Therapeutic options for *Clostridioides difficile* infections

Doctoral (Ph.D.) thesis

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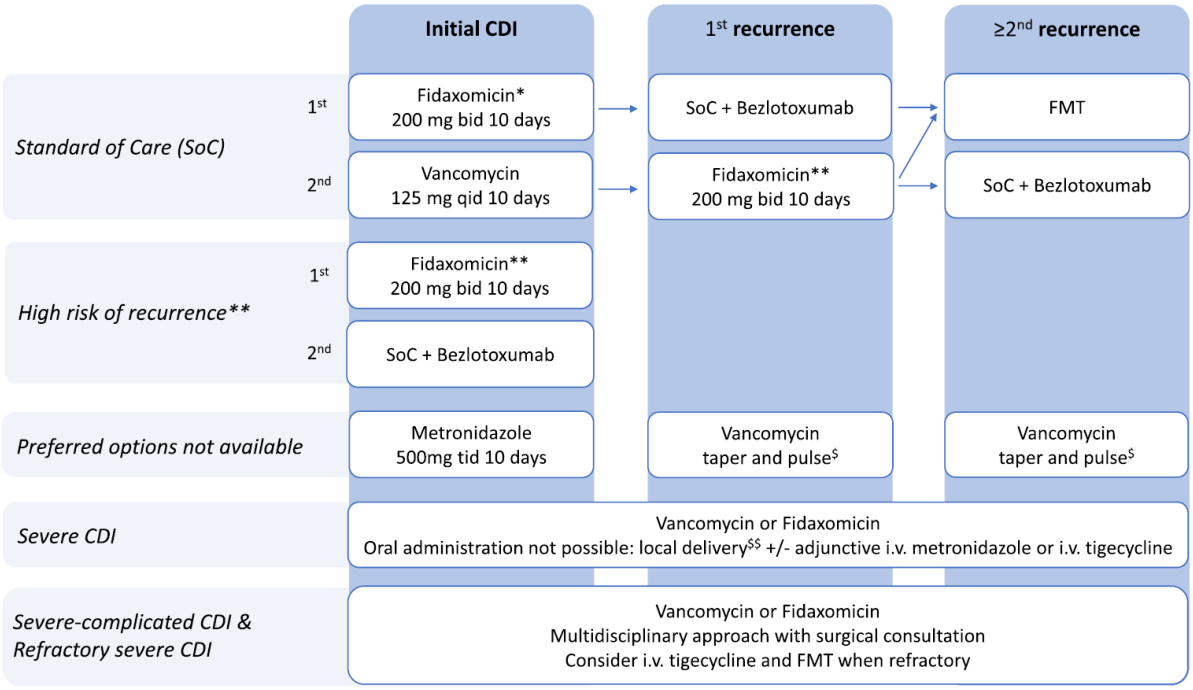
1. Introduction

The treatment of *Clostridioides* (formerly known as "*Clostridium*") *difficile* infections is currently only partially solved. In simple cases, antibiotics in protocols usually lead to resolution of symptoms, but recurrence is still common. In complicated or recurrent infections, the potential for treatment refractoriness or further recurrence varies depending on the antibiotic used.
Although it has been cited as a classic example of nosocomial infection, in the majority of cases the pathogen is carried by the individuals prior to hospital admission [1]. Severe symptoms are caused by toxin-producing strains. Spread in the hospital environment is facilitated by the resistance of the spores to alcohol-based hand disinfectants and commonly used surface disinfectants. Handwashing with soap and the use of sporocidal disinfectants can limit the spread in hospitals – this is particularly important for toxin-producing strains.
For the treatment of symptomatic infection, depending on the recurrance and severity of the course, metronidazole, vancomycin and possibly fidaxomicin as a first step are recommended in national recommendations [2, 3].Because of the frequent recurrence observed with metronidazole, the updated international recommendations currently recommend metronidazole only as a last resort. In recurrent infection, stool transplantation may be performed. Several clinical trials have compared the efficacy of these therapeutic options [4], but other drugs are also being studied for their efficacy [5-9], including bezlotoxumab and tigecycline, which are recommended by the European Society of Clinical Microbiology and Infectious Diseases (ESCMID, Figure 1).



* Risk stratification for risk of recurrence may be applied for selective use of fidaxomicin in case of limited access or resources.
** Consider extended fidaxomicin: 200 mg bid on day 1-5, 200 mg q48h on day 7-25. Most important risk factor for recurrence is age >65-70 years. Additional risk factor(s) to consider are healthcare-associated CDI, prior hospitalization ≤ 3 months, prior CDI episode, continued non-CDI antibiotic use, and PPI therapy started during/after CDI diagnosis. The risk of recurrence is assumed higher with more risk factors present.
$ Vancomycin taper and pulse: 2 weeks 125 mg qid, followed by 1 week 125 mg bid, then 1 week 125 mg qd, then 1 week 125 mg q48h, and finally 125 mg q72h for 1 week.
$$ Rectal or nasoduodenal delivery

Figure 1. ESCMID recommendation for the treatment of CDI.

In terms of mechanism of action, the methods used in the protocols can be divided into three groups: antibiotics (metronidazole, vancomycin, fidaxomicin, tigecycline), monoclonal antibodies (bezlotoxumab) and faecal component administration (faecal transplantation). Antibiotics can lead to cure by inhibiting bacterial multiplication (bacteriostatic) or killing them directly (bactericid), monoclonal antibodies by binding to toxins and inhibiting them, and stool components by restoring colonisation resistance in addition to killing bacteria directly (phages). Even with the recently published results with known bacterial composition of stool-derived preparations [10, 11], it is not clear exactly what is required from donor stool to restore colonisation resistance. For example, the

cited publication highlights specific bacterial strains, while viruses and fungi were removed in the preparation. On the other hand, other components (free fatty acids, proteins, other metabolites) may also have been present in significant amounts.
Depending on the route of administration, faecal transplantation can be stressful for patients. The lyophilised, encapsulated formula used in our research minimises the discomfort associated with transplantation. The potential role of the gut flora has been described in several diseases [12, 13], and research in this area could be boosted by the use of encapsulated faecal lyophilisation.

2. Aims

The methodology of faecal transplantation is, with a few exceptions, based on the administration through a tube (nasogastric, nasojejunal, colonoscopy). Although the 100 ml volume of our protocol is usually not burdensome for the patients, the method of administration causes discomfort.

The main topic of this thesis is the workflow we have developed, whereby the suspension doses used in the previous protocol are lyophilised, filled into capsules and stored in the freezer until use. Our aim was to improve the storability, tolerability and flexibility of the process.

In addition to testing the efficacy of capsules containing lyophilised faeces, we sought to answer the following questions:

- Does the cure rate decrease if only the supernatant or only the sediment of the suspension is used?

- What effect do storage time and temperature have on the survival of bacteria in samples?

- What effect does lyophilisation have on the protein and short-chain free fatty acid content of the samples?

- What changes in protein and short-chain free fatty acid composition and metagenome can be observed in patients' faecal samples after faecal transplantation?

- What differences can be observed between the protein and short-chain free fatty acid composition of the intestinal flora of healthy patients and patients treated for *Clostridioides difficile* infection?

- What is the predictive value of IgG levels against *Clostridioides difficile* toxin A and B for recurrence?

- What is the rate of reduction in insulin requirements after faecal transplantation in type 2 diabetic patients?

3. Methods

The production of the capsules and the related laboratory tests were performed at the Department of Medical Microbiology and Immunology, University of Pécs, Clinical Centre (Hungary), the clinical testing of the capsules was performed at the Department of Infectology of the 1st Department of Medicine, University of Pécs, Clinical Centre (Hungary).

Samples from a single donor were used throughout the study period. A total of 9 stool samples were processed and the corresponding measurements were also performed on these samples.

Between January 2018 and December 2019, a total of 28 patients received lyophilised stool capsules.

Donor selection (Table 1) and laboratory screening (Table 2) were carried out in accordance with international recommendations.

