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Title

Impact of SARS-CoV-2 vaccines on donor recruitment for faecal microbiota transplantation

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Text

Due to its clear benefits in the management of recurrent Clostridioides difficile infection (CDI), faecal microbiota transplantation (FMT) has been advocated as a non-postponable gastroenterological procedure to be continuously delivered during the COVID-19 pandemic.[1]

Specific recommendations to reorganise the whole workflow of FMT at the time of the COVID-19 pandemic have been therefore released, in order to avoid the potential risk of transmission of SARS-CoV-2 by the procedural FMT process or through the donor-recipient faecal transfer.[2]

Briefly, they included the use of remote assessment of patients and donors whenever possible, the expansion of donor screening with questionnaires and laboratory testing aimed at excluding SARS-CoV-2, and the application of specific safety measures during the endoscopic FMT procedure.[1,3]

The vaccination campaign against SARS-CoV-2 has recently started worldwide. One major category of vaccines (BioNTech/Pfizer, Moderna) is based on mRNA products that encode a genetically modified SARS-CoV-2 spike (S) protein. These vaccines are highly promising, with a 93-95% efficacy and minimal rate of side effects. An additional emerging class of vaccines – using a non-replicating adenovirus vector with SARS-CoV-2 S protein, including the ChAdOx1 nCoV-19 Oxford/AstraZeneca vaccine – have also now been given at least temporary authorisation in certain regions. Finally, a variety of vaccine technologies, including also attenuated live virus vaccines, are currently being investigated.

Overall, these efforts are expected to give a considerable boost to the global fight against COVID-19. Consequently, it points to an important discussion in the field of human tissue transfer, and specifically FMT: based on current knowledge and data, what impact will the vaccination have on FMT in clinical practice?

The first question is if there is a window period to wait between SARS-CoV-2 vaccination and donor screening. In our latest consensus report on stool biobanking, a recent (less than two months) history of vaccination with a live attenuated virus, in case of a possible risk of transmission, was included among the exclusion criteria for stool donors.[4] For those vaccines based upon mRNA

technologies (as opposed to live attenuated virus), it does not seem feasible that this would be a potential risk, and this exclusion criterion may be disregarded, as already suggested for blood donors.[5] Nonetheless, available vaccines have been associated with some adverse events, including fatigue, nausea, fever, headache, myalgia, arthralgia, pain at the injection site, and others, which can last several days after the vaccination. As these symptoms may overlap with symptoms assessed during donor screening (at the beginning questionnaire and the day of each donation), it may pragmatically be convenient to wait 7-10 days from vaccination before evaluating potential donors, to avoid the risk of inappropriate rejection of candidates. It may be reasonable to follow such line also for vaccines based on viral vectors, as suggested also in UK blood donation guidelines.[6]

Attenuated live virus vaccines are being developed and may become available for clinical use, but there are still no data about their risk of viral transmission with these candidate vaccines. In this case, the safest approach may be to adhere current guidelines for such type of vaccines and wait at least two months from vaccination before starting the donor screening.[4]

At the initial evaluation, all potential donor candidates should be asked about SARS-CoV-2 vaccination and, if vaccinated, a specific time window, depending on the type of vaccine, should elapse before moving forward with the full screening (Panel 1).

Another question is whether vaccinated donors require clinical and laboratory investigations for COVID-19 during screening. Although it is recognised that current vaccines are highly effective in preventing COVID-19, there is still uncertainty regarding their degree of impact upon the inter-human transmission of the virus. More specifically, there are no available data on the presence of SARS-CoV-2 in the faeces of vaccinated individuals if exposed, and of the risk of faecal-oral transmission of the virus. Finally, as there is not yet clear knowledge on how long the vaccine immunity lasts, it would be difficult to predict the duration of the donor's protection against the virus. So, all these open questions prevent any recommendation on changing or streamlining the current indications for the screening of stool donors, as current data do not yet assure a satisfactory level of safety for the complex procedure that is the transfer of human faeces.

However, regardless of all the above considerations, as different steps of the FMT process, including the evaluation of donors and patients, the manipulation of faeces, the FMT procedure itself, and the follow-up of patients, could expose involved individuals (donors, patients, and physicians) to SARS-CoV-2 infection, it is reasonable and wise to strongly encourage vaccination.

In conclusion, whilst the availability of vaccines is clearly expected to be a turning point in the pandemic, the alert level currently applied to the FMT workflow to prevent the transmission of SARS-CoV-2 cannot be reduced until further data emerges.

Panel 1. Summary of recommendations

- At the initial evaluation, all donor candidates should be asked about SARS-CoV-2 vaccination
- If vaccinated, a specific time window should be waited before starting the full screening

Type of vaccine	**Time window to wait**
mRNA	7-10 days
Viral vector	7-10 days
Attenuated live virus	8 weeks

Declaration of interests

AG reports personal fees for consultancy from Eisai Srl, 3PSolutions, Real Time Meeting, Fondazione Istituto Danone, Sinergie Srl, Board MRGE and Sanofi SpA personal fees for acting as a speaker for Takeda SpA, AbbVie and Sandoz SpA and personal fees for acting on advisory boards for VSL3 and Eisai. BHM reports personal fees from Finch Therapeutics Group. CRK has served as a clinical advisor, with no financial compensation, for OpenBiome since 2013; she is a local principal investigator for the PRISM-3 clinical trial, for which her institution receives some salary support for a research coordinator and compensation from Finch Therapeutics Group for each patient enrolled. FZ reports grants from the non-profit China Microbiota Transplantation System (fmtBank) and has a patent for GenFMTer for separating microbiota issued to FMT medical. GC has received personal fees for acting as advisor for Ferring Therapeutics. GI has received personal fees for acting as speaker from Biocodex, Danone, Metagenics, and for acting as consultant/advisor from Ferring Therapeutics, Giuliani, Metagenics. HS reports personal fees from Danone, Enterome, Takeda, AbbVie, Roche, Amgen, Danone, BiomX, Ferring, BMS, Astellas, MSD, Novartis, Tillotts Pharma, and Biose, and grants from Biocodex, Danone and BiomX, and is a co-founder of Exeliom Biosciences. JJK and EJK report grants from Vedanta Biosciences. JRA reports personal fees from Finch Therapeutics and has a non-financial relationship with OpenBiome as a scientific advisor. MF reports personal fees from Finch Therapeutics Group, Rebiotix, Takeda, AbbVie and Janssen. SCN reports grants from Ferring and personal fees from Takeda, AbbVie, Janssen and Tillotts. SPC reports non-financial support from Janssen and personal fees from Shire, Ferring, Microbiotica and Pfizer. ZK is an employee and shareholder of Finch Therapeutics and is an unpaid special advisor for OpenBiome.

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