

## Research Article

# Effect of probiotics in the treatment of gastrointestinal symptoms in patients with scleroderma

Afsaneh Enteshari-Moghaddam<sup>1</sup>, Shafieh Movassaghi<sup>2\*</sup>, Abdolrahman Rostamian<sup>2</sup>

<sup>1</sup>Department of Internal Medicine, School of Medicine, Ardabil University of Medical Science, Ardabil, Iran

<sup>2</sup>Department of Rheumatology, Tehran University of Medical Science, Tehran, Iran

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### \*Correspondence:

Dr. Shafieh Movassaghi,

E-mail: [shafiehmovassaghi@gmail.com](mailto:shafiehmovassaghi@gmail.com)

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### ABSTRACT

**Background:** Treatment of gastrointestinal symptoms in patients with systemic sclerosis has been a challenge for years. Drugs, immunosuppressive or anti-fibrotic have always been associated with complications. The effectiveness of probiotics as live microorganisms of nonpathogenic always was to treat the symptoms.

**Methods:** In this clinical trial, 37 patients with systemic sclerosis with mild to severe symptoms in the intervention and control groups were studied. Inventory (UCLA SCTC GIT 2.0) was used for rating the severity of the gastrointestinal tract. Collected data was analysed by statistical methods using SPSS.19.

**Results:** Improvement was seen in total score after the use of probiotics in gastrointestinal reflux condition ((P=0.001), gastric distention (P =0.001), emotional function ((P=0.001), social.

**Conclusions:** This study showed that probiotics were significantly effective in treatment of gastrointestinal symptoms in patients with systemic sclerosis.

**Keywords:** SSc, Gastrointestinal involvement, Probiotics

## INTRODUCTION

Autoimmune diseases are chronic diseases which are caused by the loss of the body's immunological tolerance to its self-antigens. Chronic nature of these diseases has a noticeable impact on the use of medical care and services directly or indirectly by economic costs and affecting the quality of life. The prevalence of autoimmune diseases is estimated about 90 cases per 100,000 people annually and the incidence rate of them is estimated at 3% of the whole population.<sup>1</sup>

Systemic sclerosis (SSc) is one of chronic multi-systemic autoimmune and idiopathic diseases, which occurs due to excessive collagen deposition and production of autoantibodies in the skin, internal organs and vasculopathy of small vessels.<sup>2</sup>

The prevalence of SSc varies from 100 to 300 people per million people worldwide and its incidence is about 20 cases per million people.<sup>3</sup>

Marie, in a study in 2006, showed that anorectal involvement is prevalent to the extent of 50%-70%, and digestive symptoms develop up to 75%-90% among patients with two main subtypes of SSc i.e, limited and diffuse SSc.<sup>4</sup> In a study by Jaovisidha et al, it has been explored that 80% of patients had diffuse SSc and 20% had limited SSc. Moreover, they have found that the gastrointestinal involvement in SSc can be extremely debilitating and even life threatening.<sup>5</sup>

Tian et al have undertaken a study and have shown that SSc diagnosis is based on manometry and endoscopic examination and treatment, besides, they have expressed that supportive and symptomatic treatment is the best strategy. However, they have suggested early diagnosis

as a determining factor in successful management of the disease.<sup>6</sup>

The involvement of gastrointestinal tract as an important part of the body occurs in about 90% of patients and SSc disease is involved from beginning to end includes inflammation, vascular damage due to ischemia, fibrosis and neuropathy in the upper and lower parts of the gastrointestinal tract.<sup>7-9</sup>

Totally speaking, there are a number of ways to treat the disease such as immunosuppressive therapy, anti-fibrotic therapy, treatment of intestinal complications, treatment of gastrointestinal complications, and treatment of pulmonary hypertension and systemic blood pressure. Probiotics are live non-pathogenic microorganisms (bacteria and yeasts) that cause adequacy of microflora in the intestines of host.<sup>10,11</sup>

The probiotics are helpful in IBS in which the abnormal functions of the gastrointestinal tract concerning motility and viscera, and the intestinal tract's hypersensitivity are dependent on psychosocial factors.

