Fecal Microbiota Transplantation for Autism

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Autism spectrum disorders (ASD) are complex neurobiological disorders that impair social interactions and communication and lead to restricted, repetitive, and stereotyped patterns of behavior, interests, and activities[1]. Many children with ASD experience gastrointestinal symptomsand have lower abundances of fermentative bacteria and lower bacterial diversity[2]. Fecal microbiota transplantation (FMT) therapy has been used to treat recurrent Clostridium difficile infection[3], ulcerative colitis[4,5] and alcoholic hepatitis[6]. A modified FMT protocol, termed Microbiota Transfer Therapy (MTT), involves 14 days of oral vancomycin treatment, followed by bowel cleansing. Finally, the gut microbiota is repopulated by administering a high initial dose of Standardized Human Gut Microbiota either orally or rectally followed by daily, maintenance oral doses with a stomach acid suppressant for eight weeks. It has been shown to improve both gastrointestinal and ASD-related symptoms[7]. We hereby report our first case of FMT- MTT for ASD.

Case Report

The patient was a four-year-old male child who had been diagnosed with autism. He had been on speech and occupational therapy for 10 hours per week. The Childhood Autism Rating Scale (CARS) score was 45, suggestive of severe autism. The CARS consists of 14 domains assessing autism-associated behavior and the 15th domain rating the general impression of autism. Each domain is scored on a scale from 1-4; higher scores corresponding with a higher level of impairment. Total scores below 30 indicate a non-autistic range, between 30 and 36.5 indicate mild to moderate autism, and from 37 to 60 indicate severe autism.

The child did not have any gastrointestinal symptoms. His parents approached us as they wanted FMT to be tried as a therapeutic option in the child. They were counseled regarding the procedure and its utility in ASD. The Institutional Ethics Committee approved the use of FMT as an experimental modality for ASD. The parents were considered as donors since there was no history suggesting gastrointestinal disease, metabolic syndrome, autoimmunity, atopic disease, chronic fatigue syndrome, or fibromyalgia. There was no recent antibiotic use within the preceding three months or a history of high-risk behavior. They were screened with serology for HIV, HBsAg, anti-HCV, and VDRL, and stool examination consisting of routine microscopy for ova and cysts, gram stain, special stains, and bacterial culture.

Patient preparation for FMT

The child was started on oral vancomycin (40 mg/kg/day) 10 days prior to the procedure, oral omeprazole two days prior, and polyethylene-glycol based oral preparation one day prior to the colonoscopic instillation.

Preparation of stool for FMT

The mother was selected as the donor. She deposited a stool sample in a sterile container in ice packing at the Microbiology laboratory two hours prior to colonoscopy. Two hundred grams of fresh stool was measured and diluted with 400ml of saline, blended, strained, and filled in centrifuge tubes of 10 ml each, which were centrifuged @800 rotations per minute(rpm) for 2 minutes, resulting in the formation of two layers of supernatant and sediment. The supernatant was collected in 8 tubes of 10 ml each and transported immediately to the colonoscopy room in an ice pack half an hour before the procedure.

Oral FMT preparation

For oral use, a fresh sample was prepared by blending, straining, and centrifugation at 1400 rpm for 10 minutes. The supernatant was separated and centrifuged again at 4800 rpm for 15 min to get a sample rich in microbiota in 5-10 ml syringes handed to the parents in an ice pack, to maintain a temperature of -20 degrees centigrade for five days.

Colonoscopic instillation

The colonoscopy was performed under sedation, and FMT material sprayed from caecum to sigmoid colon. The donation-to-FMT time was around 180 min. Post-instillation, the foot end of the bed was raised, and the child kept in the left lateral decubitus position. Stool retention time was 210 min. There were no adverse effects.Two sessions of colonoscopic instillation were done eight days apart.

Oral administration

The pre-prepared oral suspension was administered to the child every day after the first session of colonoscopy. Oral administration was given in mixed in chocolate milk to mask the taste and given twice daily(10 ml per dose) for one month.

The child showed improvement after one month of treatment with a lowering of the CARS score to 37. At three months follow up, the improvement was sustained(CARS score 36).

Discussion

The present case highlights the use of FMT for an unusual indication. Currently, very few centers in India offer FMT. Previous studies have reported the benefit of FMT in alcoholic hepatitis and ulcerative colitis in India.[5,6] The procedure is safe, technically feasible, and offers good results. We used a protocol previously reported by Kang *et al*[2] In this small open-labeled study, the authors acknowledged several limitations including their study design not allowing them to evaluate if observed improvement in their study cohort was due to vancomycin therapy, PPI therapy or fecal transplant, or a combination all three. This protocol is currently being evaluated in adults with ASD in clinical trials in the United States (NCT03408886). Fecal transplant for autism, as of date, may be regarded as experimental; well-designed double-blind placebo-controlled trials demonstrating its safety and efficacy are needed.

The exact quantification of the microbial load was not possible in our case, and oral suspension, even when refrigerated, is unlikely to be useful beyond seven days. Oral capsules for FMT are available commercially abroad but currently unavailable in India. The use of such "poop capsules" would offer greater ease in performing this form of therapy.The present case highlights fecal transplantation for the management of autism in India for the first time. Though it is an experimental therapy, it offers hope for causing sustainable improvement in patient symptoms. The need of the hour is to devise techniques for preparing poop capsules or suspensions to make FMT more patient-friendly and easy to administer.

References

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