

Adverse events and unintended consequences

Dr. Robert J Porter,
Royal Devon and Exeter NHS
Hospitals Foundation Trust

Woman who had poo transplant to treat superbug infection becomes **OBESE** after being given faeces from her overweight daughter

Weight Gain After Fecal Microbiota Transplantation

Neha Alang¹ and Colleen R. Kelly²

¹Department of Internal Medicine, Newport Hospital, and ²Division of Gastroenterology, Center for Women's Gastrointestinal Medicine at the Women's Medicine Collaborative, The Miriam Hospital, Warren Alpert School of Brown University, Providence, Rhode Island

Fecal microbiota transplantation (FMT) is a promising treatment for recurrent *Clostridium difficile* infection. We report a case of a woman successfully treated with FMT who developed new-onset obesity after receiving stool from a healthy but overweight donor. This case may stimulate further studies on the mechanisms of the nutritional-neural-microbiota axis and reports of outcomes in patients who have used non-ideal donors for FMT.

Keywords. *Clostridium difficile* infection; fecal microbiota transplantation; gut microbiota; obesity.

Microbiome and Weight

- Microbiomes in obese and lean humans
 - decreased Bacteroidetes in obesity [Nature 2006; 444: 1022-3]
 - twin studies – complex relationships at gene, organism, diversity and metabolic pathways [Nature 2009; 457: 480-85]
- Animal models
 - obese mice donors increase adiposity in recipients
 - co-housing with lean mice reverses changes (coprophagic)
 - detectable alterations in Bacteroidetes populations [Science 2013; 341: 1241214]

Obese to lean

- Metabolic syndrome
 - increased insulin sensitivity [Gastro 2012; 143:913-6]
 - higher Bacteroidetes in obesity [cf previous slide]
 - increased populations of butyrate producing organisms



PORTER'S POO

Your weight may go up as well as down
The models used are for illustration purposes only, and you may
need to be called Barbie to achieve these effects
Your house is at risk if you do not keep up repayments



Current trials for FMT on clinicaltrials. gov

C. diff
IBS
UC
Crohn's
Pancreatitis
Metabolic Syndrome
AML therapy
Resistant organisms
Primary Sclerosing Cholangitis
Constipation
NASH
Obesity
Pseudo-obstruction
Post-HSCT
Hepatic encephalopathy
Epilepsy
TIIDM
MRSA
HIV
Hep B chronic liver failure
Pouchitis
Alcoholic hepatitis
NAFLD
Kidney Transplantation
Incontinence
Liver Transplantation
Total Body Irradiation
Chemotherapy
Multiple Myeloma

Autism
Parkinsons
Behaviour
Circadian rhythm
Asthma
Hypertension
Ischaemic heart disease
Food allergy
Behçets
Colorectal Cancer
T1DM
MS
Rheumatoid
SLE
Necrotising enterocolitis
Stroke
Depression
Coeliac disease

Microbiota and cancer

- Potential implications reported in
 - gastric cancer [Sci Rep 2017; 21: 15957]
 - colon cancer [J Cancer 2017; 8: 3378-95]
 - multicentric lymphoma in dogs [Vet Comp Onc 2017; in print]
- But we test extensively for BBVs pre FMT

Published data on side effects

- Systematic Review: Adverse Events of Fecal Microbiota Transplantation, Wang et al 2016
- Adverse events in faecal microbiota transplant: a review of the literature, Baxter et al 2016

Common adverse events (FMT for CDI)

- Alteration of bowel habit (IBS-like/constipation/irregularity) (3%)
- Abdominal distension, bloating or cramping (2%)
- Flatulence (2%)
- Diarrhoea (2%)
- Abdo pain (1%)
- Fever (1%)

Common adverse events (FMT for CDI)

- Generally mild, self-limiting and GI related

Procedural related events

- Endoscopy
 - mucosal tears
 - microperforations
 - aspiration
 - at least 2 deaths reported
 - witnessed aspiration at time of sedation for colonoscopy [Kelly et al, Am J Gastro 2014]
 - witnessed aspiration of FMT at OGD [Baxter et al, CID 2015]
 - (toxic megacolon and septic shock [Solari et al, CID 2014])

Fatal aspiration

- 80 y.o. male
 - vasculopathy, osteoarthritis, gout
 - recurrent CDI
- 2 x metro, 4 x vanc, 1 x fidax
- PMC confirmed on flexi-sig
- Failed radiological placement of NJ (? anatomical)
- Failed endoscopic placement of NJ (epistaxis)
- GA with endoscopic placement in distal duodenum

Fatal aspiration

- 150ml FMT
- Aspiration during 3rd 50ml aliquot
- Sepsis ensued
- Sputum = E. coli and PSAE
- Blood cultures = f/s E.coli
- Death 48 days post FMT
- Remained negative for C.diff (days 4, 11, 13, 42)

SUI

- Lessons and actions
 - Absolute transparency
 - Literature review
 - Reduced aliquots
 - Avoid sedation/GA where possible
 - If used consider protected airway methods
 - Caution in patients where things just don't go quite to plan