The theory of the role of probiotics in replacing the intestinal harmful flora with beneficial flora and alleviating the symptoms of SSc, especially bloating and abdominal distention has led to the use of probiotics for SSc patients who develop symptoms. It is necessary to note that the intestinal microflora can play a modifying role in the immune system.<sup>12</sup>

Considering frequency of gastrointestinal symptoms in patients with systemic sclerosis, the aim of this study was to investigate the effect of probiotics in treating the symptoms in patients with SSc.

## METHODS

This clinical trial study was conducted over 37 patients with SSc who had been diagnosed in the Tehran's Rheumatology Clinic in 2014. The sample was randomly divided into two groups of control (17 persons), and intervention (20 persons). Randomization was performed as randomized blocking to eliminate the effect of nuisance factors.

In the beginning, the patients were examined and their gastrointestinal symptoms and other necessary information were recorded by the researcher. Subsequently, UCLA SCTC GIT 2.0 questionnaire was administered among patients. This questionnaire consisted of 7 scales of reflux, abdominal distention/bloating, fecal soilage, diarrhea, emotional disorders, and social functioning, and constipation that were used to elicit information from the patients. The patients were asked about the occurrence of symptoms over the last week. The obtained mean score for 7 scales was the criterion to judge the change in the situation before and after taking the drug. Those patients

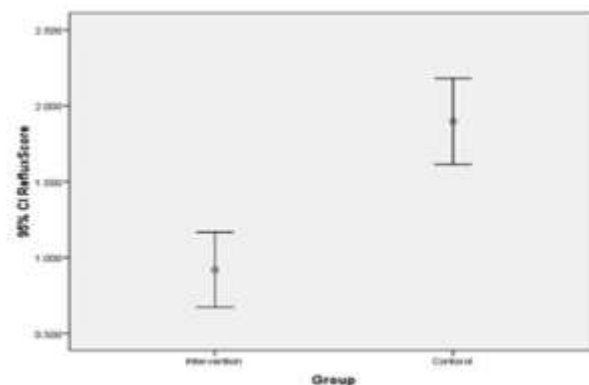
developing moderate to severe symptoms of systemic sclerosis who had scores higher than 1.25, were included in the study. Then, lactobacillus casei probiotic, in the form of tablets, were given to the patients to take for two months. Two months later, the patients were re-examined and completed the same questionnaire, and the recorded data were compared and analysed before and after intervention.

The patients were told not to make any change in their medicinal, nutritional, or behavioural pattern. Related to blinding, probiotic was prepared in packages similar to placebo and patients and therapists were unaware of which group they were allocated. Exclusion criteria involved not taking the drug on time, drug intolerance due to side effects, or incompatibility of the patient's taste with the drug, and the patient's unwillingness to participate in the study.

## Statistical analysis

The gathered data from the check-lists and test results were entered into the SPSS16 and were analysed using t-test and non-parametric test of Mann-Whitney U-test. In the present study, the patients were not imposed any extra charge. The used examinations in this study were regular techniques that were accepted in the scientific and international assemblies. Before undertaking study, informed written consent form was obtained from all the patients.

## RESULTS



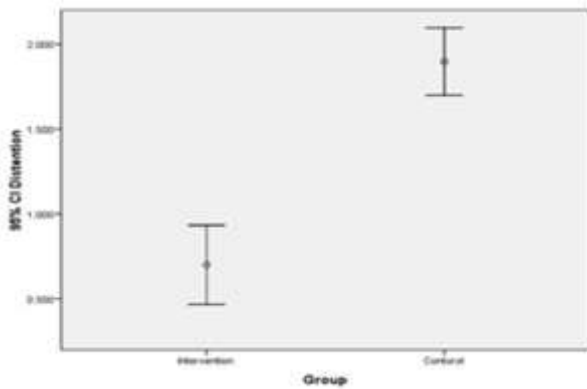
**Figure 1: The average of esophageal reflux score in two groups after intervention.**

The total number of participants in the study was 37, including 20 SSc patients in the intervention group, and 17 SSc patients in the control group. Of all the patients, 32 patients (86.5%) were females and 5 patients (13.5%) were males. Both of control and intervention groups were similar in terms of sex. The disease duration ranged from 1 to 16 years with the mean of 6 years and the standard deviation of 3.41 years. The age range of the patients was between 18 and 58 years with the mean age of 46.3 and the standard deviation of 11.8. Prednisolone taken by 34 patients (92%) and omeprazole taken by 29

patients (85%) were the most common drugs used by the patients.

