlled trials.

Data Synthesis

Given the heterogeneity of study designs, antibiotic regimens, and outcome definitions, a qualitative (narrative) synthesis was undertaken. Results were grouped by antibiotic agent (ciprofloxacin, metronidazole, combination regimens, rifaximin, vancomycin, and tinidazole) and analyzed for efficacy, safety, and comparative effectiveness.

Results

Antibiotics remain the cornerstone of therapy for acute pouchitis, with most patients experiencing infrequent, self-limiting episodes that respond promptly to short courses of treatment.[7] Evidence supporting antibiotic therapy is largely derived from small, randomized trials and observational studies, with much of current practice based on clinical experience rather than large comparative studies.

Ciprofloxacin and Metronidazole

Ciprofloxacin and metronidazole are the most widely used and well-studied antibiotics for both acute pouchitis - ciprofloxacin at a dose of 500 mg twice daily and metronidazole at a dose of 500 mg three times daily for 2 weeks.

There is limited comparative data, however ciprofloxacin is generally preferred due to its superior efficacy and tolerability.

Acute Pouchitis

An early prospective study by Hurst et al demonstrated that acute pouchitis treated with a one week course of metronidazole, resulted in complete symptom resolution in 79% of patients. Those who did not respond sufficiently or could not tolerate metronidazole due to side effects were switched to ciprofloxacin, leading to full remission in most of these cases and an overall response rate of 94%. These early results established short-course antibiotic therapy—especially with metronidazole or ciprofloxacin—as the standard initial treatment for acute pouchitis.[8]

A subsequent randomized clinical trial compared the efficacy and tolerability of ciprofloxacin and metronidazole for the treatment of acute pouchitis. Sixteen adults with a Pouchitis Disease Activity Index (PDAI) score ≥7 and symptom duration ≤4 weeks were randomized to receive ciprofloxacin 1000 mg/day (n=7) or metronidazole 20 mg/kg/day (n=9) for 2 weeks. Clinical, endoscopic, and histologic assessments were performed before and after treatment, with remission defined as a posttreatment PDAI score <7. Both antibiotics significantly reduced disease activity; however, ciprofloxacin demonstrated greater efficacy across all outcome measures: mean reductions in total PDAI (6.9 vs 3.8; P=0.002), symptom (2.4 vs 1.3; P=0.03), and endoscopic subscores (3.6 vs 1.9; P=0.03) favored ciprofloxacin. Complete remission was achieved in all ciprofloxacin-treated patients compared with 67% in the metronidazole group. Adverse effects occurred exclusively with metronidazole, including nausea, dysgeusia, and transient neuropathy. These findings suggested that ciprofloxacin is both more effective and better tolerated than metronidazole.[9]

A recent large real-world cohort using the TriNetX global database compared ciprofloxacin monotherapy, metronidazole monotherapy, and combination therapy (ciprofloxacin + metronidazole) for initial pouchitis episodes after IPAA. The main outcomes were failure of the initial antibiotic therapy and the development of recurrent pouchitis within 12 months of the first episode. One-to-one propensity score matching was used to control for potential confounders, including age, sex, race, primary sclerosing cholangitis, nicotine dependence, obesity, and previous exposure to tumor necrosis factor inhibitors. Among 271 patients (mean age at IPAA 35.8 years; 57% male), 70% experienced recurrence within 12 months. After propensity score matching, there were no significant differences in rates of early relapse, nonresponse, or recurrence between treatment groups. The adjusted odds ratio for early relapse or nonresponse with ciprofloxacin versus metronidazole monotherapy was 0.56 (95% CI, 0.23–1.34), and 0.86 (95% CI, 0.40–1.84) for recurrent pouchitis. Combination therapy did not demonstrate superior outcomes compared with either monotherapy. These data indicate similar real-world effectiveness among these antibiotic strategies.[10]

A randomized, double-blind, controlled trial by Sambuelli et al evaluated the efficacy and tolerability of budesonide enemas compared with oral metronidazole in the treatment of active pouchitis. Twenty-six patients with a PDAI ≥ 7 and no recent treatment were randomized to receive budesonide enemas (2 mg/100 mL nightly) plus placebo tablets or metronidazole (500 mg twice daily) plus placebo enemas for six weeks. Both treatments significantly improved disease activity by week 1 ($P < 0.01$), stabilizing by week 4. In the intention-to-treat analysis, clinical improvement (≥3-point PDAI reduction) occurred in 58% of the budesonide group and 50% of the metronidazole group (odds ratio 1.4; 95% CI, 0.2–8.9). Both regimens significantly reduced total, clinical, and endoscopic PDAI scores, with no histologic change. Efficacy was comparable, but budesonide showed better tolerability, with adverse events in 25% of patients versus 57% in the metronidazole group. The most frequent metronidazole-related side effects were anorexia, nausea, headache, and metallic taste, leading to discontinuation in several cases. No serious adverse events occurred. Overall, budesonide enemas provided similar efficacy with fewer side effects, representing a reasonable alternative for patients intolerant to antibiotic therapy.[11]

