Nature's therapy for recurrent *Clostridium difficile* diarrhea

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PA: With the widespread use of antibiotics, we have been detecting a large number of cases of *C difficile* colitis. Our first approach to treatment is usually metronidazole and, if the problem recurs, a course of vancomycin is often used. When the problem recurs again, there are a number of treatment options.

TL: Most patients are treated again with standard therapy to achieve a normal stool pattern, fully realizing that these patients have a high risk for a relapse. To prevent relapse and recurrence, strategies have included tapering of vancomycin dosages over four weeks, using probiotics (eg, *Saccharomyces boulardii*) or bacterial products such as VSL#3 (VSL Pharmaceuticals Inc, Canada) or over-the-counter/health food store preparations, alone or in any combination, for varying durations of several weeks to a month. There is no proof that any of these treatments are effective, and the consensus of experts is that these strategies are of unproven benefit. Nevertheless, in principle, filling the void in the intestinal flora cannot hurt in the vast majority of situations. In many ways, the strategies to stop recurrence are desperate measures.

PA: You have been an advocate for the 'stool transplant'. Can you describe the techniques for delivering this bacteria to the patient?

TL: I would not say that I have been an advocate for the procedure. I have performed them primarily because patients and referring physicians were out of options. Patients became prisoners of the threat of recurrence, and were vancomycin-dependent. It is important that patients are not on long-term courses of metronidazole, because of the risk for neurotoxicity. The normal colonic microbes, numbering in the trillions, are generally nonpathogenic and the majority are not cultivable (ie, grown in the laboratory). These organisms compete against pathogens and exclude them. It has been recognized for at least a decade that fecal flora replacement is highly effective – over 90% – in stopping the cycle of relapsing disease. Techniques for delivery range from ingestion, nasogastric/jejunal tube administration (1) (which runs the risk of colonizing the small bowel with potential pathogens), instillation with a colonoscope or simply an enema of varying volumes.

I have used an enema of 800 mL to 1400 mL of fecal slurry, generally as a once-only procedure. After 14 days of vancomycin therapy to ensure that the colon is healed and bowel motions are normal, the vancomycin is discontinued, allowing the antibiotic to clear from the colon over three to four days. At that time, the procedure is performed within the window before recurrence, when stool antibiotic concentrations that could be inhibitory are low. The volume used was recommended by radiology technicians at the Foothills Hospital (Calgary) because that amount was required to reach the right colon in most people during a barium enema examination. No cathartics are used because doing so might irritate the colon. On the day of the procedure (approximately day 18), after a normal full bowel motion, the infusion is administered over 30 min to 45 min, stopping at intervals if there are cramps. The patient is repositioned several times to facilitate transit to the right colon. Of the procedures done over 10 years, only one was performed in hospital.

PA: Why do you choose a relative to be the stool donor ?

TL: I suspect that there is a genetic basis or influence on the composition of the bowel flora, and that the bowel flora in relatives might be more compatible. Also, when I have been unable to find a related donor, opting for a spouse, I find that there is a greater likelihood of irritable bowel-like symptoms presenting after the procedure, which can last for several months or longer. The *C difficile* is gone, they indicate

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that they are better, but they are still not completely normal. The biological basis for, and confirmation of, what I have observed needs to be verified.

PA: Many of our patients have tried probiotics and yogurt, to no avail.

TL: The consensus of world experts on C *difficile* is that these treatments are of limited effectiveness. Remember that the vast majority of the microbes are not cultivable, so there is a concern that the probiotics used are not in sufficient numbers, are not the right ones or are not used in the right combinations.

PA: Are there any risks for the stool transplant?

TL: Drs John Bartlett and Ciaran Kelly in the United States have indicated that the legal barriers to the procedure are insurmountable (personal communication and also conference positions stated). At the most recent infectious disease meetings in the United States, the issue has come out in the open, and centres in Minnesota and Kansas are doing this kind of treatment. Acceptance is partly facilitated by the finding that this approach is more common in Europe. Our cultural aversion to our own indigenous flora is deeply rooted. I check the donor and recipient for transmissible blood-borne pathogens using the same testing procedures as for tissue banking and for enteric pathogens.

PA: When is the optimal time to move away from more antibiotics and to the stool transplant?

TL: That is an excellent question. As you know, each time the patient has a recurrence, there is always the probability of an adverse outcome. I have waited for patients to have six months of recurrent disease to define that they are in a difficult situation. In some ways, the process of trying a variety of treatments that are of limited effectiveness simply frustrates patients. So, it might be timely to discuss introducing the procedure after the third or fourth episode. A colleague in Netherlands wishes to be even more expedient.

REFERENCES

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