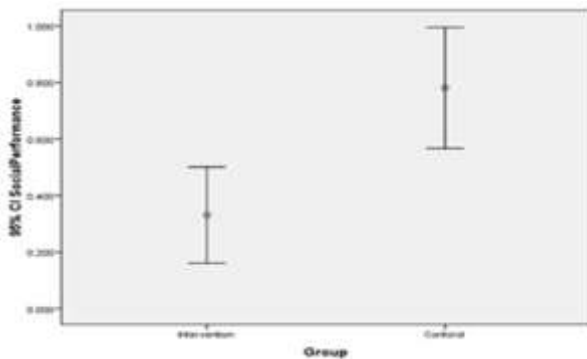
Two months after taking probiotics, a significant difference was observed between the mean score for esophageal reflux in the intervention group (mean 0.91, standard deviation 0.52) and the control group (mean 1.89, standard deviation 0.55), while the difference between groups was not significant prior to the intervention (Figure 1).

Two months after taking probiotics, abdominal distension's mean score between the intervention groups (mean 0.7, standard deviation 0.49) and the control group (mean 1.89 standard deviation 0.38) showed a significant difference, but the difference was not significant before the intervention (Figure 2).



**Figure 2: The average of gastric distention score in two groups after intervention.**

The mean of fecal incontinence scores for the intervention group (mean 0.037, standard deviation 0.16) and the control group (mean 0.058 standard deviation 0.25) didn't show statistically significant difference. Similarly, the difference between average score of diarrhea in the intervention groups (mean 0.4, standard deviation 0.5) and in the control group (mean 0.38, standard deviation 0.51) was not statistically significant.

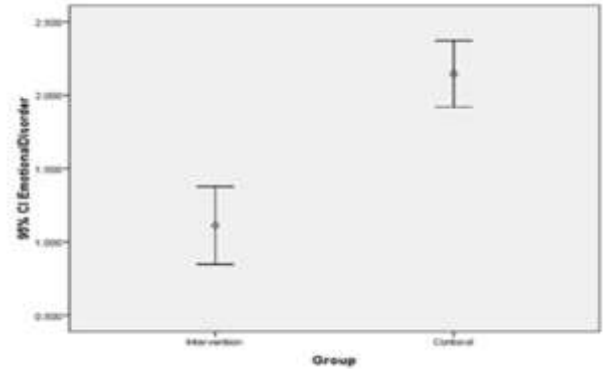


**Figure 3: The average of social performance score in two groups after intervention.**

The difference between average score of social functioning in the intervention group (mean 0.33,

standard deviation 0.36) and the control group (mean 0.78, standard deviation 0.41), was statistically significant, considering that there was no significant difference in this regard between groups before the intervention (Figure 3).

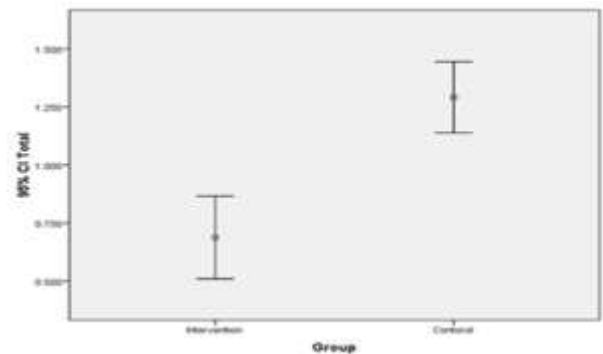
Two months after taking probiotics, the mean score of emotional disorders didn't vary significantly from the intervention group (mean 1.11, standard deviation 0.56) to the control group (mean 2.14, standard deviation 0.44) (Figure 4).