- Age <18 years or >65 years
- Body Mass Index (BMI) >30 kg/m^2
- Metabolic syndrome
- Moderate to severe undernutrition
- History of antibiotics use in the last 6 months
- Diarrhea within the last 3–6 months
- History of *Clostridioides difficile* colitis
- Immune disorder or use of immunosuppressive medications
- History of drug use or other recent risk factor for HIV or viral hepatitis
- History of travel to a tropical region in last 3 months
- Any gastrointestinal illness (IBD: Inflammatory Bowel Disease, IBS: Irritable Bowel Syndrome, gastrointestinal malignancy, or major surgery) or complaints
- History of autoimmune or atopic illness
- History of chronic pain syndrome (fibromyalgia, chronic fatigue syndrome)
- Neurologic or neurodevelopmental disorders
- History of malignancy

Table 1. Criteria of donor selection

Tests	Blood	Stool
Bacteria	*Treponema spp.*	Enteric pathogen culture: *Salmonella, Shigella, Campylobacter spp.* *Helicobacter pylori* EIA VRE antibiotic sensitivity test to prevent to use stool containing polyresistant strains (16)
Viruses	Hepatitis A virus IgM Hepatitis B surface antigen Anti-hepatitis C virus HIV 1 and 2	Norovirus EIA or PCR Rotavirus EIA
Parasites	*Entamoeba histolytica* *Strongyloides stercoralis*	Ovum and parasite *Microsporidia* *Giardia* fecal antigen/EIA *Cryptosporidium* EIA AFB for *Isospora* and *Cyclospora*
Others	Complete blood count Liver function test ESR and CRP	*Clostridium difficile* test PCR of Toxin genes Others

Table 2. Laboratory screening of the donor.

Faecal samples were collected at the donor's home. 60 g of faeces were homogenised in 200 ml of physiological saline on room temperature. The suspensions were filtered through metal pasta filters and centrifuged for 10 min (827 g). 100 ml of the resulting homogeneous suspension was further centrifuged for 15 min at 3309 g in a centrifuge precooled to 4°C. The supernatant was separated from the sediment, the latter being suspended in 10 ml of physiological salt solution for handling. The supernatant and the sediment were frozen in separate vessels at -20°C and lyophilised at -40°C under vacuum $4*10^{-4}$ mbar for 36 hours. The lyophilisates were homogenized in a mortar and filled into hard gelatine capsules of size "00" depending on their compressibility. Both the lyophilised sediment and the lyophilised supernatant required 4-6 capsules. Figure 2 summarizes the main steps of sample preparation. For comparison, note that a therapeutic dose in centres using conventional frozen stool is 30-40 capsules [14], in other protocols using lyophilised inoculum is 2-40 capsules [15-17].

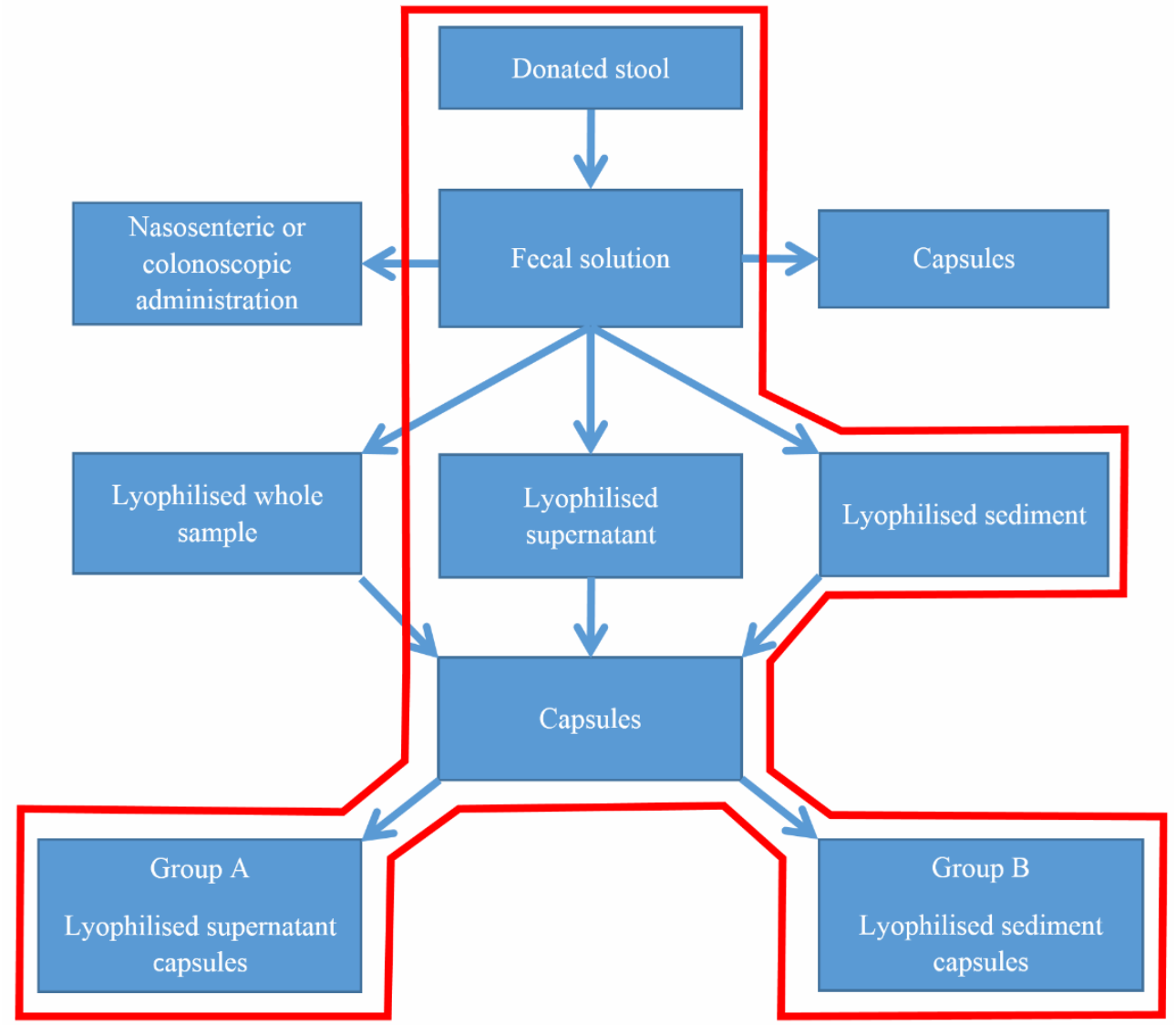


Figure 2. The main steps of sample preparation. Steps of our current protocol are marked by the red contour line.

As native capsules were found to be effective, enterosolvent capsules were not used in the clinical trial. Encapsulation of liquid faeces was also attempted, but the suspensions used to waterproof the capsules deformed the capsules and made the method more difficult, so these capsules were not used.

For the survival studies of the lyophilisates, samples were stored at four temperatures (-80°C, -20°C, +4°C and +20°C) and analysed for 6 months. Solid media (blood agar, eosin methylene agar, chocolate agar, vancomycin chocolate agar and Sabouraud agar) were used as media and colony forming units (CFU) were counted after 48 h of parallel aerobic and anaerobic incubation (30°C).

The protein analysis was performed on faecal samples from 4 patients before and after faecal transplantation and before and after donor lyophilisation at the Institute of Bioanalysis, University of Pécs, Medical School (Hungary). The samples were stored at -80°C and prepared for microchip electrophoresis according to the protocol developed by Makszin et al [18]. Calibration curves were used to determine the molecular weights of the components and the results were expressed as a percentage of the area under the curve (AUC%).