Chronic Pouchitis

A double-blind, placebo-controlled crossover study evaluated metronidazole in patients with chronic, unremitting pouchitis. Thirteen patients presented with active disease, defined by more than six bowel movements per 24 hours or persistently bloody stools accompanied by endoscopic and histological signs of mucosal inflammation, were enrolled. Each patient received metronidazole 400 mg three times daily and a placebo for seven days each, in random order,

separated by a washout period. Metronidazole significantly reduced stool frequency compared with placebo (median change −3 vs +1 bowel movements per 24 h; P<0.05), though no significant improvements were observed in endoscopic or histologic inflammation, serum C-reactive protein, or overall symptom scores.[12]

A prospective study also evaluated the efficacy of combination therapy with metronidazole and ciprofloxacin in patients with refractory or recurrent pouchitis. Eligible patients had experienced pouchitis at least twice in the preceding year or required continuous antibiotic treatment, with a baseline PDAI score of ≥7. Participants received metronidazole (400–500 mg twice daily) and ciprofloxacin (500 mg twice daily) for 28 days. Clinical, endoscopic, and histological outcomes were assessed before and after treatment using the PDAI, and remission was defined as a clinical score ≤2, an endoscopic score ≤1, and a total score ≤4. Quality of life was evaluated using the Inflammatory Bowel Disease Questionnaire (IBDQ). Among 44 participants (median age 37.5 years), 82% achieved remission. Median PDAI scores decreased from 12 (8–17) to 3 (1–10; P < 0.0001), and median IBDQ scores improved from 96.5 to 175 (P < 0.0001). No serious adverse events occurred. These results suggest that a four-week dual regimen is highly effective and well-tolerated for recurrent or refractory pouchitis.[13]

Vancomycin

Vancomycin has been studied primarily in chronic pouchitis rather than acute pouchitis. A retrospective cohort study from the University of North Carolina evaluated oral vancomycin (125 mg twice daily) in 41 patients with chronic pouchitis, including chronic antibiotic-dependent or -refractory pouchitis and Crohn's-like disease of the pouch. Over half demonstrated an initial and sustained clinical response at four weeks, with sustained benefit at three and six months. Response rates did not differ by pouchitis subtype or by the presence of primary sclerosing cholangitis. Endoscopic PDAI subscores did not significantly differ between responders and nonresponders. These findings suggest vancomycin may provide a durable option for refractory chronic pouch disorders, particularly in patients unresponsive to standard antibiotics.[14]

Rifaximin

A randomized, placebo-controlled pilot study assessed rifaximin (400 mg three times daily for four weeks) in 18 patients with acute pouchitis (PDAI ≥ 7). Clinical remission (PDAI < 7 and ≥ 3-point reduction) occurred in 2/8 (25%) rifaximin-treated vs 0/9 (0%) placebo patients, a nonsignificant difference due to small sample size. Rifaximin was well tolerated, with no reported safety concerns.[15]

An open-label study evaluated the efficacy and tolerability of rifaximin as maintenance therapy in patients with chronic antibiotic-dependent pouchitis. Patients first underwent a two-week course of various antibiotics to induce remission and subsequently initiated rifaximin maintenance therapy at doses ranging from 200 mg to 1800 mg daily, continued for up to 24 months. The primary endpoint was maintenance of remission at three months. Of the 51 patients enrolled, 33 (65%) maintained remission at three months, meeting the primary endpoint. Among these, 26 (79%) sustained remission for six months, 19 (58%) for 12 months, and two (6%) for 24 months. Only one transient rash occurred.[16]

Conclusion

The management of acute pouchitis continues to rely primarily on antibiotic therapy, with ciprofloxacin (500 mg twice daily) and metronidazole (500 mg three times daily) remaining the cornerstone agents. Among available options, ciprofloxacin demonstrates superior efficacy, endoscopic response, and tolerability, while metronidazole remains a reasonable alternative, particularly for patients that are intolerant to fluoroquinolones. Despite widespread use, the evidence base guiding antibiotic selection and treatment duration is limited, largely derived from small, randomized trials and observational studies. When selecting antibiotic therapy, factors such as prior antibiotic exposure, pregnancy or lactation status, comorbidities, allergies, and tolerance should guide decision-making. A proposed treatment algorithm is provided in Figure 1. While short antibiotic courses are generally safe, prolonged or recurrent use carries risks including dysbiosis, *C. difficile* infection, and the emergence of quinolone-resistant *Escherichia coli* strains.[17,18]

