Possible Linkage Between Intestinal Bacteria Composition Changes and Disease Activity in Patients with Rheumatoid Arthritis Treated with Natural Milk Antibodies Against Enteric Bacteria and Their Toxins

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Background: A growing body of research has indicated potential association between dysbiosis or imbalance of intestinal bacterial flora and RA. Previously, we demonstrated the natural milk antibody preparation containing high levels antibodies against pathogenic enteromicrobes and their toxins seems to be effective in a certain RA subset in an open labelled pilot study.[1]

Objectives: To investigate the effects of natural milk antibodies (Ab) on intestinal bacteria composition, and consequent therapeutic effect on disease activity of RA by multicenter randomised double blind clinical trial (UMIN CTR: 000009492).

Methods: Eighty-seven patients with RA with disease activity score of 28 joints (DAS28-ESR) values above 3.2 were divided into 3 groups (29 patients each), and treated with 600 mg of Ab, 300 mg of Ab plus 10 g of skim milk (prebiotics), and 20 g of skim milk alone, respectively, for 12 weeks. The therapeutic effects of milk antibody treatment were determined by serum and faecal LPS concentration, and faecal bacterial composition changes before and after the treatment. Bacteria composition changes was determined by quantitative PCR of bacterial 16S rRNA.

Results: A significant increase in DAS28-ESR values from 4.6 to 4.1 was observed at 4th week in Ab 300 mg plus skim milk group (figure 1). Importantly, this effect was lasted through until 12th week (p<0.01), but DAS28-ESR values gradually returned to original levels after discontinuation of the treatment. On the other hand, neither high dose of milk antibody (600 mg) nor 20 g of skim milk had little effect on DAS28-ESR. Characteristic effect of milk antibody treatment observed in the Ab 300 mg plus skim milk group was the improvement of SJC, TJC, and Pain VAS. No severe adverse events have been observed. Enteric microbe analysis before the treatment indicated lower Bacteroides fragilis (less than 1/100 compared to healthy adults) and higher Staphylococcus aureus population (1000x higher) in patients with RA, indicating a dysbiosis in RA. The DAS28-ESR value reduction in the Ab 300 mg group was associated with an increase in the Lactobacillus population. In contrast, the improvement of Pain VAS was associated with an increase in the B. fragilis population. Possible improvement in the intestinal barrier function was assumed by the reduction of serum and faecal LPS concentration ratio in the Ab 300 mg groups.

Conclusions: Adding IGU to csDMARDs with poor response in RA patients is effective, but AE should be considered. Radiographic progression by Iguratimod might be inhibited in early phase of RA.

REFERENCE:


Disclosure of Interest: None declared

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