Probiotic-derived treatment offers new hope for premature babies

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Study in the *American Journal of Physiology-Gastrointestinal and Liver Physiology* addresses critical component of problem affecting infants with necrotizing enterocolitis.

"Good" bacteria that live in our intestines have been linked with a variety of health benefits, from fighting disease to preventing obesity. In a new study, Kriston Ganguli of Massachusetts General Hospital for Children and Harvard Medical School and her colleagues have discovered another advantage to these friendly microscopic tenants: Chemicals secreted by good bacteria that typically live in the intestines of babies could reduce the frequency and severity of a common and often-lethal disease of premature infants.

This disease, known as necrotizing enterocolitis (NEC), affects between 8 and 13 percent of very low birthweight infants (those under 3 pounds, 4 ounces), and up to half of the infants with this condition will die. As babies develop the collection of gut bacteria that colonize healthy intestines, those with NEC have an extreme inflammatory reaction that leads to damage and death of these tissues that often requires surgery to correct. Steroids are one of the few currently available ways to prevent NEC, but their use can cause undesirable complications.

Recent clinical trials of probiotics—live microbes taken as dietary supplements to promote health—have shown promise in reducing both the incidence and severity of NEC. However, in the U.S., the Food and Drug Administration does not sanction the use of whole bacteria in

premature infants. Seeking a different tact that avoids the use of the bacteria themselves, scientists in the new study investigated whether secretions from probiotic bacteria could prevent NEC.

The article is titled "Probiotics prevent necrotizing enterocolitis by modulating enterocyte genes that regulate innate immune-mediated inflammation." It appears in the American Journal of Physiology —*Gastrointestinal and Liver Physiology* published by the American Physiological Society.

Methodology

As a model for a baby's immature gut, the researchers used intestinal tissue from infants with NEC as well as fetal intestinal tissues. The researchers also grew two probiotic strains of bacteria, *L. acidophilus* and *B. infantus*, in liquid culture medium, but removed the bacteria from the cultures. The material in which these bacteria were grown, known as the probiotic conditioned medium (PCM), contained secretions the bacteria left behind.

They then exposed human immature and mature intestinal tissues to either PCM or to material usually used to grow bacteria that had never contained microbes. They also exposed some tissues to a compound derived from bacteria that's known to cause an inflammatory response.

They analyzed the tissues for expression of genes known to respond to inflammation and looked at the effects of secretions from the two different probiotic strains separately to determine whether one had a greater anti-inflammatory effect than the other.

Results

The scientists found that treatment with just the PCM significantly reduced inflammation in both immature intestinal tissue and tissue from infants with NEC.

When the researchers analyzed gene expression in the PCM-exposed tissue, they found reduced activity of several genes linked with inflammation. Interestingly, PCM exposure did not affect mature intestinal tissue.

"Since an immaturity of intestinal immune responses is felt to be partially responsible for the development of NEC, the bioactive factors in PCM may be useful as an effective, targeted preventive strategy without the broad effects of steroids," explained Ganguli.

When the researchers tested the effects of secretions from *B. infantis* and *L. acidophilus* separately on fetal intestinal cells, they found that those from *B. infantis* alone showed a greater ability than *L. acidophilus* to reduce inflammation. While this does not rule out the possibility that the two together could have a greater synergistic effect, it does suggest that *B. infantis* may be primarily responsible for the anti-inflammatory effect observed.

Importance of the Findings

While NEC is a complex disease, the authors suggest that this study addresses a critical component of the problem. If purified secretions from probiotic bacteria can reduce the severity and incidence of NEC in very low birthweight infants, it could represent a very promising new avenue of clinical research, they say, and may ultimately change the standard of care for these infants.

They add that these promising findings could lead to future clinical studies to investigate these factors in greater detail. Eventually, the

researchers add, secretions from probiotic bacteria may help prevent the development of NEC in premature infants in the U.S., potentially saving thousands of lives each year.

"The specific mechanisms by which probiotic secretions reduce inflammation need to be further investigated and safety data will need to be established in live animal models of NEC," says Ganguli. "Once established, these factors should be then investigated as a standard preventive strategy in a randomized, placebo-controlled clinical trial."

More information: ajpgi.physiology.org/content/3 … 2/G132.full.pdf+html

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