Bifidobacterium lactis Bb12 Enhances Intestinal Antibody Response in Formula-fed Infants: A Randomized, Double-Blind, Controlled Trial

Holscher HD, Czerkies LA, Cekola P, Litov R, Benbow M, Santema S, Alexander DD, Perez V, Sun S, Saavedra JM, Tappenden KA.
Journal of Parenteral and Enteral Nutrition. 2012;36:106S-117S

Nestlé Nutrition Institute

Background & Purpose

- Breastmilk is the ideal source of nutrition for infants and is also a source of secretory immunoglobulin A (sIgA) and bacteria, which enhance passive and active immunity.
- Addition of probiotics to infant formula may positively affect immune function in nonexclusively breastfed infants.
- This study aimed to investigate the effect of infant starter formula containing the probiotic *Bifidobacterium animalis* subspecies *lactis* (Bb12) on intestinal immunity and inflammation.

Methods

Participants & Study Design

- A prospective, randomized, double-blind, controlled clinical trial with two groups of 6 week-old healthy, full-term infants studied in parallel to a breastfed comparison group (n=172).
- Healthy formula-fed (FF) infants were randomized to receive either 100% whey protein partially hydrolyzed formula (CON) or the same formula with 10^6 colony forming units Bb12/g powder (PRO) for 6 weeks.
- Randomization of FF infants was stratified by delivery (vaginal vs. cesarean section).
- The self-selected breastfed (BF) group was exclusively breastfed and followed for 6 weeks.
- All participants were asked to receive immunizations according to the US Department of Health and Human Services schedule, which included rotavirus and poliovirus vaccines at 8 weeks of age.
- Stool samples were collected prior to vaccinations, and within 72 hours of each study visit.
  - — sIgA, calprotectin, lactate, Bb12 abundance and pH were assessed in fecal samples collected at baseline and after 2 and 6 weeks of feeding.
  - — Anti-poliovirus specific IgA and anti-rotavirus-specific IgA levels were analyzed in fecal samples collected prior to vaccination (2 weeks) and following vaccination (6 weeks).

Results

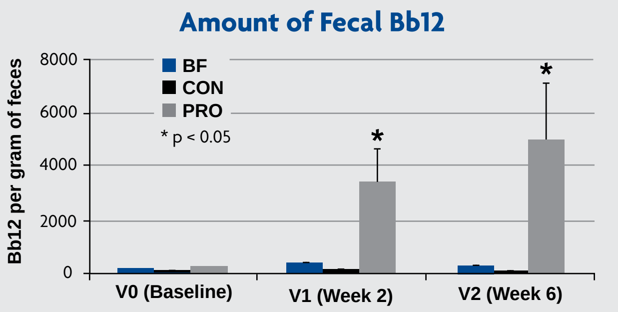
- Of the 172 recruited infants, 40 BF (30 vaginally delivered and 10 by cesarean section), 75 FF randomized to CON (34 infants; 19 vaginally delivered and 15 by cesarean section) or PRO (41 infants; 25 vaginally delivered and 16 by cesarean section) completed the study.
- No significant differences were seen in **fecal pH, fecal lactate, and stool frequency in FF groups.**

Amount of Fecal Bb12

- Fecal Bb12 was present in 93% and 88% of PRO fecal samples at week 2 and week 6, respectively.

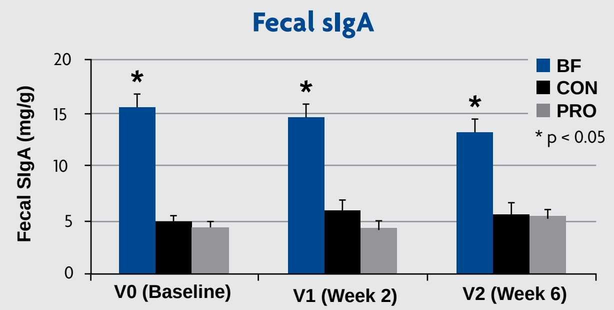
Fecal sIgA

- BF infants had significantly higher ($p<0.001$) concentrations of fecal sIgA in stool samples as compared to FF infants at all time points.
- Vaginally delivered PRO infants had increased ($p=0.046$) fecal sIgA concentration from baseline to 6 weeks of feeding compared to CON.
- Bb12 supplementation also tended to enhance the change of fecal sIgA at week 2 (8 weeks of age) in PRO, vaginally delivered infants as compared to CON. ($p = 0.063$)
- There was no effect of formula on fecal sIgA in cesarean delivered infants.



