EDITORIAL

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Is Adsorptive Granulocyte and Monocyte Apheresis Effective as an Alternative Treatment Option in Patients with Ulcerative Colitis?

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See "Adsorptive Granulocyte and Monocyte Apheresis in the Treatment of Ulcerative Colitis: The First Multicenter Study in China" by Ya-Min Lai, et al. on page 216, Vol. 11. No. 2, 2017

Although more than one-third of patients with active ulcerative colitis (UC) are treated successfully using 5-aminosalicylic acid (5-ASA) as the first-line therapy, other agents such as steroids, immunosuppressants, or biologics may be used in untreated patients.[1,2] Even, in the era of biologis, approximately 25% patients remain in clinical remission and off steroids during the follow-up after 1 year of treatment. Twenty percentage of patients with UC 20% of patients with UC are expected to undergo colectomy.[3,4] Therefore, an alternative treatment strategy is needed for patients who do not respond to conventional therapy and to complement the limited efficacy of current medications.

Although the mechanisms of inflammatory bowel diseases, including UC, are not well understood, increased infiltration of myeloid leucocytes into the intestinal mucosa can be correlated with the severity of the mucosal damage. Activated granulocytes play an important role in enhancing proinflammatory cytokines such as factor-α, interleukin-1β, -6, -8, free radicals, and matrix metalloproteinases and prolong inflammation.[5] Therefore, the selective removal of these circulating myeloid leucocytes through adsorptive granulocyte/monocyte apheresis (GMA) using Adacolumn has been applied as an alternative nonpharmacological option in UC.[6]

In the current issue of *Gut and Liver*, Lai *et al*.[7] have evaluated the efficacy and safety of GMA as an alternative therapy in Chinese UC patients who showed an inadequate response to 5-ASA and refractoriness to prednisolone. To identify the predictive factors for GMA response, Lai *et al*.[7] also analyzed and compared the clinical characteristics between GMA responders and nonresponders. A total of 30 patients who completed all 10 GMA sessions were enrolled and grouped as per the effectiveness of GMA (poorly effective, n=6 vs effective, n=24). In this retrospective study, clinical response and remission rates of GMA were 70.6% and 44.1%, respectively. This result was not significantly different from that of previous studies. However, according to results of those studies, clinical remission rate was significantly different between steroid-naïve and steroid-dependent patients (78% to 84.6% vs 57.9% to 59%, respectively).[8,9] In the study by Lai *et al*.,[7] the authors did not analyze the difference in clinical outcome of patients with or without steroid use. While evaluating adverse effects, GMA using Adacolumn was found to have a better safety profile. Likewise, in the present study, GMA-related adverse effects such as headache were found in 8.8% patients. No GMA-related serious adverse effects were observed and most patients showed good tolerance. Therefore, in Japan and Europe, the clinical application of GMA is expanding.

In the first multicenter trial conducted in Japan in 2001,[10] steroid refractory UC patients with a severe acute flare were shown to achieve remission and their steroid dosage was reduced after five GMA sessions. Although GMA has a significantly higher cost than steroid therapy, the adverse effects of GMA compared to those of steroid therapy were reported less. The Japanese guidelines for UC treatment mention that the combined use of GMA can be more effective for reducing the amount of steroids. However, in the previous studies evaluating factors affecting clinical and endoscopic efficacies, GMA was revealed to be more effective in steroid-naïve patients, patients on the low cumulative steroid dose, patients with short interval between relapse and the first GMA session, or patients without

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deep colonic ulcers.[8,9] These reports have indicated that clinical response and remission rates are higher in patients with mild or short duration UC than in patients with long-term or steroid-refractory disease. Although the various factors mentioned above had not been analyzed together in the study by Lai *et al*.,[7] a relatively lower Mayo score (≤5.5) at entry, was the only factor to predict a good GMA responder. The outcomes of these studies, suggest that patients with short duration UC with inevitable use of steroid show relapse; therefore, implementing GMA as soon as possible can be expected to have a better response. However, most studies including the one by Lai *et al*.[7] have several limitations such as heterogeneous study design, small number of patients, varying frequency (1 to 2/week) and duration (5 to 10 weeks) of GMA therapy, diverse control therapy, and short observation period. Nevertheless, current data consistently indicate that GMA is effective as an adjunct treatment to conventional drug therapy to achieve remission, spare steroids, and prevent relapse without compromising safety of patients with UC. However, in order to clarify clinical characteristics and outcomes (GMA methods, long-term outcome including avoidance of colectomy and hospitalization, and cost-effectiveness) of GMA in patients with UC, large, prospective, randomized trials are required.

CONFLICTS OF INTEREST

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

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