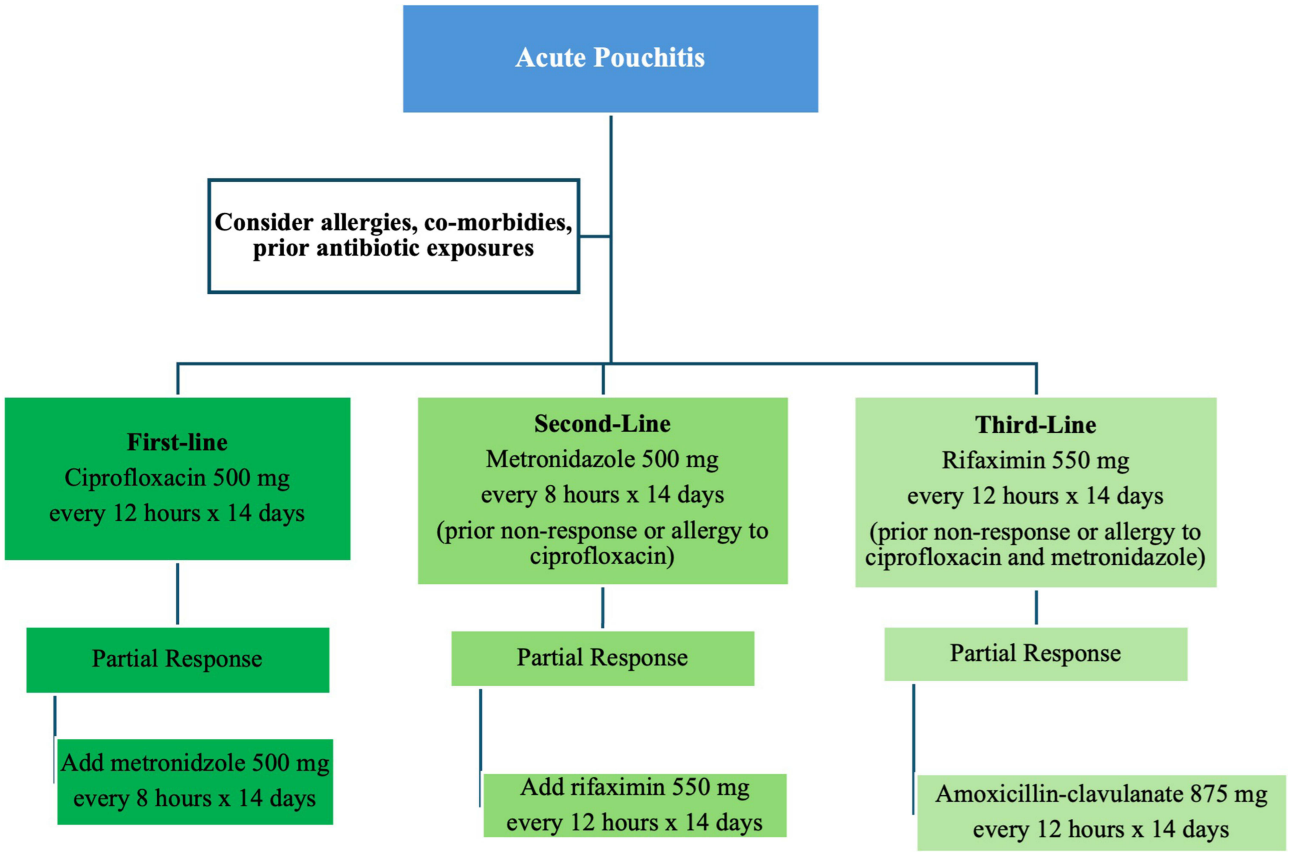

Figure 1 Proposed Treatment Algorithm for Pouchitis.

As recurrent and chronic forms of pouchitis emerge as therapeutic challenges, optimizing the initial antibiotic approach is critical to long-term pouch preservation. Future research should aim to establish standardized treatment algorithms through high-quality comparative studies and integrate microbial and immunologic profiling to guide precision-based therapy. Until such data are available, short-course ciprofloxacin or metronidazole remains the evidence-supported standard for acute pouchitis, representing the most effective and practical approach within current clinical practice.

Data Sharing Statement

Data sharing is not applicable to this article as no data were created or analyzed in this study.

Author Contributions

SB; Conceptualization, Methodology, Writing- original draft. MK; Conceptualization, Methodology, Writing – review & editing.

All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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