

Hydroxychloroquine (Plaquenil®) for recurrence prevention of Crohn's disease after curative surgery.

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Crohn's disease (CD) is a chronic inflammatory bowel disease characterized by frequent relapses. Surgical resection of the diseased intestine is followed by a high rate of clinical relapse reaching as much as 50 % over a 10-year period. Moreover, typical endoscopic recurrent lesions have been described in 70 to 80 % of the patients within 3 months after curative ileocolic resection (1). In most cases these lesions are localized to the neoterminal ileum and to the anastomosis. The severity of these early endoscopic findings is often correlated with later clinical relapse and the development of serious complications requiring surgical therapy. Effective prevention of recurrences could therefore strongly influence the long-term outcome of surgery in CD. Two drugs have recently been tested in the prevention of these early endoscopic lesions. Mesalazine was not more efficient than placebo in a recent French study (2), although metronidazole did not modify the frequency of recurrence but was associated with less severe lesions (3).

The pathophysiology of these recurrences is poorly known, but they could be associated with abnormal immune regulation mechanisms in the mucosa and particularly with abnormalities of antigen presentation. Interestingly, hydroxychloroquine has potent immunosuppressive effects partly mediated through the inhibition of antigen processing by the antigen-presenting cells. Preliminary studies have demonstrated beneficial effects of hydroxychloroquine in active CD (4).

On these basis, we tested the prophylactic efficacy of a 3-month treatment with hydroxychloroquine (400 mg/day po) in 4 patients with ileocolic resection for active CD. Three months after the beginning of hydroxychloroquine treatment, a clinical and endoscopic staging was carried out. The lesions were scored according to Rutgeerts et al. (1).

Three out of 4 patients were asymptomatic at 3 months. One of these patients presented without any endoscopic lesion, while severe diffuse aphthoid ileitis with inflamed mucosa (grade i3) was demonstrated in the other ones.

The 4th patient experienced a severe symptomatic relapse with diarrhoea, bloody stools, abdominal pain and fever, 1 month after surgery. His CDAI was 420 and laboratory examination revealed signs of inflammation. Stool cultures were negative. Colonoscopy showed severe colitis with large and deep ulcerations along the left colon. Gastrographin X-ray of the colon and the ileum confirmed the severe lesions in the left colon and demonstrated superficial ulcerations of the right colon and ileum.

Therefore, 3 out of 4 patients treated with hydroxychloroquine presented with endoscopic recurrence. This frequency is actually close to the spontaneous rate of recurrence. Furthermore, the lesions observed were unusually severe with grade i3 ileal lesions in 2 patients and nearly transmural colic lesions in one. To our knowledge, severe clinical relapse as observed in the 4th patients is highly uncommon within 3 months after surgical resection.

Although realized with a limited number of patients, our study suggests that hydroxychloroquine does not prevent recurrences of CD after surgery and could even be associated with more severe lesions. These results explain that we decided to stop the trial. However, large studies would be required to further evaluate hydroxychloroquine in this indication.

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