A retrospective outcome study of 42 patients with Chronic Fatigue Syndrome, 30 of whom had Irritable Bowel Syndrome. Half were treated with oral approaches, and half were treated with Faecal Microbiome Transplantation

J.N. Kenyon⁎, Shelly Coe, Hooshang Izadi

⁎ The Dove Clinic for Integrated Medicine, The Old Brewery, Twyford, Winchester, Hampshire SO21 1RG, United Kingdom

ABSTRACT

The gut microbiome comprises the community of microorganisms in the intestinal tract. Research suggests that an altered microbiome may play a role in a wide range of disorders including myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS).

Methods: 42 participants with ME/CFS with Irritable Bowel Syndrome (IBS) were allocated into one of two groups, 21 were treated with standard oral approaches, which centred around various nutritional remedies, probiotics, prebiotics, dietary advice and lifestyle advice. The second group who had mostly failed using oral approaches, were treated with Faecal Microbiome Transplantation (FMT). Each patient received 10 Implants, each from a different screened donor, and the Implants were processed under anaerobic conditions. The transplant is delivered via a paediatric rectal catheter, which is inserted through the anus to reach the lower part of the sigmoid colon.

The results were assessed on a percentage basis before and after treatment, 0% being no improvement, 100% being maximum improvement. An exact non-parametric Mann-Whitney (one-tailed) test was used to compare medians from those on FMT compared with those receiving oral approaches only. On clinical experience over many years, the only way to judge improvement in Chronic Fatigue Syndrome as there is no test for Chronic Fatigue Syndrome, is my clinical assessment.

Results: The median for the FMT group was found to be significantly higher compared to the oral treatment group (Mann-Whitney U=111.5, p=.003). Therefore, the FMT group improved to a greater extent (z=−2.761).

Conclusion: This study shows that FMT is a safe and a promising treatment for CFS associated with IBS. Adequately powered randomised controlled trials should be carried out to assess the effectiveness of FMT in patients with CFS and IBS.

1. Introduction

The gut microbiome comprises the community of microorganisms in the intestinal tract. Over the last five years, interest in the gut microbiome has grown considerably driven by new techniques in DNA sequencing allowing for characterisation of gut bacteria and the recognition of the potential impact the microbiome may have on health [1,2]. The large intestine has the highest number of microbial organisms, with less found in the more hostile low-pH environment of the small intestine. The large intestine is dominated by anaerobic bacteria which survive and thrive by anaerobically digesting our food [3–5]. The gut microbiome has coevolved with humans to match our modern lifestyles [6] and is beneficial for our health, supplying essential nutrients, synthesizing vitamins (i.e. vitamin K) and facilitating digestion of undigested carbohydrates [7–9]. Furthermore, bacteria also help maintain the integrity of the mucosal barrier by preventing antigens and pathogens entering the gut mucosa [10,11].

In healthy adults, 80% of the identified faecal microbiota can be classified into three dominant phyla: Bacteroides, Firmicutes and Actinobacteria. In general terms, the Firmicutes to Bacteroides ratio is regarded to be of significant relevance in the human gut microbiota composition. High Firmicutes and low Bacteroides usually correlates with a healthy diverse microbiome and reflects a largely plant-based diet. In unhealthy microbiomes the opposite is the case and may well be due to a more western type diet [12,13]. Alterations in the composition of the microbiome has the potential to significantly impact on our health and wellbeing. One of the side effects of antibiotic use is a change in gut microflora that allows overgrowth of harmful micro-organisms [14]. Clostridium Difficile-associated diarrhoea for example is a well-recognised infection linked to previous antibiotic use [15]. Furthermore, studies on young children with a developing microbiome have shown that antibiotics are especially likely to cause long lasting
Recent changes in lifestyle including reduced exposure to pathogens in early life, dietary changes to a high intake of carbohydrates and fats from processed foods and reduced dietary fibre have been proposed to play a role in the rise of inflammatory conditions such as inflammatory bowel disease (IBS/D) and Crohn’s disease [19,20]. The microbiome has been shown to have profound effects in the development of gut-associated lymphoid tissue, differentiation of gut immune cells and production of immune mediators such as IgA’s and microbial defence peptides [21]. Recent research suggests that an altered microbiome may play a role in a wide range of disorders including Parkinson’s disease [22,23] chronic liver disease [24,25], myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS) [26,27] and also impact cancer patient recovery after treatments such as chemotherapy and radiotherapy [28].

