Bovine serum albumin detected in infant formula is a possible trigger for insulin-dependent diabetes mellitus

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A constituent of cow's milk, bovine serum albumin (BSA), has recently been implicated as a possible trigger of insulin-dependent diabetes mellitus (IDDM) (1). Levels of serum antibodies to BSA were significantly elevated in children newly diagnosed with diabetes compared with normal control subjects (1,2), and cow's milk protein was diabetogenic in animal models of IDDM (3,4). In the latter studies, rats fed cow's milk protein at the onset of weaning (day 13) had an incidence of diabetes 2.6-fold greater than animals receiving milk-free protein during weaning and milk protein after weaning (day 23) (4). A Finnish study demonstrated that children who were older than 4 months of age when supplementary feeding (food or formula) was started had a lower risk of IDDM than those whose diets were supplemented before this age (5). Hence, there may be a window of time in early infancy when the consumption of cow's milk protein raises the risk for later development of IDDM.

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RESULTS AND DISCUSSION

Three of the four powdered infant formulas and cow's milk tested positive for BSA; all five of the liquid formulas and human milk tested negative for BSA. The three powdered formulas with BSA contained 0.47 to 1.14 μg BSA per liter (31.2 to 75.5 μg BSA per milliliter) compared with 2% cow's milk, which contained 1.14 μg BSA per liter (75.5 μg BSA per milliliter) (Table). However, because protein concentrations in formula are low compared with cow's milk (1.4% vs 3.3%), BSA concentration in infant formula as a percentage of total protein is equal to, or in the case of one formula, almost twofold greater than that of cow's milk (Table). The single powdered formula that tested BSA-free contained whey as the primary ingredient; however, unlike the other powdered formulas, the whey was "enzymatically hydrolyzed," a process that may predigest the protein into peptides that are not immunogenic.

We were concerned that the heat of sterilization required by the retorted liquid product or the hydrolysis process might denature the peptides to the degree that they would not migrate through the agarose gel. Hence, if BSA was present in the formula but could not migrate, our method for detecting BSA would not be adequate, because radial immunodiffusion only measures migrating proteins.

To examine this question, we prepared antibody-free agarose gels and allowed proteins from all samples tested to migrate into the gels for 30 minutes. The gels were then rinsed, dried, and stained for protein. The powdered formula that tested BSA-free did not display any migrating protein, whereas the three powdered formulas containing BSA and all of the liquid formulas displayed a band of migrating protein around the well. Our methodology, therefore, cannot determine whether the powdered formula that tested BSA-free by radial immunodiffusion is truly free of BSA, but because no protein migration was observed.

However, all of the liquid formulas tested BSA-free by radial immunodiffusion and demonstrated protein migration on antibody-agarose; hence, these preparations do appear to be BSA-free. Liquid formulas are generally heat treated (240°F) for preservation, and apparently this procedure destroys the immunogenicity of BSA. (During the pasteurization process, milk is heated only to 185°F and BSA is not denatured.)

Although some of the formulas tested BSA-free, the radial immunodiffusion procedure is not sensitive enough to determine whether the BSA subunit, ABBOS, is present; hence, the BSA-free formulas may still possibly contain ABBOS. More sensitive assay procedures (e.g., the enzyme-linked immunosorbent assay) will be necessary to demonstrate that formulas, or even human milk samples, are free of ABBOS.

If BSA is a trigger for IDDM, the presence of BSA in some infant formulas is particularly distressing, because formulas are consumed at a point in life when the digestive tract permits large protein chains to pass directly into the bloodstream. Encouragingly, our data indicate that perhaps certain processes may be adapted by the manufacturer during formula preparation to solve this dilemma.

Human milk did not test positive for BSA and, interestingly, infants breast-fed exclusively are at a lower risk for IDDM (12).

APPLICATIONS

Not every baby who drinks cow's milk or cow's milk-based infant formulas will develop IDDM. Genes have been identified that predispose individuals to the development of autoimmune diseases; furthermore, the timing of exposure to BSA and the timing and number of viral infections in early childhood are all implicated in the development of IDDM. Infants with a high risk of developing IDDM, however, should be breast-fed or given soy-based infant formula. Furthermore, manufacturers of infant formulas should be encouraged to develop processing procedures to destroy the BSA and its ABBOS subunit. Of course, breast milk is best, and the revised recommendations of the American Academy of Pediatrics state that infants should be breast-fed for the first 6 to 12 months of life and that whole cow's milk should be avoided for the first year of life (13).

References

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