Short-chain free fatty acids were also determined in pre- and post-transplant samples from four patients and before and after donor lyophilisation. In addition, samples from 6 healthy volunteers were analysed. The sample preparation and measurements were also performed at the Institute of Bioanalysis, according to the protocol developed there. Components were identified from the gas

chromatographic measurement data using an internet database (NIST MS Search 2.0 library [19]) and peaks of known internal standards.
For metagenomic analysis, pre- and post-transplant samples from the same 4 patients selected for protein and fatty acid analysis, as well as native donor stool, lyophilised stool sediment and lyophilised stool supernatant from the donor were sent to the Institute of Clinical Molecular Biology, Kiel, Germany. These samples were subjected to 16S rRNA sequencing according to the protocol described in this thesis [20, 21]. From the data obtained, alpha distribution, beta diversity and differential abundance analysis were determined.
Blood samples from patients treated for CDI (n=47, 15 negative controls from healthy volunteers) were used to measure antibody titres against *Clostridioides difficile* toxin A and B. Blood sera were prepared and measured according to a protocol developed by von Bechtolsheim et al. [22] at the Department of Medical Microbiology and Immunology, University of Pécs, Clinical Center (Hungary), using enzyme-linked immunosorbent assay (ELISA).
The rate of necessity of insulin needs after stool transplantation among patients with type 2 diabetes admitted for CDI who were concurrently treated with insulin was assessed by follow-up telephone interview (n=11).

4. Results

The main result of our research is a low tool- and labour-intensive workflow. With the exception of the centrifuge and the lyophilisation equipment, all equipment can be easily and cheaply obtained and replaced, and the whole workflow takes about 8 man-hours. 72 hours after the donor stool arrives at the laboratory, with the work of one assistant, we can offer patients a dose of 4-6 capsules containing lyophilised stool or store them at -20°C for later use. Accordung to the results of our clinical trial, samples stored in this way can be used effectively up to 6 months later. The capsules can be administered to patients immediately after removal from the freezer, without the need for thawing and other preparations as with frozen stool suspensions. Although lyophilisation requires additional equipment compared to the methodology used to produce capsules containing frozen faeces, the reduction in volume, ease of encapsulation and the flexibility of administration all tip the scales in favour of lyophilisation.

None of the 28 patients treated with the lyophilised stool capsules experienced any side effects. Group A patients (n=16) received lyophilised supernatant. Fifteen of them recovered after a single dose of capsules (93.75%). The history of the patients who did not respond to treatment prior to transplantation included 22 relapses. Relapses were seen in two cured patients and were successfully treated with fidaxomicin later on. One patient from group 1 passed away during follow-up, the cause of death was a comorbidity unrelated to CDI.

Patients in group B (n=12) received lyophilised faecal sediment. 8 patients were cured after one treatment and no recurrence was reported. One patient recovered after another stool transplantation and one after fidaxomicin administration.

The combined cure rate of the two groups after one treatment was 23/28 (82.14%) (Table 3).

	Successful	Non-succesful	Total
Group A	15	1	16
Group B	8	4	12

Table 3. Results of FMT on our study population.

Based on the bacterium culture tests, there is a 600-fold difference between the numbers of colony forming units of the faecal supernatant and the sediment. Survival showed an inverse correlation with storage time and temperature, which was in line with our preliminary expectations. Storage at -20°C was found to be an acceptable compromise between storage at -80°C and storage in a refrigerator or room temperature (Figure 3).

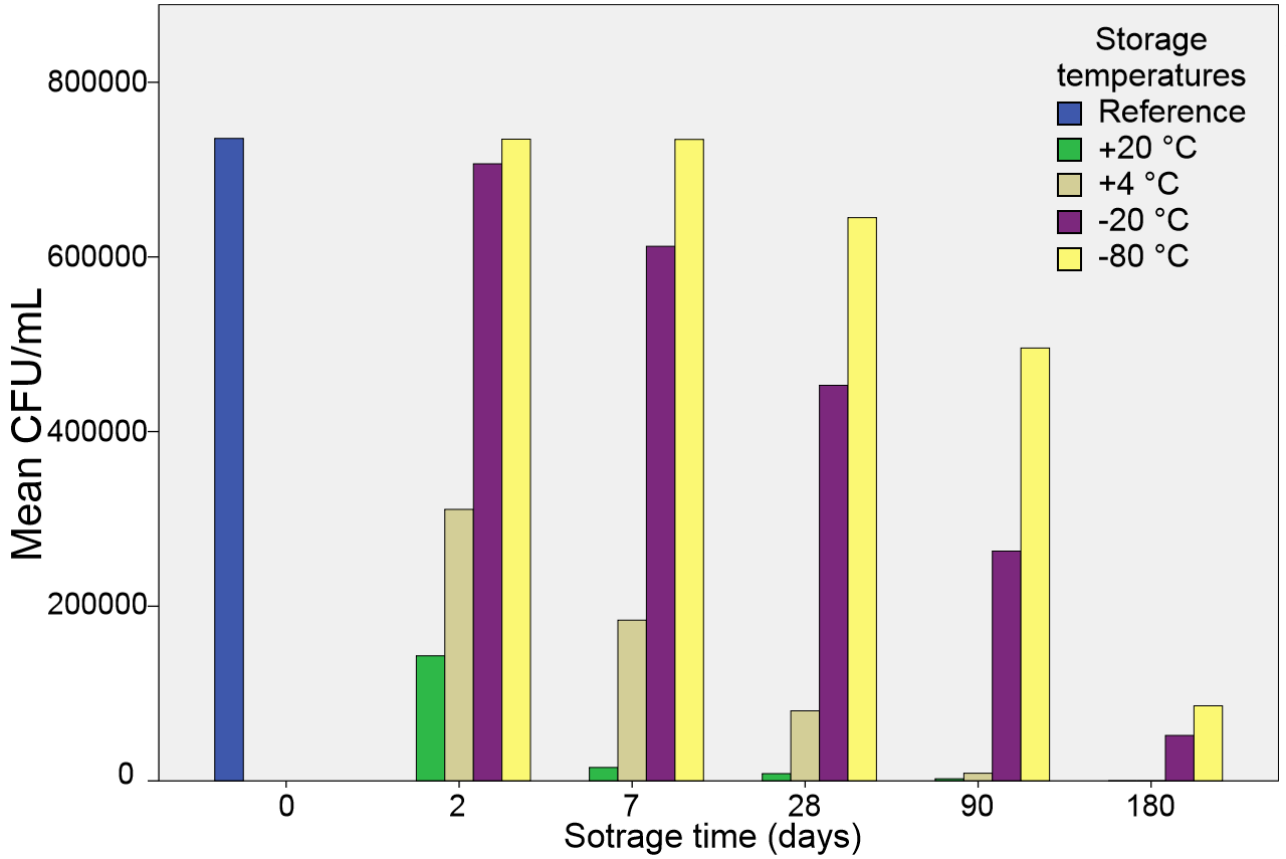


Figure 3. Colony forming unit counts of stored donor samples over time and storage temperatures.

Based on the results of the protein analyses, it is likely that lyophilisation and storage affect the protein content of the samples. Changes in components 5 and 7 were observed as a result of lyophilisation (Figure 4). Faecal transplantation had no effect on the relative proportions of proteins tested, based on the results of the 3 pairs of successful measurements.