In this study we randomly chose 21 patients from our sizeable population of Chronic Fatigue Syndrome patients. These patients were treated using oral approaches and also lifestyle and dietary advice. Then, 21 patients with Chronic Fatigue Syndrome who were treated with Faecal Microbiome Transplantation (FMT).

2. Materials and methods

All our Chronic Fatigue Syndrome patients were assessed using the agreed international consensus criteria for Chronic Fatigue Syndrome and Myalgic Encephalomyelitis [29].

Other possible diagnoses in all of these patients were ruled out with appropriate clinical examination and appropriate investigations by their General Practitioners prior to seeing us.

We divided the patients into two groups of 21 per group. 21 were treated with standard oral approaches, which centred around various nutritional remedies, probiotics, prebiotics, dietary advice and lifestyle advice. The second group were treated with FMT and the second group had mostly failed using oral approaches.

In the Faecal Microbiome Transplantation population in this study, each patient was implanted with 10 Implants, each from a different screened donor and we have found in clinical practice that 10 Implants is an optimal number, the Implants are processed under anaerobic conditions. The criteria for Chronic Fatigue Syndrome is as per Carruthers BM, van de Sande MI, et al. [29].

Donors are screened and undergo testing for many common communicable diseases to ensure that the procedure is done as safely as possible, but it is not possible to test donors for all possible organisms and some infections may be undetectable. To date there have not been any documented cases of an infection transmitted through FMT. The donor verifies that he/she has no history of:

1. Risky sexual behaviour
2. Use of illicit drugs
3. Tattoos or piercings in the last six months
4. Communicable disease
5. Metabolic syndrome (overweight, high blood pressure, fatty liver and/or Diabetes)
6. Any type of Cancer or active Autoimmune Disease
7. Risk factors for acquisition of HIV, Syphilis, Hepatitis B, Hepatitis C, Prion Infection or any Neurological Disease
8. Gastrointestinal comorbidities: e.g. Inflammatory Bowel Disease, Irritable Bowel Syndrome, Chronic Constipation or Diarrhoea
9. Receipt of Blood Transfusion in the preceding six months
10. Antibiotic use or any systemic immunosuppressive agent in the past three months prior to stool donation
11. Receipt of any type of Live Vaccine within three months prior to stool donation
12. Chemotherapy in the last three months.
The aim is to encourage proper Randomised Control Studies to be Observational Outcomes Study, it is not a Randomised Control Trial. Pathogenic state known as (Dysbiosis'). Crobes is the gut microbiome (especially when it shifts composition to a microbiome in non-communicable diseases. The chief origin of these microbioces is the gut microbiome (especially when it shifts composition to a pathogenic state known as (Dysbiosis').

A recent very interesting study shows that in patients with Irritable Bowel and Chronic Fatigue Syndrome, there is an authentic blood microbiome (especially when it shifts composition to a pathogenic state known as (Dysbiosis').

This study has significant limitations as it is a retrospective Observational Outcomes Study, it is not a Randomised Control Trial. The aim is to encourage proper Randomised Control Studies to be carried out in this area, because our Observational Outcomes Study here showed benefits amongst many patients, so this area is worth investigating further.

From our current study and from the effectiveness of Faecal Microbiome Transplantation, it would appear that this hypothesis is the first event that can result in Chronic Fatigue Syndrome associated with Irritable Bowel Syndrome [40].

6. Conclusion
Faecal Microbiome Transplantation is a safe, and from this study, an encouraging treatment for Chronic Fatigue Syndrome associated with Irritable Bowel Syndrome. This study argues for carrying out a Randomised Controlled Study of Chronic Fatigue Syndrome and Irritable Bowel Syndrome patients.
Table 2  
Chronic Fatigue Syndrome treated with oral approaches.

