Wales faecal microbiota transplant (FMT) procedural guidance for recurrent *Clostridioides difficile* infection

Gweithgor *C. difficile* Cymru
Wales *C. difficile* Working Group

INTRODUCTION

Recurrent Clostridioides difficile infection (rCDI) is defined as recurrence of CDI within 30 days of a previous CDI episode. rCDI occurs in approximately 25% of cases and is associated with significant morbidity and mortality. As the number of recurrences a patient experiences increases the likelihood of successful treatment with antibiotics decreases. After a second recurrence the risk of further recurrence is 50%. Some patients do not respond to antibiotics, and this is termed refractory CDI. This may also be an indication for FMT.

Faecal microbiota transplant (FMT) is an evidence-based treatment which restores microbiota diversity and cures rCDI in approximately 90% of cases, regardless of the prior number of recurrences.[1] NICE and All-Wales Medicines Strategy Group guidance recommends FMT in adults who have had two or more episodes of CDI.[2,3]

Despite the evidence of FMT efficacy in treating rCDI, uptake is not widespread and, where it is used, it is sometimes only used after multiple episodes (i.e., >2)[4], which leads to unnecessary delays in treatment and subsequently excess patient morbidity. FMT is cost effective, saving at least £1500 per patient with 2 or more episodes of rCDI.

Evidence suggests that barriers to FMT delivery relate predominantly to physician rather than patient factors.[5,6]

The aim of this document is to provide a practical guide to clinicians wanting to provide FMT, giving them confidence to deliver this highly effective therapy to appropriate patients. Briefly, it will cover:

1. Patient selection
2. Donor material
3. Route of administration
4. Patient preparation
5. The procedure
6. Post procedure

PATIENT SELECTION

- Any patient who has had two or more episodes of CDI.
- FMT can be used in immunocompromised patients in whom evidence indicates there is no increased rate of adverse events.

DONOR

- National guidance recommends using material from a stool bank, for example, the Microbiome Treatment Centre (MTC), Birmingham.
- Material is extensively screened and is from healthy donors who have passed a medical assessment.
- The MTC is licensed by the MHRA to provide material on a named-patient basis for use in rCDI.
- Requests are made via email and material delivered by the Blood Bikes.
- Current cost is £1300 for 50ml, which is the dose for upper gastrointestinal (GI) treatment (note that treatment through the lower GI route requires 3 times the volume, and cost).

ROUTE OF ADMINSTRATION

FMT can be delivered either by upper GI (nasogastric tube [NGT], nasojejunal tube [NJT] or gastroscopy) or lower GI (colonoscopy) route. Colonoscopy, with delivery to the terminal ileum or caecum, is the most efficacious route with an approximate cure rate of 90%, compared with approximately 82% via the upper GI route .[7]

Given the morbidity of the majority of patients with rCDI, many are not ideal candidates for colonoscopy and, due to the increased costs associated with this delivery route, it is not recommended by NICE. Upper GI treatment, in particularly via NGT, is easy to deliver and is highly efficacious. Only 50ml of material is administered and is tolerated well. A NJT is much more difficult to place but reduces the small risk of vomiting/regurgitation and can be performed without sedation.[6]

Gastroscopy is less well tolerated, compared with an NG treatment, but increases the risk of retching and aspiration.

PATIENT PREPARATION

- The patient should be treated with CDI antibiotics for 4 days prior to FMT. If the patient is severely symptomatic, treatment can be continued until FMT is arranged.
- Antibiotics should be stopped the evening prior to FMT.
- Bowel preparation is needed for lower GI administration, but not for the upper GI route. Patients should be nil by mouth for 6 hours before the FMT.
- For the upper GI route consider giving a dose of a PPI 2 hours prior to FMT.

THE PROCEDURE

UPPER GI (NGT / NJT)

- NGT/NJT placed according to local protocol and position confirmed.
- Consider administering a prokinetic (metoclopramide) 2 hours prior to FMT if concerned about nausea and vomiting (N.B. in the rare situation where patients may be “nil by mouth” but have a NG tube in situ, PPI and prokinetic agent may be administered parenterally).
- Draw material into a 60ml enteral syringe and have a syringe of sterile water available.
- Position patient on a trolley sat up to at least 45 degrees.
- Position yourself behind the patient with the NGT/NJT over the patient’s shoulder.
- For patient reassurance, it is helpful to have an assistant in front of the patient to talk to and reassure the patient.
- Allow the patient to sip water or cordial.
- Ensure the NGT/NJT is flushing easily with water.
- Switch to the FMT syringe and ensure it is securely connected.
- Ensure the patient is comfortable before starting to, slowly, administer the material over 2-3 minutes.
- Disconnect the syringe and flush the NGT/NJT with sterile water.
- Give loperamide (4mg) after transplant completion and repeat at 4 hours.
- Leave NGT/NJT in situ for 1 hour before removal.
- Patients can then be discharged and can eat 1 hour following the procedure if, the clinician is happy with the patient's condition.

LOWER GI (COLONOSCOPY)

- Patient is prepared as per local protocol.
- Consent patient that this is not a diagnostic procedure as withdrawal time will be suboptimal for a diagnostic colonoscopy.
- Draw up the material (3x aliquots) into syringes prior to the procedure and cap the syringes.
- Scope the patient as far into the colon as possible (ideally proximal transverse), keeping insufflation to a minimum.
- In the terminal ileum or caecum, all material is infused through the working channel of the scope.
- If possible, the patient should be given loperamide (2mg) whilst the scope is still in the caecum.
- Withdraw the scope rapidly and remove air.
- Patient should remain on the trolley for two hours post procedure.
- Patient can then be discharged as per local endoscopy protocol.

POST PROCEDURE

- The patient should be aware that mild GI side effects, such as bloating and cramps, are common after FMT.
- If the patient is asymptomatic, there is no need to repeat *C. difficile* testing to confirm cure.
- Patients will need a telephone review at 7 days, or on discharge (whichever is sooner) and 90 days post procedure, as per MTC protocol.
- Good antimicrobial stewardship should be closely observed for FMT patients as the greatest risk of recurrence is from further antimicrobial treatment.

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