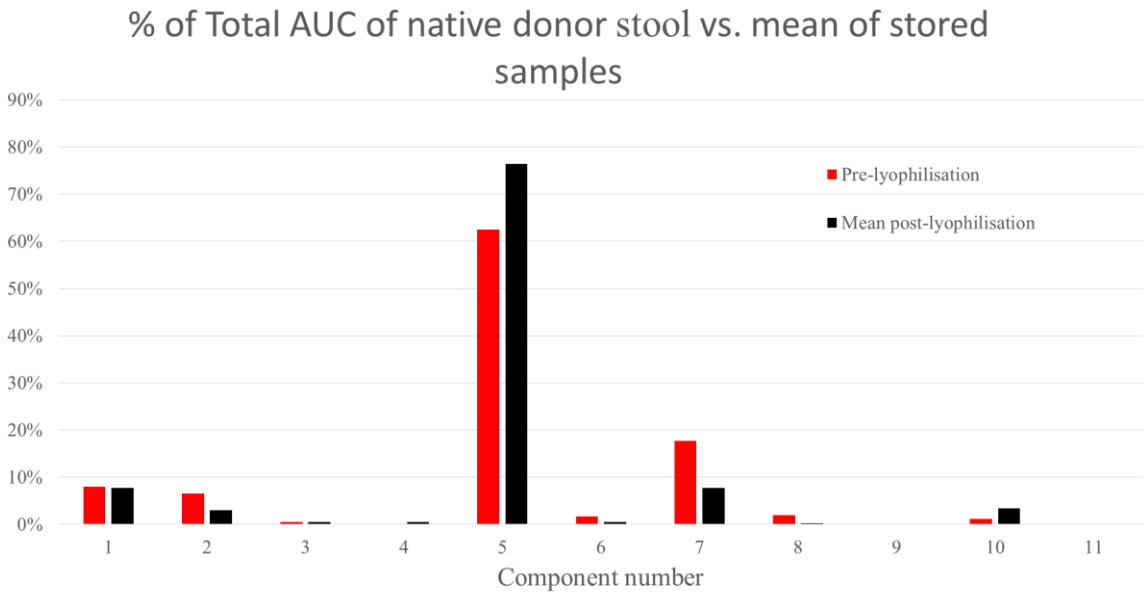


Figure 4. Changes of relative abundances of protein components after lyophilisation

Short-chain free fatty acid analysis found stools with a more diverse fatty acid composition in 5 of the 6 healthy controls (including donor) than in CDI patients before transplantation (Figure 5). After stool transplantation, we saw an increase in fatty acid diversity in the recipient samples, which became more similar to the values measured in the donor samples. In particular, the C4:0 (butyric acid) ratio increased in recipient samples after treatment (Figure 6-8).

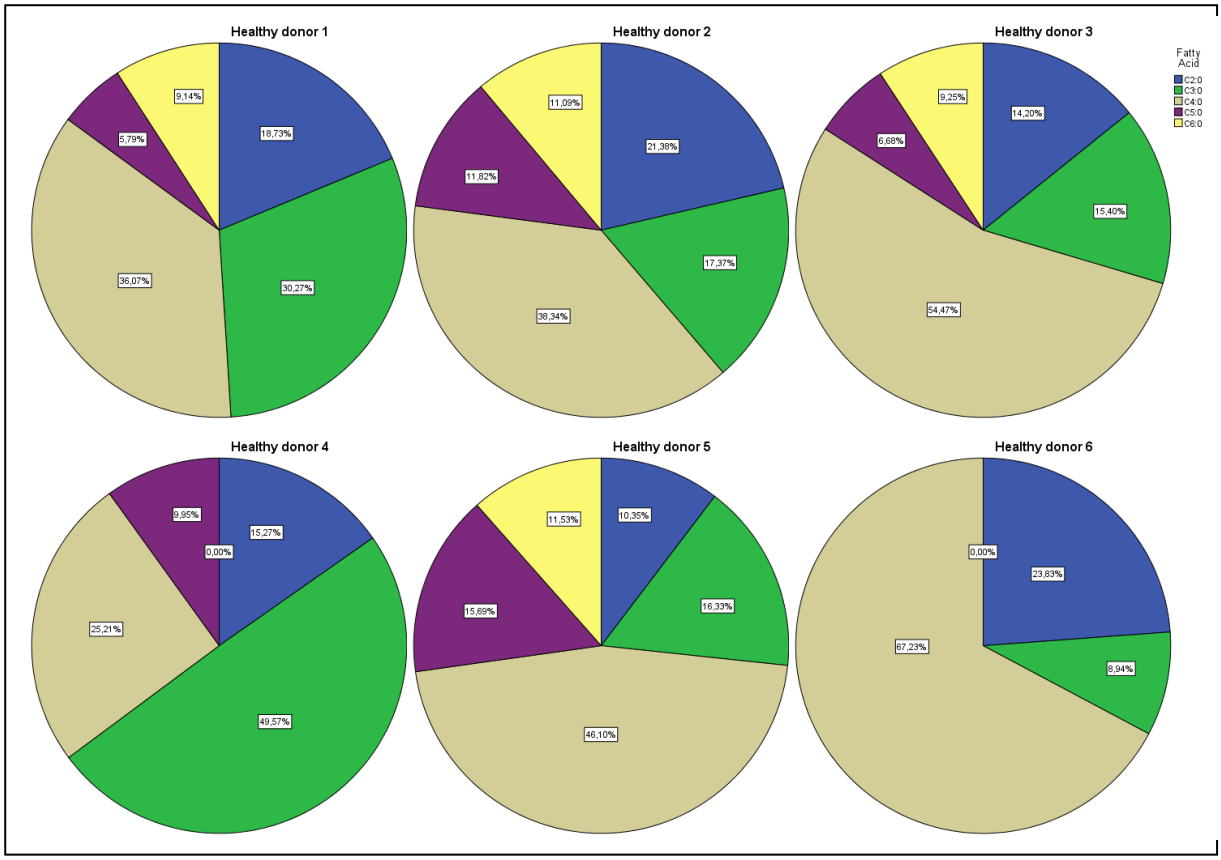
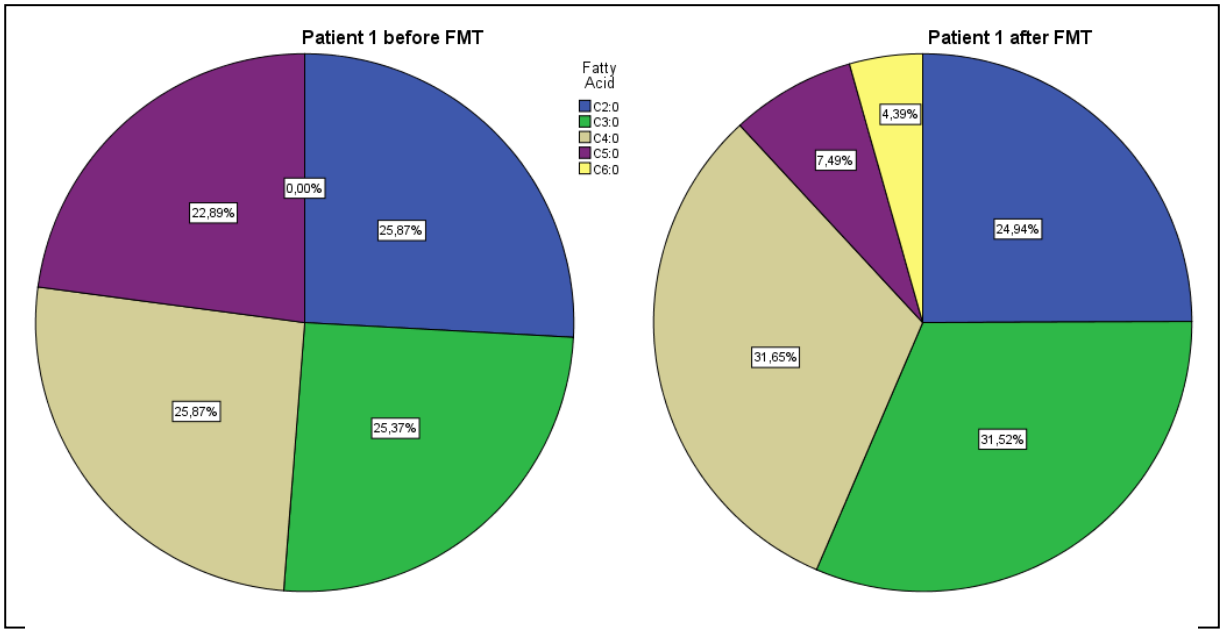


Figure 5. Short chain fatty acid compositions in samples from healthy donors.