<table>
<thead>
<tr>
<th>Patient</th>
<th>% Improved</th>
</tr>
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<tbody>
<tr>
<td>(F) Age 67 Chronic Fatigue Syndrome since 2007, associated with Insomnia, we have been treating her since 2010 and the response has been modest, but we have managed to maintain that modest degree of response.</td>
<td>35%</td>
</tr>
<tr>
<td>(F) Age 31 This patient has had Chronic Fatigue Syndrome since childhood, we have been treating her since the early 1990s. We have had modest improvement and we have managed to maintain that, but nothing further than that and her energy remains well below that of her peers.</td>
<td>40%</td>
</tr>
<tr>
<td>(F) Age 71 Chronic Fatigue Syndrome and Irritable Bowel Syndrome for 20 years. We have been treating her since 2000. We have had modest but maintained improvement in the Irritable Bowel Syndrome and Chronic Fatigue Syndrome.</td>
<td>35%</td>
</tr>
<tr>
<td>(F) Age 75 This patient has had Chronic Fatigue Syndrome since 1986. We have been treating her using various approaches over these years and have had marginal improvement only</td>
<td>10%</td>
</tr>
<tr>
<td>(F) Age 49 30-year history of Chronic Fatigue Syndrome, moderate improvement only. I have been seeing her for 20 years.</td>
<td>30%</td>
</tr>
<tr>
<td>(M) Age 40 25-year history of Chronic Fatigue Syndrome, using oral approaches. Also, Irritable Bowel Syndrome for the same period of time. Moderate improvement only. I have been seeing him for 15 years.</td>
<td>30%</td>
</tr>
<tr>
<td>(F) Age 64 40-year history of Chronic Fatigue Syndrome, I have been treating her for 20 years, modest improvement only in her Chronic Fatigue symptoms.</td>
<td>35%</td>
</tr>
<tr>
<td>(F) Age 49 Chronic Fatigue Syndrome and Irritable Bowel Syndrome for 20 years. I have been treating her since June of this year. She has more or less complete improvement with oral approach.</td>
<td>90%</td>
</tr>
<tr>
<td>(M) Age 68 Chronic Fatigue Syndrome for 30 years, Irritable Bowel Syndrome for the same time. We have been treating her for nine months. She has had modest improvement.</td>
<td>35%</td>
</tr>
<tr>
<td>(F) Age 27 Chronic Fatigue Syndrome since 2002. We treated her for a year when I saw her initially in 2012, no significant improvement.</td>
<td>0%</td>
</tr>
<tr>
<td>(F) Age 70 Chronic Fatigue Syndrome for 30 years, Irritable Bowel Syndrome for the same time. We have been treating her for nine months. She has had modest improvement.</td>
<td>35%</td>
</tr>
<tr>
<td>(M) Age 44 10-year history of Chronic Fatigue Syndrome and Irritable Bowel Syndrome. We have been treating him for 18 months. We have had modest improvement only.</td>
<td>35%</td>
</tr>
<tr>
<td>(F)Age 71 Irritable Bowel Syndrome and Chronic Fatigue Syndrome for over 40 years. We have been treating her for 20 years with modest improvement only.</td>
<td>40%</td>
</tr>
<tr>
<td>(F) Age 30 10-year history of Irritable Bowel Syndrome and Chronic Fatigue Syndrome. We have been treating her for 2 years with modest improvement only.</td>
<td>20%</td>
</tr>
<tr>
<td>(F) Age 60 She has had Chronic Fatigue Syndrome and Irritable Bowel Syndrome for 20 years, we have been treating her intermittently since 2010. We have obtained modest improvement only.</td>
<td>30%</td>
</tr>
<tr>
<td>(F) Age 75 Chronic Fatigue Syndrome, Irritable Bowel syndrome for 20 years. Some significant improvement, by about 50%.</td>
<td>50%</td>
</tr>
<tr>
<td>(M) Age 42 Chronic Fatigue Syndrome for over 20 years as well as Irritable Bowel Syndrome. Marginal improvement only obtained.</td>
<td>10%</td>
</tr>
<tr>
<td>(F) Age 34 Chronic Fatigue Syndrome and Irritable Bowel Syndrome for 15 years. We have been treating her since 2013 and she has had significant improvement.</td>
<td>75%</td>
</tr>
<tr>
<td>(F) Age 54 Chronic Fatigue Syndrome and Irritable Bowel Syndrome for 20 years, we have been treating her for five years and she has obtained significant improvement by 70%.</td>
<td>70%</td>
</tr>
<tr>
<td>(F) Age 25 10-year history of Chronic Fatigue Syndrome. We have been treating her since 2014, she has obtained very good improvement, up to 90%.</td>
<td>90%</td>
</tr>
<tr>
<td>(F) Age 35 Chronic Fatigue Syndrome and Irritable Bowel Syndrome for 6 years, we have been treating her for three years and she has obtained 90% improvement.</td>
<td>90%</td>
</tr>
</tbody>
</table>

### Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

### References


