Immune status of infants fed soy-based formulas with or without added nucleotides for 1 year: part 1: vaccine responses, and morbidity


Introduction
This paper addresses knowledge gaps regarding immunologic development of soy protein-based formula-fed infants. Early studies of soy flour-based formulas had shown decreased immunoglobulin production, but these results were not replicated with modern soy protein isolate-based formulas.

Study Purpose
This study examined the relative immune status over the course of the first year of life of full-term, healthy infants fed soy protein-based formula with and without added nucleotides. A reference group of infants fed human milk/cow milk-based formula was also included.

Study Design
Using data from a masked, 12-month feeding trial by Lasekan et al., the authors looked at immune status as determined by antibody response to standard childhood immunizations as well as parent- and/ or physician-reported morbidity. Formula-fed infants in this study were randomly assigned to one of two groups:
1) Infants fed soy protein-based formula (n=92) (SOY)
2) Infants fed soy protein-based formula with 74 mg added nucleotides/L (n=94) (SOYN)
A nonrandomized group of infants fed exclusively human milk for at least 2 months and human milk and/or milk-based formula (HM/F) was also included (n=81).

Immunizations were administered according to the 1994 immunization schedule of the American Academy of Pediatrics. Data was collected at 0.5, 1, 2, 4, 6, 7 and 12 months, and telephone contacts were made with parents when infants were 9, 10, and 11 months of age.

Study Results
Of the 267 infants enrolled, a total of 213 infants successfully completed the study (73 SOY, 73 SOYN, 67 HM/F). Of the seven immune indicators measured at 6, 7 and 12 months, five showed no significant differences between all three groups at all three
measurement points. However, the infants fed SOYN showed significantly higher levels of antibody to Hib (a standard childhood immunization) at 7 and 12 months compared to the infants fed HM/F ($p=0.007$ and 0.008 respectively), and the infants fed HM/F had a significantly higher poliovirus neutralizing antibody response at 12 months only compared to infants fed SOY ($p=0.016$).

Morbidity data was collected for physician-recorded diarrhea, parent-recorded diarrhea and physician-recorded otitis media. When analyzed based on presence or absence of diarrhea, physician-reported diarrhea was less frequent in infants in the HM/F group ($p=0.011$), but the difference was not significant when the frequency of diarrhea was analyzed. There were no significant differences in parent-reported diarrhea (either presence/absence or frequency) or in the occurrence of otitis media. In addition, there were no significant differences in antibiotic usage among the groups.

**Discussion**

The findings in this study are generally consistent with earlier studies. The anti-diarrheal effect of breastfeeding is well-documented.\(^3\) Although many of the vaccine response increases did not reach statistical significance, they did indicate an upward trend, which is consistent with findings in cow milk-based studies. Unlike nucleotide unsupplemented cow milk-based formulas, soy protein-based formulas are naturally rich in nucleotides which may account for the lesser effect of supplementation in these formulas.

**Study Conclusions**

The results from this study indicate that infants fed soy protein-based formula through one year of age have normal immune development based on their normal immunoglobulin levels, normal responses to vaccine antigens and similar morbidity associated with otitis media when compared with infants who are exclusively breastfed for at least the first two months of life.

This study also found that, unlike studies in nucleotide supplementation of cow milk-based formula, nucleotide supplementation of soy protein-based formula provided only a marginal benefit in response to Hib immunization, which did not reach statistical significance when compared to unsupplemented soy protein-based formula.

**References**


**Key Point:**

Soy protein-based formula-fed infants in this study had normal immune development relative to infants exclusively breast-fed for at least the first 2 months of life.