Gut and Liver
https://doi.org/10.5009/gnl210246
pISSN 1976-2283 eISSN 2005-1212

Letter to the Editor

Infliximab versus Adalimumab: Can We Choose the Right One for the Right Patients with Ulcerative Colitis?

Sang Hyoung Park, Byong Duk Ye, and Suk-Kyun Yang

Department of Gastroenterology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea

Article Info

Received May 31, 2021
Accepted June 22, 2021
Published online August 11, 2021

Corresponding Author

Suk-Kyun Yang
ORCID https://orcid.org/0000-0003-2772-2575
E-mail sky@amc.seoul.kr

To the Editor:

We read with great interest the article by Lee *et al.*[1] comparing the efficacy of infliximab and adalimumab for biologic-naïve patients with ulcerative colitis (UC). The authors emphasize the similar efficacy and long-term outcomes between these two anti-tumor necrosis factor (TNF) agents for biologic-naïve patients with moderate-to-severe UC. In their retrospective study, the authors compared various outcomes, including clinical remission and response, hospitalization, discontinuation or switching of drugs, and rescue corticosteroid use, between biologic-naïve UC patients who received infliximab (n=83) and those who received adalimumab (n=30). During the median 26 months of follow-up, the above outcomes were comparable between infliximab and adalimumab users. However, there were differences between the two groups. At baseline, the Physician Global Assessment subscore of the Mayo score was significantly better in the adalimumab group (p=0.028), and the rates of UC-related hospitalization and corticosteroid use during follow-up seemed higher in the infliximab group, but these differences were not statistically significant (p=0.085 and p=0.082, respectively). Additionally, colectomies (n=2) were performed on only patients treated with infliximab, and the rates of adverse events seemed higher in the infliximab group than in the adalimumab group, although this difference was not statistically significant. With their article, Lee *et al.* fill the knowledge gap on the comparative efficacy of representative anti-TNF agents, i.e., infliximab and adalimumab, for UC among biologic-naïve patients, particularly Korean patients, for whom there are limited data on this topic.

Although a head-to-head trial has not been performed to compare the efficacy of these two drugs directly, there have been several relevant observational studies conducted in Western countries. A recent study using a nationwide Danish cohort and a propensity score matching analysis reported a higher risk of hospitalization and serious infections among UC patients treated with adalimumab (n=104) than among those treated with infliximab (n=171).[2] Another population-based study from the United States addressing this issue showed no difference in all-cause and UC-related hospitalization between the infliximab (n=1112) and adalimumab (n=288) groups; however, adalimumab users may have had a higher risk of corticosteroid use and a lower rate of drug persistence.[3] In network meta-analyses, infliximab seemed superior to adalimumab in the induction or maintenance phase of UC treatment.[4-6] These studies reported that infliximab is slightly more efficacious than adalimumab, whereas the study by Lee *et al.*[1] seemed to favor adalimumab over infliximab. This discrepancy among studies comparing these two drugs for UC treatment could be partly due to the different study designs, the heterogeneity of the study populations, or adalimumab being relatively underdosed in Caucasian populations whose body weights are usually higher than those of Asian patients.