F [illegible] **FMT.**

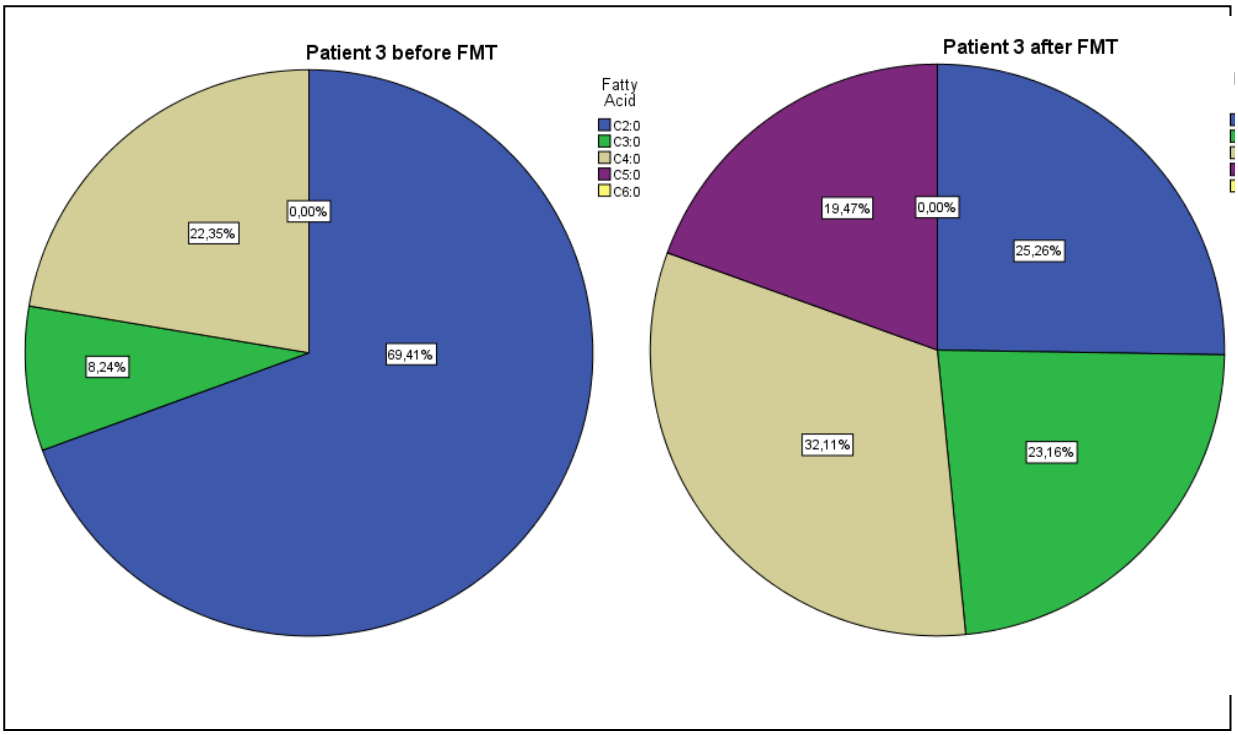


Figure 7. Short chain fatty acid compositions in samples from *Patient* #3 after FMT.

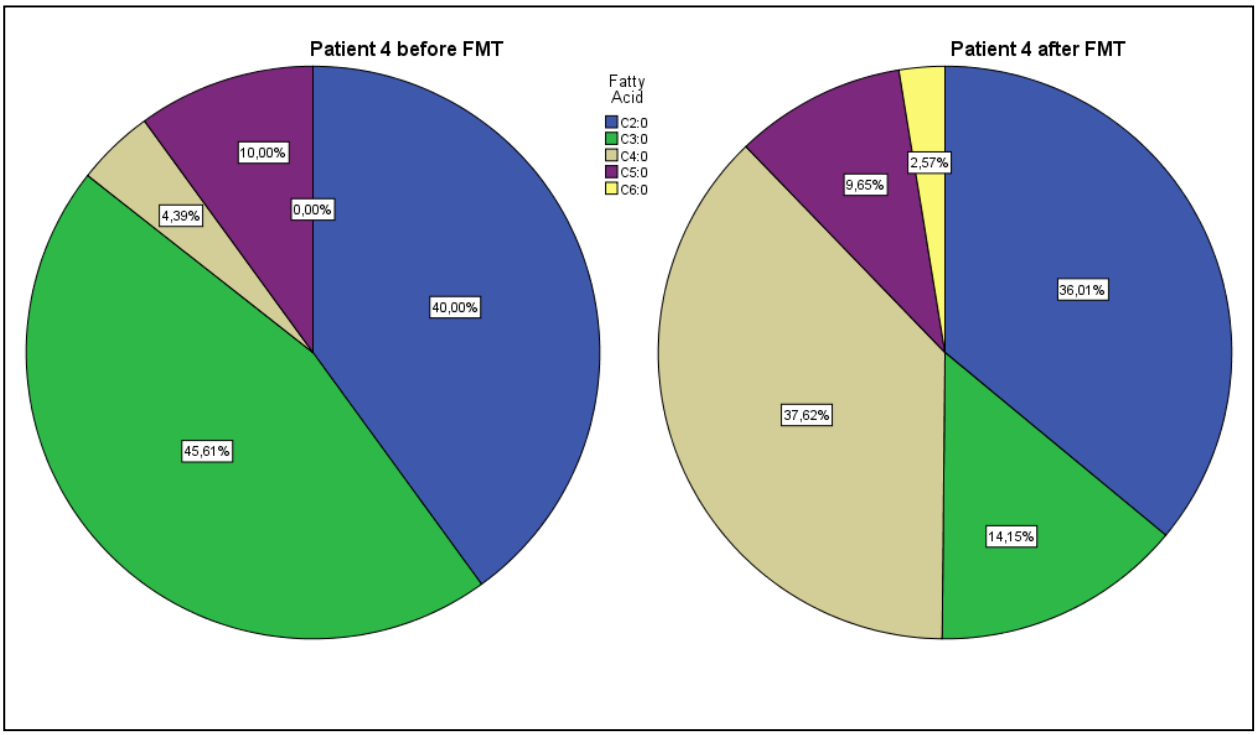


Figure 8. Short chain fatty acid compositions in samples from *Patient #4* before and after FMT.

Metagenomic studies showed a diversity shift in patient samples after faecal transplantation. The results showed that the diversity of patients' samples after transplantation was similar to that of the donor (Figure 9). The post-FMT sample of patient 4 could not be adequately sequenced. Given the low number of cases, no significant interindividual differences have been found. Comparison of donor samples (native, lyophilised supernatant and lyophilised sediment) showed differences at both genus and phylum level.

