FPIN's clinical inquiries: effects of soy protein-based formula in full-term infants

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Introduction

The Family Physician Inquiries Network (FPIN) is a non-profit consortium of medical professionals whose mission is to make evidence-based family medicine and clinical scholarship more accessible to family physicians in clinical practice. FPIN’s Clinical Inquiries provide answers to clinical questions using a structured search, critical appraisal, authoritative recommendations, clinical perspective, and rigorous peer review.

Clinical Inquiry Question

- To evaluate evidence for the long-term safety of soy protein-based formula in full-term infants.

Inquiry Summary

While no large randomized and controlled trials were found on this topic, the FPIN made recommendations based on extrapolation from limited data and observational studies.

13 variables were evaluated for potentially adverse outcomes: bone mineralization, calcium phosphate levels, cognitive development, menstrual discomfort, growth, immune cell populations, menstrual duration, nutritional status, protein metabolism, vaccine response, sensitization allergy, thyroid effects, and visual acuity. The supporting studies ranged in sample size from five to 811 participants and employed a range of design methodologies: prospective cohort, structured review, historical cohort and randomized, controlled trials.¹⁻⁷

In addition, the FPIN reported that The Center for the Evaluation of Risks to Human Reproduction (CERHR), a joint program for the Centers for Disease Control and Prevention, the FDA, and the National Institutes of Health, convened a 14-member panel to evaluate the data regarding the health effects of soy protein-based formula. The panel reviewed 229 studies. While this panel concluded that the human studies it evaluated were of limited utility because of poor study design, lack of experimental detail, or small sample size, it identified no long-term detrimental effects on growth or sexual maturation. No recommendation was issued by the CERHR.⁸
The FPIN identified only one study that specifically addressed the long-term effects of soy protein-based formula. In this historical cohort study, adults who were 20-34 years of age and had previously participated in a controlled feeding study as an infant (soy protein-based formula n=248, cow milk-based formula n=563) were contacted and interviewed on a range of health issues. There was no association between exposure to soy protein-based formula and general health or reproductive outcomes but there was a slight correlation between an increased duration of menstrual bleeding later in life and receiving a soy protein-based infant formula. However, the applicability of the findings in this study is limited by several confounding variables which were not controlled for in the original study, including the use of older soy protein-based formulations.

Inquiry Findings
- Of 13 variables evaluated for potentially adverse outcomes attributable to soy protein-based formula, no detrimental effects were found in 11 variables, and the remaining 2 were found to have only a slight detrimental effect: a slight increase in the pain associated with menstruation (dysmenorrhea), and a slight increase in menstrual duration (~8 hours).\(^1\)-\(^7\)
- The Center for the Evaluation of Risks to Human Reproduction (CERHR), in a review of 228 studies, identified no long-term detrimental effects of soy protein-based formula on growth or sexual maturation.
- The American Academy of Family Physicians (AAFP) and the AAP recommend the use of breast milk exclusively for at least the first six months of life. The AAP recommends that, for full-term infants whose nutritional needs are not being met from maternal breast milk or cow milk-based formulas, soy protein-based formula is a safe and effective alternative. The AAFP has no current policy recommendation regarding the use of soy protein-based formula.

Discussion
While both the FPIN and the CERHR found no significant long-term detrimental effects associated with the use of soy protein-based formula, the value of both reports was weakened by a lack of quality data. To date, recommendations on this topic are reassuring but need to be further strengthened by the results of well-controlled, long-term studies.
Conclusions

There are no significant long-term detrimental effects associated with the use of currently available, commercially produced, isolated soy protein-based formula in full-term infants. This recommendation is given a Strength of Recommendation of ‘B’ by the FPIN because it is based primarily on cohort studies and the number of well-controlled, long term studies is limited.

References