Fellowship Report

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Time frame of training: 01.09.2023-29.02.2024
Host institute and country: Oslo University Hospital, Norway
Scientific coordinator: Prof. Anna-Maria Hoffmann-Vold
Summary of planned outlined project: Disease Burden and Impact of Fecal Incontinence in Systemic Sclerosis - data from the randomized ReSScue trial

My research aimed to understand the disease burden of fecal incontinence (FI) in systemic sclerosis (SSc) patients with moderate to severe lower gastrointestinal (GI) disease, and explore the potential of fecal microbiota transplantation (FMT) in alleviating FI symptoms. Although the ReSScue trial (1) did not find efficacy of FMT by standard 'Anaerobic Cultivated Human Intestinal Microbiota' (ACHIM) on primary outcome (diarrhea or bloating), the exploratory endpoint, impact of FMT on fecal incontinence (FI), has not been assessed.

In this post-hoc analysis, we examined: (1) the prevalence and burden of FI symptoms by two different patient-reported outcome measures, (2) potential associations between FI and baseline SSc characteristics, (3) predictive factors for worsening of FI-related quality of life over time, and (4) the efficacy of FMT on FI symptoms within the randomized ReSScue trial. FI symptoms were assessed at baseline, 12 and 20 weeks using the Fecal Incontinence Quality of Life (FIQL) scale (2) and University of California Los Angeles Scleroderma Clinical Trial Consortium GIT 2.0 (UCLA GIT) scale (3). The Bristol Stool Form Scale assessed stool consistency at baseline and week 12 (4). Using multivariable logistic regressions, we assessed associations between baseline FI and frequency of FI symptoms with patient characteristics. Next, we assessed associations between FI, by UCLA GIT fecal soilage score and FIQL subscales, as well as ScleroID, HAQ-DI, EuroEQ-5D, patient and physician global assessment and VAS fatigue scale, using Pearson's correlation analysis. Linear mixed-effect models were applied to unveil predictors of FIQL score behavior over time. One-way repeated measure analysis explored the behavior of FI symptoms over time. Changes meeting the minimally clinically important difference (MCID) threshold at week 20 were considered meaningful (3,5). Effect size was calculated by Cohen's index (0.2 = small, 0.5 = moderate, 0.8 = large). Analyses were conducted for all patients, and a subset defined as the "severe" FI cohort, comprising those reporting FI at all time points (baseline, 12 and 20 weeks).

In the entire cohort, 72% (48/67) reported FI on the FIQL scale, in contrast to 33% (22/67) using the UCLA GIT. Compared to patients without FI, those reporting FI were more often anti-centromere positive and had a lower body mass index. Overall, 14 SSc patients met the definition of "severe" FI. We found that "severe" FI was associated with modified Rodnan Skin Score, digital ulcers, loose stools and diarrhea. The FIQL subdomains, particularly coping ($r=-0.74$, $p<.001$) and embarrassment ($r=-0.63$, $p<.001$), correlated with both mild and moderate to severe UCLA fecal soilage scores, notably in "severe" FI patients. Age and disease duration predicted worsening of FI-related quality of life over time in all patients and those with "severe" FI, with no associations between baseline FI severity and score changes in either cohort. No correlation was found between FIQL subdomains and ScleroID lower GI domain and no other patient-reported outcome measures correlated with the severity of fecal soilage. Regarding the efficacy of FMT on FI symptoms, at baseline, 48 patients reported FI, with 24 in each treatment arm. The "severe" FI cohort included 14 patients, 8 in the ACHIM group and 6 in the placebo group. By week 20, FMT-treated patients showed numerical improvements in UCLA fecal soilage scores, surpassing the MCID thresholds of "somewhat better" compared to the placebo group. Furthermore, the subset characterized by "severe" FI sustained improvement from 12 to 20 weeks. Fewer FMT-treated patients reported loose stool at week 12, specifically 3 out of the initial 9 in the entire cohort and 6 in the "severe" FI cohort. In contrast, the placebo group had an additional two patients reporting watery stool. Despite changes in FI and stool consistency over 20 weeks, patients did not perceive a corresponding improvement in their quality of life, consistently rating themselves as "about the same" on the FIQL scale.

The ReSScue trial provided valuable insights for future studies in SSc patients with GI involvement. The cohort had a high prevalence of FI, with the FIQL scale showing greater sensitivity compared to the UCLA GIT score. Recurrent FI episodes were linked to more severe SSc-related GI issues. Early FI assessment appears key to prevent considerable daily life restrictions. Although FMT did not improve bloating and diarrhea in the ReSScue trial, current analyses demonstrate significant relief of FI symptoms with consistent improvement over 20 weeks, possibly due to improved stool consistency. However, caution is warranted in interpreting these positive results due to the limited number of participants and short study duration.

The diagnosis and management of FI in SSc patients present challenges, primarily due to patients' reluctance to discuss embarrassing symptoms and the absence of a clear diagnostic approach. This is notable despite the availability of universal tools such as the Wexner score (7) and Vaizey score (8), along with the Fecal Incontinence Quality of Life scale (FIQL), and the disease-specific UCLA GIT 2.0 scale. Nevertheless, the current understanding of the severity and behavior over time of SSc-related FI symptoms is generally limited. Furthermore, few data are available regarding the coping mechanisms employed by SSc patients to manage their bowel issues, and the true impact that FI symptoms exert on the overall health status of these individuals.

References:

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