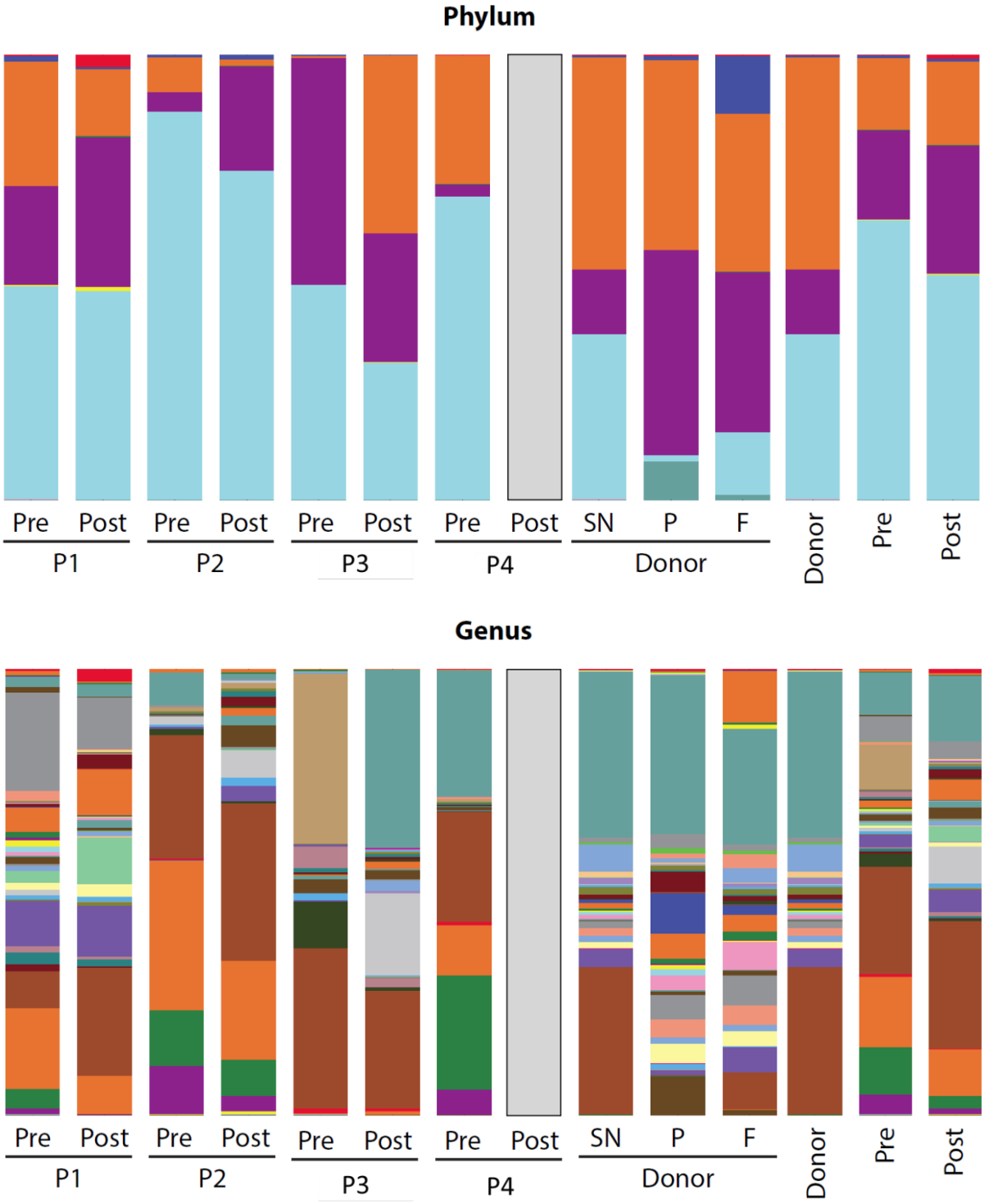


Figure 9. Taxa summaries on phylum and genus level. Pre: the mean of the four pre-FMT samples. Post: the mean of three post-FMT samples. SN: Supernatant. P: Pellet. F: Native faeces.

Studies on anti-toxin antibodies and recurrence have shown mixed results. Of the 47 patients who subsequently developed recurrence, all had low anti-toxin A antibody titres. The anti-B toxin titer assay did not show such consistency, with low levels measured in only 30% of recurrent cases (Figure 10).

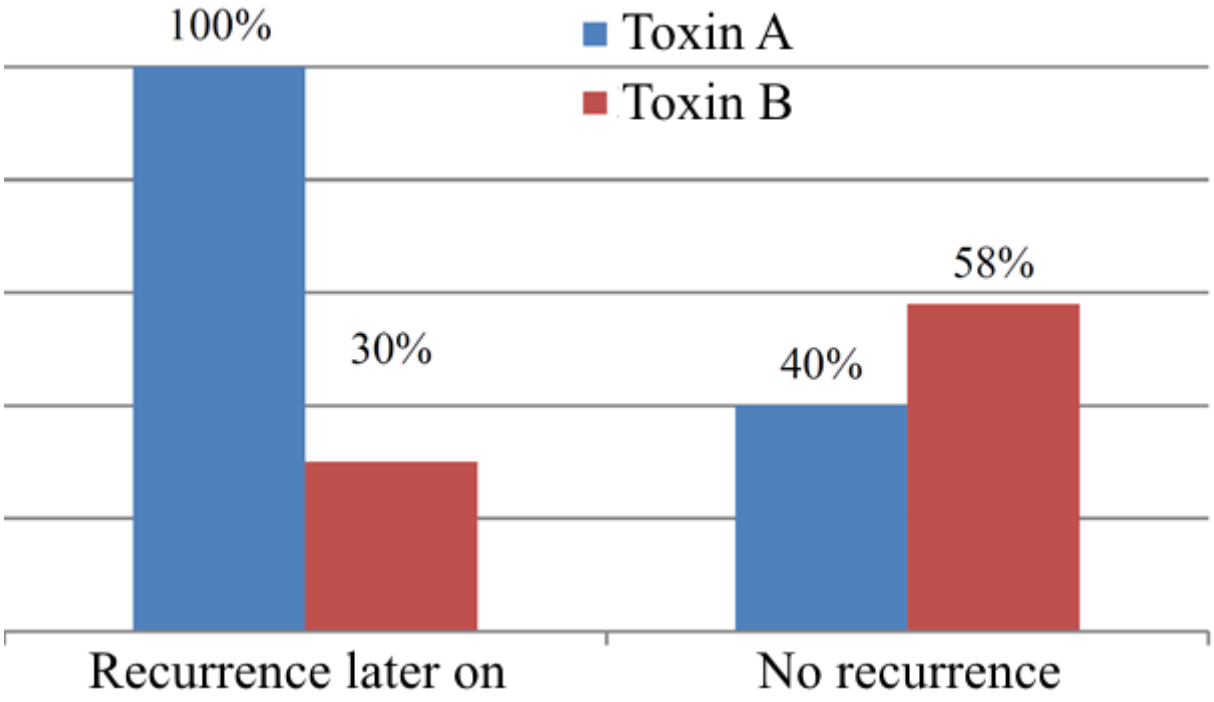


Figure 10. Low Toxin A (blue) and Toxin B (red) serum titer among CDI patients with and without recurrence later on.

In the group of insulin-treated diabetic patients who underwent stool transplantation, insulin doses had to be reduced in 6 patients and remained unchanged in 5 patients after the intervention (Figure 11).

