Faecal microbiota transplants and microbial ecosystem therapeutics as a treatment for recurrent *Clostridium difficile* infections

**Background**

*Clostridium difficile* infection (CDI) is one of the most common hospital-acquired infections. It is originated by a gram-positive strict anaerobic rod shaped bacteria, which can induce from watery diarrhoea to pseudomembranous colitis and toxic megacolon, becoming recurrent in most cases.

In the United States, during the 2011, caused about 500,000 infections and 15,000 deaths, achieving a higher mortality rate than the human immunodeficiency virus (HIV). His pathogenesis seems to be related to perturbations of the intestinal microbiota, caused mainly by broad spectrum antibiotics altering the balance of microbial populations, allowing the pathogen grow and infect. It can be contracted by eating vegetable cells or spores. During the passage through the stomach most viable cells die, but spores persist, germinate in the small intestine, and multiply in the colon. The intestinal mucosa promotes the adhesion of *C. difficile* to the epithelium, where it produces enzymes and A and B toxins, responsible for causing severe inflammation, tissue degradation, watery diarrhoea and pseudomembranous colitis.

As it is difficult to treat and shows high failure rates for antibiotic therapy, there is an increasing interest in finding new promising therapies, as faecal microbiota Transplantation (FMT) and Microbial Ecosystem Therapeutics (MET), both aimed to restore the gut microbiota.

**What are FMT and MET?**

These are two techniques used to restore the normal intestinal microbiota composition, both aimed to remove *C. difficile* infection, especially in recurrence cases. The FMT consists in donating stool from a healthy person to a sick one, they were implemented in 1985 as a clinical treatment addressed to humans. With the time, have evolved to MET, which are microbial communities synthesized in vitro, simulating faces composition, making the practice more reproducible, simple and safe.

**Microbiota: healthy vs ill people**

- Healthy
  - Bacteroides and Firmicutes
  - γ-Proteobacteria

- Ill
  - Bacteroides and Firmicutes
  - γ-Proteobacteria

**Obtaining the microbiota**

Donor selection

- Questionnaire in order to see if candidates are quality
- If they are printing, undergo blood and faecal tests

Acceptation or derangement of stool

**C. difficile endospores**

**FMT: There is no need to be related with the patients because there is no problem of compatibility. Also there are faecal banks like OpenSis.**

MET: Only donor selection in the first phase of isolation. There are laboratories that produce MET like the probiotic RePOOPulate.

**Why are FMT and MET useful?**

They are useful because restore the normal microbiota, while antibiotics still cause more damage, promoting recurrent infections.

- How does microbiota suppress *C. difficile*?
- -Competing for the same nutritional nche
- -Producing molecules and bacteriocins with toxicogenic activity
- -Interacting indirectly with its lifecycle

It is a simple, safe and effective technique, normally without complications. If it occurs, usually is due to the administration form and not because of the technique itself.

**Results and success of the techniques**

Van Nood et al., 2013, evaluated efficacy of FMT vs antibiotics.  
- Vancomycin + bowel lavage: 23% resolution
- Vancomycin: 31% resolution
- Bowel lave + FMT: 81% resolution

Brand et al., 2012, analysed the response to FMT of 77 patients with recurrent CDI.  
- The primary cure rate was 91% (resolution of symptoms ≤90 days after treatment)
- The secondary cure rate was 98% (after one further course of vancomycin with or without repeat FMT)

Petrol et al., 2013, develop a MET called RePOOPulate. Have been tested in two patients, both remained symptom-free after the treatment and restore the normal bowel pattern.

**Legislation**

FMT and MET are considered by the Food and Drug Administration (FDA) as drugs with biological origin.

In July 2013 FDA accepted FMT as a treatment for patients those do not respond to the conventional procedure with antibiotics.

In other cases, if someone wants to apply those techniques, the responsible must request a new investigational drug application, in order to be accountable for the practice.

**Conclusions**

- FMT and MET are promising techniques, but there is still a lot of work to do: understand how they exactly work, optimize the composition of the infusions, doses, routes of administration, study the long-term effects and define the legal issues.
- There is a tendency to prioritize the investigation of the MET not only for treating CDI, but also other diseases. In the future it might be synthesized different MET aimed at specific groups of patients.
- It’s surprising how a natural technique with stool or derived stool products, could work even when antibiotics can’t remove the infection.

**References**