Regarding the clinical applications of the authors' findings, we would like to report some of our observations and impressions. First, as discussed by the authors, dose optimization strategies for infliximab and adalimumab have differed due to the Korean reimbursement policy during the study period. UC patients experiencing secondary loss of response have been allowed to shorten their adalimumab injection intervals to every week, whereas infliximab dose-doubling and interval shortening have not been allowed in the same setting. Although the authors performed subgroup analyses comparing the outcomes between weekly adalimumab (n=8) and biweekly adalimumab (n=22) as well as biweekly adalimumab and infliximab groups, which showed no differences in efficacy, the sample size was too small to yield a clinically meaningful conclusion on this issue. We suggest that patients who experienced secondary loss of response to standard doses of infliximab or adalimumab should be considered as showing "poor outcomes" to allow for a valid efficacy comparison between these two agents and minimize selection bias during the analyses. Second, in line with the dose optimization issue, pharmacokinetic data were not reported in the article, maybe because therapeutic monitoring for anti-TNF agents was not feasible during the study period in Korea (between 2012 and 2017). Given that checking the trough levels of anti-TNF drugs and anti-drug antibodies in the setting of secondary loss of response would be helpful for treatment planning,[7,8] future studies using pharmacokinetic data to evaluate the efficacy of anti-TNF agents in Korean inflammatory bowel disease (IBD) patients are warranted. Third, in Korea, the reimbursement policy requires an assessment of the Mayo score using sigmoidoscopy at weeks 0 and 8–10 for every patient receiving infliximab or adalimumab induction therapy for UC.[9] Therefore, the comparison of these two drugs would have been more objective if this study had presented the data on endoscopic subscores after the infliximab and adalimumab induction regimens.

The incidence and prevalence of IBD have been rapidly increasing in recent decades, especially in Asian countries, including Korea.[10-14] Along with the increasing disease burden, the requirement of immunomodulators and anti-TNF agents for managing IBD patients has also been increasing.[15,16] Although efficacy data for anti-TNF agents in Asian IBD patients have been reported,[17-22] there has been a lack of comparative efficacy data for biologic agents used to treat IBD, especially for non-Caucasian populations. Realistically, head-to-head clinical trials comparing infliximab and adalimumab, so-called first-generation anti-TNFs, would not be feasible in the future; therefore, the real-world data garnered from studies like that conducted by Lee *et al.*[1] are helpful for guiding optimal therapies for IBD patients in Korea. In addition to the findings of this study, we should consider other factors, such as patients' preferences, costs, and safety profiles, to optimize IBD care under a shared decision-making paradigm because one size does not fit all in this context. Of course, in the future, the therapeutic patterns and real-world efficacy and safety of these medications should be validated by prospective, observational cohort studies enrolling Korean patients.[23]

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

ORCID

Sang Hyoung Park https://orcid.org/0000-0002-5366-5749
Byong Duk Ye https://orcid.org/0000-0001-6647-6325
Suk-Kyun Yang https://orcid.org/0000-0003-2772-2575

REFERENCES

1. Lee YI, Park Y, Park SJ, Kim TI, Kim WH, Cheon JH. Comparison of long-term outcomes of infliximab versus adalimumab treatment in biologic-naïve patients with ulcerative colitis. Gut Liver 2021;15:232-242.
2. Singh S, Andersen NN, Andersson M, Loftus EV Jr, Jess T. Comparison of infliximab and adalimumab in biologic-naive patients with ulcerative colitis: a nationwide Danish cohort study. Clin Gastroenterol Hepatol 2017;15:1218-1225.
3. Singh S, Heien HC, Sangaralingham LR, et al. Comparative effectiveness and safety of infliximab and adalimumab in patients with ulcerative colitis. Aliment Pharmacol Ther 2016;43:994-1003.
4. Danese S, Fiorino G, Peyrin-Biroulet L, et al. Biological agents for moderately to severely active ulcerative colitis: a systematic review and network meta-analysis. Ann Intern Med 2014;160:704-711.
5. Stidham RW, Lee TC, Higgins PD, et al. Systematic review with network meta-analysis: the efficacy of anti-tumour necrosis factor-alpha agents for the treatment of ulcerative colitis. Aliment Pharmacol Ther 2014;39:660-671.
6. Thorlund K, Druyts E, Toor K, Mills EJ. Comparative efficacy of golimumab, infliximab, and adalimumab for moderately to severely active ulcerative colitis: a network meta-analysis accounting for differences in trial designs. Expert Rev Gastroenterol Hepatol 2015;9:693-700.
7. Oh EH, Ko DH, Seo H, et al. Clinical correlations of inflix-