B. animalis subspecies *lactis* strain Bb12 was detected within the collected stool samples following ingestion of the probiotic Bb12-containing study formula.

Adapted from Figure 2. Effects of probiotic supplementation on Fecal Bb12 per gram of feces



A significantly higher concentration of total fecal sIgA was observed in BF infants than in FF infants due to the exogenous contribution of sIgA through the mother's breastmilk.

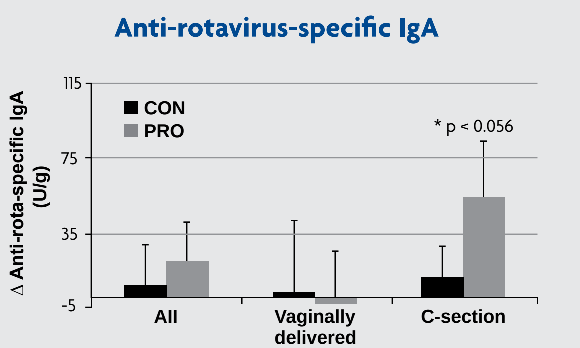
Adapted from Figure 3. Effects of Probiotic Supplementation on Fecal sIgA concentration.

Anti-rotavirus-specific IgA

- In cesarean-delivered infants, PRO tended to increase (p=0.056) anti-rotavirus-specific IgA concentrations from week 2 to week 6 (V1 to V2), but no change was observed with CON.

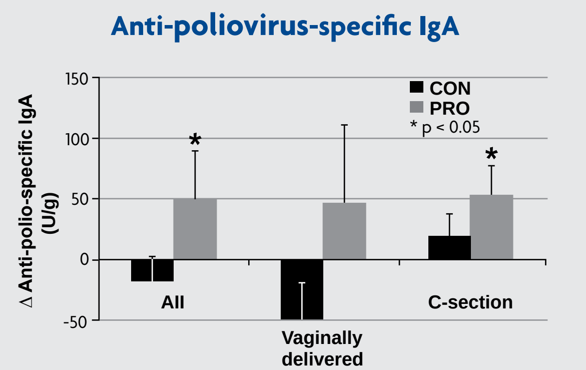
Anti-poliovirus-specific IgA

- From week 2 to week 6 (V1 to V2), the increase in anti-poliovirus-specific IgA concentration was higher in all PRO vs. CON stool samples (p=0.031), including those from cesarean-delivered infants.



Cesarean-delivered PRO infants saw an increase in anti-rotavirus-specific fecal IgA after 6 weeks of feeding.

Adapted from Figure 5. Probiotics increase anti-rotavirus—specific IgA in infants born by cesarean delivery.



Cesarean-delivered PRO infants saw a significant increase in anti-poliovirus-specific fecal IgA after 6 weeks of feeding.

Adapted from Figure 6. Fecal anti-poliovirus-specific IgA concentration increased in infants consuming probiotic formula.

Discussion

- "It is possible that Bb12 provided immune modulating bacterial exposure that was more pronounced in the cesarean-delivered infants".
- "...per protocol PRO infants experienced an increase in anti-poliovirus-specific fecal IgA, suggesting that the addition of Bb12 to infant formula may be helpful in mitigating some of the negative immune-related effects associated with formula feeding (not breastfeeding)".

Conclusion

- **"Infants fed formula supplemented with Bb12 had significantly higher levels of Bb12, and infants born by vaginal delivery had increased concentrations of sIgA. In addition, infants born by cesarean section who received the probiotic formula had enhanced immune response to poliovirus and rotavirus vaccines, as evidenced by an increase in anti-rotavirus and anti-poliovirus-specific IgA."**
- **"These results demonstrate that negative immune-related effects from the absence of breastfeeding and cesarean-section delivery may be mitigated by including *B. animalis* subspecies *lactis* Bb12 in infant formula and thereby providing infants a safe, dietary, immune-modulating bacterial experience."**

Please see attached clinical study for complete information.