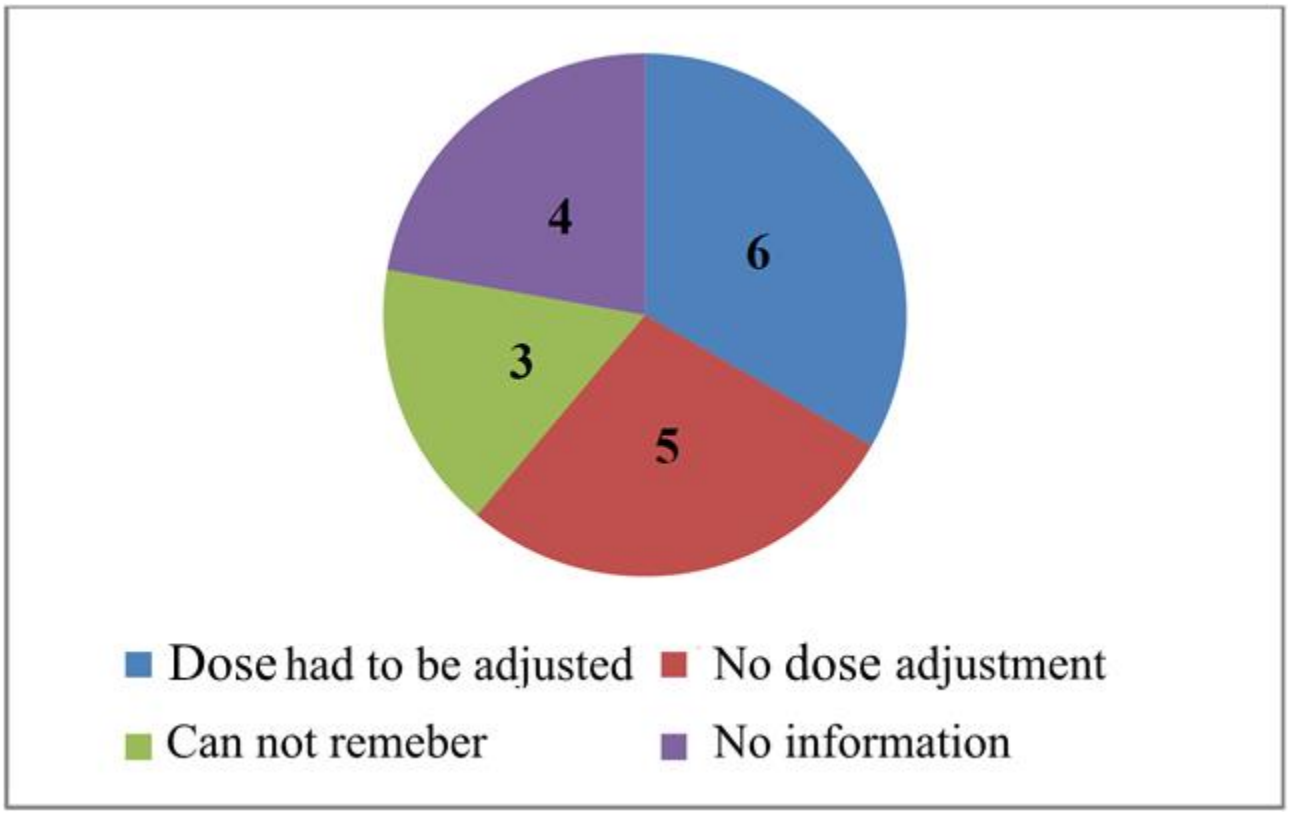


Figure 11. Retrospective survey on adjustment of insulin dose needed after FMT.

5. Discussion

Our research has been limited to the use of faecal transplantation in the treatment of CDI, but always with a view to its possible wider application. Our capsule preparation protocol both makes stool transplantation more flexible in current indications and facilitates research in additional areas. The equipment used in sample processing is easy to obtain and use, and the capsules can be stored efficiently and administered without any special preparation.

The question remains open as to which components of the faeces are responsible for the beneficial effects. The capsules containing lyophilised supernatant that we used were not germ-free, but contained orders of magnitude fewer colony-forming units than those containing lyophilised sediment. It should also be mentioned that we found a difference (not significant in this number of cases) between the efficacy of the two types of capsules, in favour of capsules containing the supernatant, i.e. the lower germination number. Furthermore, the importance of the other components is supported by the fact that capsules containing supernatant were still effective after six months of storage, even though the results of the bacterial culture tests showed that after six months of storage at -20°C, these samples no longer contained viable bacteria. There is apparently conflicting literature on this subject. Ott et al. obtained good results with sterile stool filtration [23], while another study found a combination of certain bacterial strains to be effective [10, 11]. Neither our research nor the sources I have found have explored the exact role of viruses. Even before the advent of metagenomics, it was clear that they constitute a significant part of the intestinal flora. Research into their interactions and roles has been made possible by metagenomics, but the wealth of new information has also made the task of researchers more difficult.

The results of anti-toxin antibodies can help predict whether a patient will develop a recurrence in the future.

The use of faecal transplantation in other diseases is currently under intense scrutiny, one example being the relationship between diabetes and gut flora. In our study population, there were also patients with reduced external insulin requirements after transplantation. Lyophilised, encapsulated stools may facilitate targeted investigation of other potential indications.

6. Summary

- The workflow we designed for lyophilisation and encapsulation of standard faecal suspensions is simple and quick to perform and can be integrated into daily clinical routine.
- Our method requires more time and equipment than the production of frozen stool-filled capsules, but the preparation, storage and administration of the capsules is more flexible.
- Our developed protocol has proven to be effective in administering 6 capsules compared to the 30-40 capsule doses used in large centres.
- The efficacy of the lyophilised stool capsules is not inferior to the efficacy of the conventional procedure, which is still comparable to the most effective antibiotic treatment (fidaxomicin).
- The capsulated formula is less burdensome for patients and more flexible for healthcare personnel.
- Although the CFU count of capsules containing lyophilised faecal supernatant is 600 times lower than that measured in capsules containing lyophilised sediment, this does not reduce efficacy.
- Capsules can be stored at -20°C for up to 6 months without loss of efficacy
- Lyophilisation and storage are likely to affect the protein content of faecal samples.
- Short-chain free fatty acid diversity measured in recipient samples after stool transplantation is more similar to that measured in donor samples than before the intervention.
- Bacterial strains also showed an increased diversity similar to that of the donor following faecal transplantation.
- Antibody titres against toxin A were low in all patients who subsequently developed recurrence following infection.
- Among type 2 diabetic patients, 6 out of 11 patients required a reduction in insulin dosage after faecal transplantation.

Results and observations:

1. We have developed and standardised a methodology for the encapsulation of lyophilised faecal filtrate for transplantation.
2. Capsules containing lyophilised faeces are effective for treating *Clostridioides difficile* infections.
3. Using centrifugation, a 600 times concentration diffenrence of the colony-forming unit between the sediment and the supernatant can be achieved.
4. Faecal supernatant and sediment lyophilisate are effective separately as well.
5. The hard gelatine capsules are also suitable for the administration of lyophilisates without a gastric acid resistant coating.
6. Storage of encapsulated, lyophilised faeces at -20°C for 6 months does not reduce the cure rate.
7. The diversity of short-chain free fatty acids in faeces increases after faecal transplantation, becoming more similar to that measured in donor faeces.
8. A low *Clostridium difficile* A toxin antibody titer after infection correlates well with subsequent recurrence.

The practical significance of the thesis

An essential part of the toolkit for treating *Clostridioides difficile* infections is faecal transplantation. Making this method more flexible will help to increase its use. At the same time, the removal of nasogastric and nasojejunal probes from the methodology and the improved transportability and storability due to the smaller volume will simplify research for other indications. The observation that efficacy is not reduced even at very low germ counts suggests the possibility of further dose reduction or omission of other components. The results of the protein and free fatty acid analyses may contribute to the identification of the components necessary for the effect in CDI. The results of anti-toxin antibody tests can be used to predict recurrence, thus allowing us to prepare for, or even avoid, a recurrence of infection in a given patient. The reduction in insulin needs following faecal transplantation in diabetic patients is a good example of the further

potential of this method, although it is not yet being considered as a therapeutic option for diabetes, for example.

8. Publications

Articles related to the thesis:

2019. December - von Bechtolsheim Felix, Varga Adorján, Szereday László, Polgár Beáta, Balassa Timea, Kocsis Béla, Péterfi Zoltán, Mikó Éva: *Development of a new serological assay for the diagnosis of Clostridium difficile infections with prognostic value.* JOURNAL OF MICROBIOLOGICAL METHODS 167 Paper: 105777 , 6 p. (Q3, IF: 1,707)

2021. March - Mintál Kitti, Tóth Attila, Hormay Edina, Kovács Anita, László Kristóf, Bufa Anita, Marosvölgyi Tamás, Kocsis Béla, Varga Adorján, Vizvári Zoltán, Cserjési Renáta, Péczely László, Ollmann Tamás, Lénárd László, Karádi Zoltán: *Novel probiotic treatment of autism spectrum disorder associated social behavioral symptoms in two rodent models.* SCIENTIFIC REPORTS. doi: 10.1038/s41598-022-09350-2 (Q1, IF: 4,380)

2021. June - Varga Adorján, Kocsis Béla, Sipos Dávid, Kása Péter, Vigvári Szabolcs, Pál Szilárd, Dembrovszky Fanni, Farkas Kornélia, Péterfi Zoltán: *How to Apply FMT More Effectively, Conveniently and Flexible – A Comparison of FMT Methods.* Frontiers in Cellular and Infection Microbiology. doi: 10.3389/fcimb.2021.657320 (Q1, IF: 5,293)