imab trough levels and antibodies to infliximab in South Korean patients with Crohn's disease. World J Gastroenterol 2017;23:1489-1496.
8. Vande Casteele N, Herfarth H, Katz J, Falck-Ytter Y, Singh S. American Gastroenterological Association Institute technical review on the role of therapeutic drug monitoring in the management of inflammatory bowel diseases. Gastroenterology 2017;153:835-857.
9. Park SH, Yang SK, Hong SM, et al. Severe disease activity and cytomegalovirus colitis are predictive of a nonresponse to infliximab in patients with ulcerative colitis. Dig Dis Sci 2013;58:3592-3599.
10. Yen HH, Weng MT, Tung CC, et al. Epidemiological trend in inflammatory bowel disease in Taiwan from 2001 to 2015: a nationwide populationbased study. Intest Res 2019;17:54-62.
11. Park SH, Kim YJ, Rhee KH, et al. A 30-year trend analysis in the epidemiology of inflammatory bowel disease in the Songpa-Kangdong district of Seoul, Korea in 1986-2015. J Crohns Colitis 2019;13:1410-1417.
12. Ng SC, Leung WK, Shi HY, et al. Epidemiology of inflammatory bowel disease from 1981 to 2014: results from a territory-wide population-based registry in Hong Kong. Inflamm Bowel Dis 2016;22:1954-1960.
13. Okabayashi S, Kobayashi T, Hibi T. Inflammatory bowel disease in Japan: is it similar to or different from westerns? J Anus Rectum Colon 2020;4:1-13.
14. Zeng Z, Zhu Z, Yang Y, et al. Incidence and clinical characteristics of inflammatory bowel disease in a developed region of Guangdong Province, China: a prospective population-based study. J Gastroenterol Hepatol 2013;28:1148-1153.
15. Cha JM, Park SH, Rhee KH, et al. Long-term prognosis of ulcerative colitis and its temporal changes between 1986 and 2015 in a population-based cohort in the Songpa-Kangdong district of Seoul, Korea. Gut 2020;69:1432-1440.
16. Aniwan S, Limsrivilai J, Pongprasobchai S, et al. Temporal trend in the natural history of ulcerative colitis in a country with a low incidence of ulcerative colitis from 2000 through 2018. Intest Res 2021;19:186-193.
17. Park SH, Hwang SW, Kwak MS, et al. Long-term outcomes of infliximab treatment in 582 Korean patients with Crohn's disease: a hospital-based cohort study. Dig Dis Sci 2016;61:2060-2067.
18. Oh EH, Kim J, Ham N, et al. Long-term outcomes of adalimumab therapy in Korean patients with ulcerative colitis: a hospital-based cohort study. Gut Liver 2020;14:347-356.
19. Hisamatsu T, Suzuki Y, Kobayashi M, et al. Long-term safety and effectiveness of adalimumab in Japanese patients with Crohn's disease: 3-year results from a real-world study. Intest Res. Epub 2020 Nov 20. Intest Res 2021;19:408-418.
20. Ogata H, Hagiwara T, Kawaberi T, Kobayashi M, Hibi T. Safety and effectiveness of adalimumab in the treatment of ulcerative colitis: results from a large-scale, prospective, multicenter, observational study. Intest Res 2021;19:419-429.
21. Seo H, Chang K, Lee SH, et al. Long-term outcomes of infliximab treatment and predictors of response in 195 patients with ulcerative colitis: a hospital-based cohort study from Korea. Scand J Gastroenterol 2017;52:857-863.
22. Seo H, Ye BD, Song EM, et al. Long-term outcomes of adalimumab treatment in 254 patients with Crohn's disease: a hospital-based cohort study from Korea. Dig Dis Sci 2017;62:2882-2893.
23. Lee CK, Lee KM, Park DI, et al. A new opportunity for innovative inflammatory bowel disease research: the Moderate-to-Severe Ulcerative Colitis in Korea (MOSAIK) cohort study. Intest Res 2019;17:1-5.