MedicalXpress

'Infect and forget': A dose of hookworms could help patients manage inflammatory bowel disease

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Could a dose of hookworms provide a medication-free alternative to people with inflammatory bowel disease? The Malaghan Institute's Hookworm Therapy team, who recently published the results from their year-long clinical study, think it's possible. Published in *Inflammatory Bowel Diseases*, the feasibility study found that hookworms were a safe and long-lasting treatment for participants with ulcerative

colitis—paving the way for wider clinical studies.

The Malaghan Institute has been exploring the potential therapeutic benefits of human hookworms for patients suffering allergic and inflammatory disease for a number of years. This current study was the first of its kind to investigate whether hookworms could offer a medication-free alternative for patients living with ulcerative colitis to manage their disease.

"This pilot study is the first controlled evidence in the use of hookworm as a therapy in ulcerative colitis," says Malaghan Institute clinician and gastroenterologist Dr. Tom Mules who led the study alongside Rutherford Clinic gastroenterologist Dr. Stephen Inns. "Our study has shown this kind of therapy is well-tolerated, safe and feasible to take into a full-scale trial."

In this pilot randomized controlled trial, patients currently in remission from ulcerative colitis were infected with a controlled dose of hookworm larvae or given placebo, and followed up over twelve months. Patients would provide regular feedback on any changes to their gut health or discomfort. Samples were collected throughout the year-long infection to test a range of scientific parameters such as gut inflammation, microbiome and immune cell composition.

"We deliberately chose to target patients with ulcerative colitis in remission," says Dr. Mules.

"We believe that the effect of hookworms may not be strong enough to push someone from an active disease state into disease remission. However, once someone is in remission hookworm could keep them there, prevent them from having disease flares and reduce the need to take medication, such as steroids, which suppresses the immune system and has adverse effects."

Living in remission from an inflammatory disease typically means that patients experience less pain and discomfort associated with active disease. In order to stay in remission patients generally have to take daily medications to prevent flare ups. However, Dr. Mules explains that there are significant barriers to taking daily medication, particularly when you do not have active symptoms to remind you to take pills morning and night. Importantly, not taking the medication increases the risk of having a flare. Disease flares impact quality of life, can lead to disease complications and need strong medications to bring under control.

"One of the key findings from this study was that a single dose of hookworm can reside in the body for several years, if not longer," says Dr. Mules. "This means that if hookworm is effective at preventing disease flares you can get infected and potentially no longer have to daily medicate. 'Infect and forget'. The worms just sit there in the background and do their thing. I think that's where the power of this therapy lies."

However, before the team could truly test this "infect and forget" theory in a full-scale trial, they had to confirm its safety.

"We did see that around the 6–8 week mark participants reported mild tummy symptoms, but those had all resolved by week 10–12," says Dr. Mules. "Otherwise, compared to the placebo group there was no significant differences in adverse events.

"The fact that these worms are well tolerated and safe to give to people with inflammatory disease is really important. One of the big safety questions was if the immune response triggered by the hookworm in the early stages of the infection could trigger a flare of ulcerative colitis. We did not see this, again highlighting that this therapy is safe in these patients."

With no effective cure for severe inflammatory and allergic diseases the

idea of using hookworms to manage harmful and aggressive symptoms is something many people have latched onto. There exists a thriving "underground" market of people self-medicating with hookworms, and significant anecdotal evidence indicating they are helpful in treating disease and managing symptoms, says Dr. Mules.

"We know that people with inflammatory bowel disease, including ulcerative colitis, already use medically unsupervised hookworms to manage their symptoms and regain some semblance of quality of life, however the evidence needed to support this is lacking. The aim of this study was to provide some solid scientific groundwork, to hopefully one day make this a real, legitimate therapy to help people living with debilitating disease."

Moving forward, the team plans to progress to larger clinical trials and to apply their findings to other diseases.

"The power of our study's findings is that we can apply them to other diseases as well," says Dr. Mules. "We are in the process of deciding what the best disease target is. It could be ulcerative colitis but there are also early findings demonstrating hookworm therapy could be beneficial to a wide-range of autoimmune, allergic and metabolic diseases.

"We're extremely grateful to the participants for taking part in this important study which will let us apply hookworm therapy where it will have the biggest impact."

More information: Thomas C Mules et al, Controlled Hookworm Infection for Medication-free Maintenance in Patients with Ulcerative Colitis: A Pilot, Double-blind, Randomized Control Trial, *Inflammatory Bowel Diseases* (2023). DOI: 10.1093/ibd/izad110

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