**Figure 4: The average of emotional disorder score in two groups after intervention.**

The average score of constipation for two groups of intervention (mean 0.55, standard deviation 0.77), and control (mean 0.58, standard deviation 0.63) didn't differ significantly.

Two months after taking probiotics, the difference between mean of total scores in the intervention group (mean 0.68, standard deviation 0.38) and the control group (mean 1.29 standard deviation 0.29) was not statistically significant (Figure 5).



**Figure 5: The average of total score in two groups after intervention.**

**DISCUSSION**

Scleroderma or systemic sclerosis (SSc) is a connective tissue disorder and autoimmune disease that cause skin and internal organs like gastrointestinal tract to be affected. Scleroderma is a chronic inflammatory disease

that produces a variety of symptoms through different mechanisms. The symptoms of this disease appear in various systems of body and different medications are used to relieve them. In the gastrointestinal tract depending on the symptoms that occur, suitable medication is prescribed for the patient. As mentioned in the introduction, slow gastrointestinal motility brings on gastroesophageal reflux. To treat this problem various medicines, such as pump inhibitor drugs like omeprazole are prescribed.

Besides, constipation as other problem also arises that some medicines like cisapride or domperidone are prescribed to increase motility and treat the problem. In any case, these drugs because of their side effects may not be used by patients or bring about some problems for them in the long run. In the recent years, researchers and specialists are looking for drugs that have fewer side effects and at the same time are more effective. And it was why probiotics were introduced to this area. The mean scores of reflux, abdominal distension, social functioning, emotional disorders, and total score in the intervention and the control groups were significantly different from each other, suggesting that the use of probiotics could reduce gastrointestinal symptoms in the intervention group.

In the same study Firch and et al in America, showed that 4 scales of the esophageal reflux, abdominal distension, emotional disorders and the average total score reduced significantly. In this study, in addition to above four aspects, the patients' social functioning improved as well, while in the Firch et al study there was no improvement in this regard.<sup>13</sup>

The results of Capello's study in Italy on symptoms of patients with irritable bowel syndrome have shown that the amount of bloating and feeling flatulence significantly decreased by taking probiotics, which is in line with the present study's finding.<sup>14</sup>

Pourfarzi et al in a study over patients with irritable bowel syndrome who had consumed probiotics for four weeks, reported that abdominal pain and bloating of patients significantly alleviated, this finding also confirms the results obtained in the present study.<sup>15</sup>

Several studies have shown that gastrointestinal tract is involved in 70-90% of patients with SSc. A recent study by Schmeiser and colleagues displayed that 98.9 patients with SSc are suffering from gastrointestinal discomfort. Generally, the severity of gastrointestinal symptoms from mild to severe are pain, dysphagia, nausea, diarrhea, constipation and fecal incontinence. The results of above studies are consistent with the results of this study in which all patients had gastrointestinal involvement.<sup>16-20</sup> In this study, the duration of disease varied from 1 to 16 years with the mean of 6 years and the standard deviation of 3.41 years, which was less than the average duration of disease reported in Al-Dhaher et al's study. In Al-Dhaher

et al's study, the duration of SSc was considered until the last visit or the death of patient which was 9.1 years (7.9 years in diffuse SSc, and 9.8 in limited SSc). Moreover, it was also revealed that cardiac involvement, dcSSc and hypertension are associated with poor survival.<sup>21</sup> In the present study, the survival of patients with scleroderma improved compared to previous reports in other studies.

## CONCLUSION

This study is among the first studies undertaken on the role of probiotics in patients with SSc in Iran, and one the rare studies conducted in the world. The high power (0.99) and the large sample size of this study are the strong points of the present study. It is worth mentioning that since probiotics are harmless, they can be consumed along with other medications that scleroderma patients receive. And in the case of being effective, taking other medicines with gastrointestinal side effects can be reduced gradually. It is suggested that systematic studies and meta-analysis to be conducted on the effect of probiotics on gastrointestinal symptoms in patients with scleroderma, and in the case of yielding better results to be used as alternative way for treating the gastrointestinal symptoms in these patients.

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*Ethical approval: The study was approved by the institutional ethics committee*

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