Local application of fidaxomicin in a patient with subtotal colectomy following recurring *Clostridium difficile* infection

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Introduction: *Clostridium difficile* is the leading cause of antibiotic-associated diarrhoea and is a major burden to healthcare services worldwide. Fidaxomicin is a first-in-class macrocyclic antibiotic that was approved for the treatment of *C. difficile* infection (CDI) in 2011, demonstrating a narrow spectrum of activity and comparable efficacy to vancomycin in clinical trials.

Case presentation: We present the case of a patient with recurrent CDI who was non-responsive to standard treatment with metronidazole and vancomycin. The patient subsequently developed toxic megacolon, which had to be treated surgically by subtotal colectomy. Fidaxomicin at 200 mg twice daily was delivered in small-volume enemas directly to the oral part of the sigmoid colon to preserve the remaining rectosigmoid colon and improve the chances of restoring gastrointestinal tract continuity. After 11 days of local fidaxomicin therapy, diagnostic tests revealed that the patient was *C. difficile* negative and no recurrence of CDI was observed. Restoration of the gastrointestinal tract was successfully completed 5 months after hospital discharge.

Conclusion: This report describes a novel concept of local fidaxomicin delivery to the rectosigmoid colon, with an improved clinical outcome compared with metronidazole and vancomycin treatment. The study suggests that topical application of fidaxomicin may be beneficial in some CDI patients following surgical treatment for toxic megacolon.

Keywords: *Clostridium difficile*; colectomy; fidaxomicin; rectosigmoid colon; recurring.
C. difficile
Colonoscopy performed up to hepatic flexure showing toxic megacolon at day 29 post-admission (a), continuous circular pseudomembranous colitis at day 33 post-admission (b) and revitalized mucosa of the rectosigmoid colon without any signs of inflammation following local fidaxomicin application at day 50 post-admission (c).
directly to the oral part of the sigmoid colon. The enema composition was prepared by dilution of a fidaxomicin 200 mg tablet in 100 ml normal saline and was applied via infusion set for 30 min for each dose. At this time, metronidazole, fluconazole and vancomycin (local sigmoid colon dose) were discontinued. On day 45, vancomycin via the nasogastric tube was discontinued. On day 50, a third-look colonoscopy was carried out, which demonstrated revitalized mucosa of the rectosigmoid colon without any signs of inflammation (Fig. 1c). Diagnostic tests were negative for C. difficile GDH and toxin; therefore, fidaxomicin was discontinued. On day 52, the patient was discharged from the ICU and on day 65 the patient was discharged home. A control colonoscopy was performed in an outpatient setting and showed the mucosa without any inflammation; restoration of the gastrointestinal tract was successfully completed 5 months after hospital discharge.

Discussion

In this case, locally applied fidaxomicin was used successfully to treat a 74-year-old patient with recurrent CDI and subtotal colectomy following a total knee replacement. Initially, CDI was adequately treated with a combination of metronidazole and vancomycin for 15 days. However, 11 days after discontinuation of antibiotics, CDI recurrence was noted and a colonoscopy indicated toxic megacolon that required subtotal colectomy. After 11 days of local fidaxomicin therapy, the patient was C. difficile negative and there was no recurrence of CDI. A recent systematic review concluded that total colectomy with end ileostomy (subtotal or total colectomy without primary anastomosis) is the preferred surgical procedure in patients with severe CDI (Bhangu et al., 2012). Clinical cure of the rectosigmoid stump is essential for facilitating gastrointestinal tract restoration post-colectomy. This study describes a new concept of local fidaxomicin delivery to the rectosigmoid colon, with an improved clinical outcome compared with combined metronidazole and vancomycin treatment. The study indicates that topical application of fidaxomicin may be beneficial in some CDI patients following surgical treatment for toxic megacolon. Furthermore, because the rectosigmoid stump is safely accessible through colonoscopy, the progress of treatment can easily be monitored.

However, fidaxomicin is not currently licensed for topical administration. Therefore, further studies are necessary to demonstrate the efficacy and safety of this method of administration.

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References


