Dainekhuto (DKT), a Japanese Traditional Herbal Medicine Ameliorated Gastrointestinal Hypermotility by Downregulated the Interleukin-17A in a Murine Functional Gastrointestinal Disorder Model

Hirotada Akiho, Harutai Ogino, Mitsuru Esaki, Eikichi Ibara, Kazuhiko Nakamura, Masahiro Yamamoto

Background and Aim: Intestinal inflammation and immune activation are accompanied by alterations of gastrointestinal motility associated with alterations of smooth muscle function. We have previously reported that IL-17A directly enhanced gastrointestinal transit and small intestinal smooth muscle contraction. We evaluated the effects of dainekhuto (DKT) on the hypermotility of gastrointestinal transit persisting after acute inflammation induced by a T-cell activating anti-CD3 antibody (CD3). DKT is a pharmacological cholinergic drug widely prescribed for patients with functional gastrointestinal disorders like irritable bowel syndrome or postoperative ileus in Japan. Methods: Wild-type or IL-17A KO BALB/c mice were injected with CD3 (12.5 mg, i.p.) and DKT (2700 µg/kg) was administered orally daily for 1 week. The gastrointestinal motility was evaluated by using geometric center analysis. For estimation of gastrointestinal transit, mice were orally administered with 200 µL of fluorescein-labelled dextran of 70,000 MW and the gastrointestinal tract was excised after 30 min. Fluorescence was visualized and quantified using the G-box system and the geometric center was calculated using the formula: geometric center = x = ∑x/∑, where n is the number of specimens. Plasma albumin-protein expressions of small intestine were evaluated on days 1, 3, and 7 after CD3 injection from mice. Results: The small intestinal tissue damage in the early phase (1-3 days after CD3 injection) is characterized by enterocyte apoptosis, epithelial damage and villous atrophy which had recovered by day 7 in terms of histology. However, αCD3-treated mice on day one (the inflammatory phase) showed hypomotility (p<0.01), but then displayed hypermotility on day 7 in the recovery phase (p<0.03). Prolonged upregulation of IL-17A was prominent (p<0.05) and IL-17A injection directly enhanced gastrointestinal transit (p<0.01). In IL-17A KO mice, while the hypermotility of gastrointestinal transit in the inflammatory phase was shown (p<0.05), the hypermotility in the recovery phase was not observed. There were no apparent differences in the enteropathy of small intestine between wild-type and IL-17A KO mice. DKT inhibited the immune cell infiltration and downregulated the IL-17A protein in the intestine induced by CD3 (p<0.05). DKT ameliorated the CD3-induced gastrointestinal hypermotility on day 7 in the recovery phase (p<0.05). Conclusions: DKT ameliorated the hypermotility of gastrointestinal transit by downregulating the IL-17A. DKT may lead to the development of new pharmacotherapeutic strategies aimed at a wide variety of functional gastrointestinal disorders.

Inflammatory Responses Associated With Postoperative Ileus Contribute to Anastomotic Leakage - A Post-Hoc Analysis of a Prospective Randomized Controlled Trial

Emmeline Peters, Marloes Dekkers, Francesca W van Leeuwen-Hillers, Freek Daams, Wouter De Jonge, Willem A. Buurman, Misha Luyer

Background: Anastomotic leakage (AL) following abdominal surgery is a critical determinant of postoperative recovery. The etiology of AL is largely unknown. Interestingly, interventions such as chewing gum and early enteral nutrition, aimed at reducing the inflammatory response and postoperative ileus (POI) also have a beneficial effect on AL co-occurrence. The aim of this study was to investigate the relation of POI with inflammation and AL after colorectal surgery. The etiology of AL is largely unknown. Interventions such as chewing gum and early enteral nutrition, aimed at reducing the inflammatory response and postoperative ileus (POI) also have a beneficial effect on AL co-occurrence. This raises questions about a possible overlap between IBS and allergic contact enteritis (ACE).

Methods:

Objective:

To evaluate if identified type 4 food allergens, when tolerated in the diet, may lead to the development of new pharmacotherapeutic strategies aimed at a wide variety of functional gastrointestinal disorders.

Results:

A questionnaire was distributed at this time, to be completed and returned by the patient after one month of avoiding the identified allergens. This questionnaire asked the patient to report their baseline IBS symptoms as well as how they changed after one month of food avoidance. Results: Thirty-nine patients were included in this study. Average age was 43 ± 17 years and 76.9% were female. Subcategories of IBS included 44% diarrhea predominant, 18% constipation predominant, 28% mixed, and 10% unknown. Common allergens which showed a response included casinum casein, barley, gluten, soy, milk, fish, shellfish, egg, and almon. Seventy-eight patients showed either some or total improvement in their global IBS symptoms and 87% had some or total improvement in abdominal pain/discomfort alone. Conclusion: In this post hoc study, our results show that 85% of patients with IBS had some or complete improvement with avoidance of known type 4 food allergens identified by skin patch testing. This raises questions about a possible overlap between IBS and allergic contact enteritis. Larger studies will be needed to investigate dose-related response and to more fully address the placebo effect.