



Adalimumab or infliximab: which is better for perianal fistula in Crohn's disease?

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Article: Clinical efficacy of adalimumab versus infliximab and the factors associated with recurrence or aggravation during treatment of anal fistulas in Crohn's disease (**Intest Res 2017;15:182-186**)

Perianal fistula complicating CD is common with up to 90% in patients with rectal involvement. Of importance, perianal disease is more commonly detected in East Asia, involving 58.8% of CD patients in Guangdong (China), 30.3% in Hong Kong, and 33.3% of pediatric and 43.1% of adult patients in Korea.^{1,2}

Treatment goals for perianal fistula are reduction of abscess drainage and symptoms, and ultimately resolution of fistula discharge, improvement in quality of life, with preservation of continence, fistula healing, and avoidance of proctectomy and a stoma.³ The treatment of perianal fistula should be individualized according to fistula location, presence of abscess, and disease activity, and multidisciplinary approaches are helpful, especially in cases of both medical and surgical treatments are required.⁴

Simple asymptomatic perianal fistulas usually do not require treatment. For symptomatic simple perianal fistulas, antibiotics, most commonly metronidazole and ciprofloxacin, are considered first-line treatment. Although antibiotics improve fistula symptoms and may contribute to healing, they do not induce complete fistula closure, and the fistula often deteriorates after their discontinuation. In addition, metronidazole should be used cautiously, because of ad-

verse events associated with long-term use.^{3,4}

Fistulotomy alone induced remission in 85% of patients with simple perianal fistula without rectal inflammation. However, if active inflammation is present in the rectum, the risk of delayed healing or fecal incontinence increases after fistulotomy. Therefore, a noncutting seton placement is preferred, along with appropriate medical treatment when active inflammation is present.⁴

The introduction of anti-tumor necrosis factor (anti-TNF) agents has significantly changed the management of fistulizing CD. Anti-TNF agents are recommended in conjunction with adequate drainage, using a seton for a complex perianal fistula.⁴ The first placebo-controlled study included 94 CD patients with fistulas (including 85 with perianal fistulas), and showed that 68% (infliximab 5 mg/kg group) and 56% (infliximab 10 mg/kg group) achieved the primary endpoint, defined as a reduction of $\geq 50\%$ from baseline in the number of draining fistulas.⁵ The ACCENT II study showed a higher remission rate in the infliximab maintenance group, compared with the placebo group at 54 weeks (36% vs. 19%, $P=0.009$).⁶ No placebo-controlled randomized studies have evaluated the efficacy of adalimumab as a primary outcome variable in patients with fistulizing CD. However, the effect of adalimumab on Crohn's perianal fistula has been reported as a secondary endpoint in three large, multicenter, double-blind, placebo-controlled trials.⁷ Currently, there are no head-to-head comparison trials with infliximab and adalimumab. An observational cohort study involving 327 patients (183 infliximab and 144 adalimumab) reported that both

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anti-TNF agents showed similar response characteristics in CD patients.⁸

In the current issue, Ji and Takano⁹ reported the clinical efficacy of adalimumab, and compared the results with those for infliximab in CD patients with perianal fistula. They enrolled 47 perianal CD patients treated with either infliximab (n=31) or adalimumab (n=16). Of 26 patients with a simple fistula (55%), 17 were in the infliximab group and nine in the adalimumab group. The cumulative rate of fistula recurrence/aggravation was 37.5% in the adalimumab group and 16.1% in the infliximab group at 2 years after treatment. They found that seton placement was an independent risk factor for recurrence/aggravation of the fistula tract. Patients with a complex fistula who underwent seton placement were more likely to experience recurrence, but neither infliximab nor adalimumab influenced the clinical course. This study is meaningful in that the clinical efficacy of two anti-TNF agents was assessed in perianal fistula patients. However, this small retrospective study has several limitations. Two groups were enrolled at different times in the infliximab group between 2005 and 2010, and in the adalimumab group between 2010 and 2012. More than 50% had a simple fistula, which can be managed effectively with drainage and antibiotics. In addition, only nine patients received immunomodulators, which had a beneficial effect, especially in those on infliximab.¹⁰

Optimal treatment guidelines for fistulizing CD are needed; however, their development may be difficult because of diagnostic and treatment complexity, and the fact that high-quality clinical data for fistulizing CD are lacking.⁴ Both infliximab and adalimumab can be used for perianal fistulas in CD, with consideration of the clinical setting and patient preferences, based on their similar efficacy.⁹ However, combinations of anti-TNF agents with antibiotics or immunomodulators resulted in a better response; therefore, further studies with use of combined medications are warranted.

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