All probiotics are not the same in protecting premature infants from common, life-threatening illness

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Treating premature infants with probiotics, the dietary supplements containing live bacteria that many adults take to help maintain their natural intestinal balance, may be effective for preventing a common and life-threatening bowel disease among premature infants, researchers at UC Davis Children's Hospital have found.

The study, "A comparison of two probiotic strains of bifidobacteria in premature infants," recently was published online in the *Journal of Pediatrics*. The bowel disease, necrotizing enterocolitis (NEC), is the second most common cause of death among premature infants, said Mark Underwood, lead study author, neonatologist and professor in the Department of Pediatrics at UC Davis Children's Hospital. It affects 3 to 10 percent of premature infants; about 25 percent of those with the severe form of this NEC succumb to the infection.

Underwood and his collaborators evaluated the effectiveness and safety of two types of probiotics of known purity and composition in a clinical trial that included nine breastmilk- and 12 formula-fed premature infants in the Neonatal Intensive Care Unit (NICU) at UC Davis Children's Hospital.

The products tested in the study were two genetically different strains of bifidobacteria, normal inhabitants of the gastroentestinal tract that inhibit the growth of harmful pathogens and bacteria, *Bifidobacterium*

longum subspecies infantis (*B. infantis*); and *Bifidobacterium animalis lactis* (*B. lactis*).

Laboratory analysis of the bacterial contents of fecal samples from the infants, *B. infantis* was more effective at colonizing bifidobacteria, the healthy bacteria, in the newborns' gastrointestinal tracts than was *B. lactis*. The highest fecal levels of bifidobacteria were found in the infants who were breastmilk-fed and received the *B. infantis* probiotic, Underwood said.

No side effects were identified from administration of the two probiotic strains, Underwood said. One of the breast milk-fed infants treated with *B. lactis* developed NEC early in the trial, Underwood said, "indicating that *B. lactis* may not be as effective as *B. infantis* in protecting against NEC, though the study was not designed to answer that question."

Because earlier research conducted in Europe, Japan, and Australia has demonstrated the potential benefits of probiotic therapy in preventing NEC, many NICUs in the United States treat premature infants with the supplements, said Underwood. Probiotic therapy is not, however, the standard of care for premature infants in the United States. The American Academy of Pediatrics has not established a policy about using the products in newborns, and the U.S. Food and Drug Administration (FDA) currently regards probiotics as food supplements, not drugs.

The study was conducted in premature infants born between 24 to 33 weeks gestation and weighing less than 1,500 grams, or three pounds. It was conducted in two phases. In the first, the formula-fed infants were randomly assigned to receive either *B. infantis* or *B. lactis* in increasing doses over a five-week period. The second-phase evaluated the probiotics in breastmilk-fed premature infants. Each infant was treated with one strain for two weeks and after a one-week break, received the

other strain for two weeks.

In both the formula-fed and breast milk-fed newborns, greater increases in fecal bifidobacteria occurred in the *B. infantis* groups than in the *B. lactis* groups.

"*B. lactis* colonization was not sustained in the infants," Underwood said.

"The highest total numbers and percentages of bifidobacteria were found after two weeks of *B. infantis* treatment in the breast milk-fed babies," said Underwood. "In addition, during the one week break in the phase of the study that involved the breast milk-fed infants, the relative abundance of bifidobacteria was significantly greater for those treated with *B. infantis*."

During periods of administration of *B. infantis*, the diversity of the beneficial microbes inhabiting the breast milk-fed babies' GI tract increased. In addition, the harmful bacteria known as γ-Proteobacteria decreased in the breast milk-fed babies who received *B. infantis*.

However, the formula-fed infants treated with *B. infantis* and *B. lactis* did not experience a decline in the γ-Proteobacteria, which typically increases at the onset of NEC and can cause serious tissue-damaging infections in the gastrointestinal system, lungs and other organs of the body.

The two strains of bifidobacteria used in the study were grown for UC Davis by a food-grade commercial facility, to insure that the infants in the study would receive probiotics of known purity and composition, Underwood said.

Specimens were obtained from the stool of the formula-fed infants at baseline, the beginning of the study, and then weekly for five weeks. In

the breast milk-fed babies, the stool specimens were collected at baseline and following the first probiotic course, the one-week break and the second probiotic course.

Underwood is submitting an application for a new investigational drug to the FDA for a multi-centered second phase clinical trial to evaluate the safety and effectiveness of the *B. infantis* probiotic in preventing NEC in premature infants. If the application is approved and funded by the National Institues of Health, Underwood and his colleagues will conduct a larger trial involving more babies.

Provided by UC Davis