

Infliximab “Top-Down” Strategy is Superior to “Step-Up” in Maintaining Long-Term Remission in the Treatment of Pediatric Crohn Disease

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ABSTRACT

Objectives: We aimed to compare the efficacy of remission maintenance between infliximab “top-down” and “step-up” strategies in moderate to severe pediatric Crohn disease during 3 years. We also aimed to determine prognostic factors that may influence the relapse-free rate in these patients.

Methods: The present study was a retrospective review of a prospective cohort, based on an infliximab treatment protocol for pediatric Crohn disease used at Samsung Medical Center. A total of 31 patients (group A) were treated with early infliximab induction (“top-down” strategy) and 20 patients (group B) refractory to conventional therapy underwent infliximab treatment (“step-up” strategy). The efficacy of infliximab treatment was assessed by relapse-free rate and remission period rate for 3 years. A total of 11 prognostic factors that may influence the relapse-free rate were further analyzed.

Results: The relapse-free rates at 3 years were 35.5% (95% confidence interval [CI] 0.194–0.519) in group A and 15.0% (95% CI 0.037–0.335) in group B ($P = 0.0094$). Overall remission period rate for 3 years also showed a significant difference between the 2 groups ($92.1\% \pm 7.2\%$ vs $78.3\% \pm 16.6\%$; $P = 0.005$). Multivariable analysis revealed that the duration from the initial diagnosis to infliximab infusion was the only factor associated with relapse-free remission for 3 years (hazard ratio = 1.077; 95% CI 1.025–1.131).

Conclusions: “Top-down” strategy had a longer remission period compared with the “step-up” strategy in pediatric Crohn disease during a study period of 3 years, based on relapse-free rate and remission period rate. Earlier introduction of infliximab is recommended in pediatric patients with moderate to severe Crohn disease.

Key Words: Crohn disease, infliximab, pediatric, step-up, top-down

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What Is Known

- Infliximab in children with luminal Crohn disease is usually commenced when treatment fails with conventional medication including corticosteroids (“step-up” strategy).
- Early introduction of infliximab with or without immunomodulators is known as the “top-down” strategy.
- “Top-down” is superior to “step-up” in inducing and maintaining clinical remission in pediatric Crohn disease for 1 year.

What Is New

- Pediatric patients with Crohn disease under “top-down” treatment are more likely to achieve deep remission at 1 year compared with those under “step-up” treatment.
- “Top-down” is superior to “step-up” in maintaining clinical remission in pediatric Crohn disease for 3 years.

Crohn disease (CD) is a chronic inflammatory disorder involving the gastrointestinal tract, which is characterized by relapsing and remitting episodes (1–3). Various factors such as environmental factors, infectious microbes, and genetic susceptibility are known to play a role in its pathogenesis, which ultimately leads to mucosal inflammation of the intestine (4).

Medical therapy of CD is becoming more complex as the choices of drugs increase. Practical guidelines recommend the following drug categories as first-line treatments: 5-aminosalicylates, budesonide, corticosteroids, azathioprine, 6-mercaptopurine, and infliximab (5,6). Conventional therapy guidelines recommend treatment with corticosteroids initially. Although corticosteroids are efficient in controlling symptoms, their long-term use has many adverse effects and dependency or resistance (7).

After receiving Food and Drug Administration approval for pediatric use in May 2006, infliximab has become widely used in the treatment of pediatric CD (8,9). The efficacy of infliximab suggests that early intense induction may reduce complications associated with conventional treatment and improve quality of life. Intensive early therapy with infliximab is known as the “top-down” strategy. The “top-down” strategy with infliximab has proven to be more intensive than the traditional “step-up” approach in patients newly diagnosed as having moderate to severe CD (10).