2022. March - Mintál Kitti, Tóth Attila, Hormay Edina, Kovács Anita, László Kristóf, Bufa Anita, Marosvölgyi Tamás, Kocsis Béla, Varga Adorján, Vizvári Zoltán, Cserjési Renáta, Péczely László, Ollmann Tamás, Lénárd László, Karádi Zoltán: Novel probiotic treatment of autism spectrum disorder associated social behavioral symptoms in two rodent models. SCIENTIFIC REPORTS 12 : 1 Paper: 5399 , 14 p. doi: 10.1038/s41598-022-09350-2 (Q1, IF: 4.379)

2023. January - Varga Adorján, Makszin Lilla, Bufa Anita, Sipos Dávid, Kása Péter, Pál Szilárd, Rosenstiel Philip, Sommer Felix, Kocsis Béla, Péterfi Zoltán:Efficacy of lyophilised bacteria-rich faecal sediment and supernatant with reduced bacterial count for treating patients with *Clostridioides difficile* Infection – A novel method for capsule faecal microbiota transfer. FRONTIERS IN CELLULAR AND INFECTION MICROBIOLOGY 13 Paper: 1041384 , 15 p. doi: 10.3389/fcimb.2023.1041384 (Q1, IF: 6,073)

2023. January - Péterfi Zoltán, Varga Adorján, Vigvári Szabolcs, Sipos Dávid. Széklettranszplantáció aktuális hazai helyzete; Central European Journal of Gastroenterology and Hepatology / Gasztroenterológiai És Hepatológiai Szemle. In press

Cumulative impact factor related to the thesis: 21,832

Articles not related to the thesis:

February, 2018 - Ács Kamilla, Kocsis Béla, Balázs Viktória Lilla, Kerekes Erika Beáta, Csikós Eszter, Varga Adorján, Krisch Judit, Vágvölgyi Csaba, Horváth Györgyi: *Illóolajok, illóolaj-komponensek és antibiotikumok együttes alkalmazásának lehetőségei légúti infekciók esetén.* Gyógyszerészet, ISSN 0017-6036 , 2018. (62. évf.), 2. sz., 73-79. p.

July, 2018 – Balázs Viktória L., Horváth Barbara, Varga Adorján, Ács Kamilla, Kerekes Erika, Kocsis Béla, Széchenyi Aleksandar, Krisch Judit, Horváth Györgyi: *A borsmenta, a fahéj, a kakukkfű és a szegfűszeg illóolajok különböző emulzióinak hatása Pseudomonas*

aeruginosa által képzett biofilm képződésre. ACTA PHARMACEUTICA HUNGARICA, in press

August, 2019 - Balázs Viktória Lilla, Horváth Barbara, Kerekes Erika, Ács Kamilla, Kocsis Béla, Varga Adorján, Böszörményi Andrea, U. Nagy Dávid; Krisch Judit, Széchenyi Aleksandar, Horváth Györgyi:*Anti-Haemophilus Activity of Selected Essential Oils Detected by TLC-Direct Bioautography and Biofilm Inhibition*. MOLECULES. doi: 10.3390/molecules24183301 (Q1, IF: 3.060)

November, 2019 - Horváth Barbara, Balázs Viktória L., Varga Adorján, Böszörményi Andrea, Kocsis Béla, Horváth Györgyi, Széchenyi Aleksandar: *Preparation, characterisation and microbiological examination of Pickering nano-emulsions containing essential oils, and their effect on Streptococcus mutans biofilm treatment*. SCIENTIFIC REPORTS. doi: 10.1038/s41598-019-52998-6 (Q1, IF: 4.525)

Cumulative impact faktor: 29,417

Oral presentations:

28.10.2017. Doktoranduszok a Klinikai Kutatásokban – Pécs

Clostridium difficile colitis terápiás lehetőségei

Varga Adorján, Kappéter Ágnes, Feiszt Zsófia, Sipos Dávid, Vigvári Szabolcs, Kocsis Béla, Mikó Éva, Szereday László, Felix von Bechtolsheim, Péterfi Zoltán

18.05.2018. Interdisciplinary Doctoral Conference – Pécs

Options and future possibilities in the treatment of Clostridium difficile infection
Adorján Varga, Béla Kocsis, Ágnes Kappéter, Zsófia Feiszt, Dávid Sipos, Szabolcs Vigvári, Éva Mikó, László Szereday, Felix von Bechtolsheim, Zoltán Péterfi

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31.08.2018. Magyar Laboratóriumi Diagnosztikai Társaság 59. Nagygyűlése – Pécs

Treatment options of Clostridium difficile infection: our latest experiences with fecal microbiota transplant

A. Varga, B. Kocsis, D. Sipos, Sz. Vigvári, P. Kása, Sz. Pál, É. Mikó, L. Szereday, F. Bechtolsheim, Z. Péterfi

21.09.2018. 12th Central European Symposium on Pharmaceutical Technology and Regulatory Affairs – Szeged (CESPT2018)

Our experiences with freeze-dried fecal supernatant capsules in *Clostridium difficile* infection

Adorján Varga, Béla Kocsis, Dávid Sipos, Szabolcs Vigvári, Péter Kása, Szilárd Pál, Lilla Makszin, Péter Hantz, Tamás Kovács, Zoltán Péterfi

27.10.2018. Medical Conference for PhD Students and Experts of Clinical Sciences (MedPÉCS)

Capsules against *Clostridium difficile* infections - our first experiences

Adorján Varga, Béla Kocsis, Dávid Sipos, Szabolcs Vigvári, Péter Kása, Szilárd Pál, Lilla Makszin, Péter Hantz, Tamás Kovács, Zoltán Péterfi

13.09.2019.. Szintentartó tanfolyam oxiológia, Pécs

Az a csodálatos mikrobiom

Péterfi Zoltán, Sipos Dávid, Varga Adorján, Kocsis Béla

29-31.03.2019. FIGAMU, Balatonalmádi

A széklet-transzplantáció új kérdései

Varga Adorján, Kocsis Béla, Sipos Dávid, Vigvári Szabolcs, Kása Péter, Pál Szilárd, Makszin Lilla, Hantz Péter, Kovács Tamás, Péterfi Zoltán

2022.10.01. Magyar Infektológiai és Klinikai Mikrobiológiai Társaság 49. kongresszusa, Miskolc

A mikrobiom szerepe a bélbetegségekben és széklet transzplantáció

Péterfi Zoltán, Vigvári Szabolcs, Sipos Dávid, Varga Adorján, Kocsis Béla

Poster presentations:

23.03.2018. - Fiatal Gasztroenterológusok Munkacsoportjának XIII. Kongresszusa - Balatonalmádi

Salmonellosist követő *Clostridium difficile* fertőzés – avagy a bélflóra nem felejt

Varga Adorján, Kocsis Béla, Kappéter Ágnes, Feiszt Zsófia, Sipos Dávid, Vigvári Szabolcs, Mikó Éva, Szereday László, Felix von Bechtolsheim, Péterfi Zoltán

16-19.09.2018. - The Human Microbiome, Heidelberg

Microbial and bacteriophage communities of food, fecal, and environmental samples

Ildikó Miklóssy, Adorján Varga, Ildikó Katalin Nagy, Maria Antoniadou, Mihály Óvári, Klára Pásztorné Huszár, Krisztina Kovács, Erzsébet Takács, Erwin Rosenberg, Béla Kocsis, Björn Rotter, Zoltán Péterfi, Tamás Kovács, Péter Hantz

20-22.09.2018. - 12th Central European Symposium on Pharmaceutical Technology and Regulatory Affairs, Szeged

Enteric film coating of capsules with freeze-dried fecal supernatant in *Clostridium difficile* infection

Kása, P., Varga, A., Kocsis, B., Nagy, R., Péterfi, Z. , Pál, Sz.

27.10.2018. Medical Conference for PhD Students and Experts of Clinical Sciences (MedPÉCS)

Salmonellosis followed by *Clostridium difficile* infection

Adorján Varga, Béla Kocsis, Ágnes Kappéter, Zsófia Feiszt, Dávid Sipos, Szabolcs Vigvári, Péter Kása, Szilárd Pál, Lilla Makszin, Zoltán Péterfi

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