Role of Breast Milk in a Mouse Model of Maternal Transmission of Asthma Susceptibility


PURPOSE OF THE STUDY. There is some epidemiologic evidence that the risk of asthma in children born to asthmatic mothers increases with breastfeeding; however, this association remains controversial. This study used a mouse model of maternal transmission of asthma risk to investigate the effect of adoptive nursing on asthma susceptibility in offspring.

METHODS. Future maternal mice were sensitized as neonates by intraperitoneal ovalbumin injections followed by repeated exposure to aerosolized ovalbumin at 4, 8, and 12 weeks of age. The mice then mated, and some litters from asthmatic mothers were nursed by normal mothers; similarly, some litters from normal mothers were nursed by asthmatic mothers. The offspring received a single intraperitoneal ovalbumin injection on day 4 (intentional suboptimal sensitization, which did not provoke any allergic response in infants born to normal mothers) followed by aerosolized ovalbumin exposure on days 13 to 15. A similar protocol was applied for studies of a second allergen, casein. Pulmonary-function testing was performed on day 16, followed by pathologic analyses on day 17. Cytokines were also analyzed in expressed breast milk from mothers, as well as breast milk retrieved from infant stomachs.

RESULTS. Infant mouse born to asthmatic mothers, but not those born to normal mothers, exhibited airway hyperresponsiveness to methacholine and allergic airway inflammation, specifically increased eosinophils on bronchoalveolar lavage and eosinophilic and mononuclear cell infiltration around airways and vessels on lung pathology. After adoptive nursing, both groups (normal infant mice nursed by asthmatic mothers and infants of asthmatic mothers nursed by normal mice) showed airway hyperresponsiveness to methacholine and airway inflammation, exhibited as eosinophilia on bronchoalveolar lavage and histology. Similar results were observed when infant mice born to ovalbumin-allergic and -exposed mothers were suboptimally sensitized to an unrelated allergen, casein, suggesting that allergens and/or specific antibodies are not responsible for the transmission of susceptibility through breast milk. Assays for cytokines (interferon γ, interleukin 2, interleukin 4, interleukin 5, tumor necrosis factor α, and interleukin 13) were negative in both expressed breast milk and milk-rich stomach contents.

CONCLUSIONS. These findings suggest that breast milk contains factors that are sufficient, but not necessary, to mediate allergen-independent transmission of asthma susceptibility from mothers to offspring mice.

REVIEWER COMMENTS. The results of this study in a mouse model of maternal asthma support some of the epidemiologic data showing that the risk of asthma may increase with breastfeeding. In this study, the increased asthma susceptibility observed in infant mice born to normal mothers and nursed by asthmatic mothers suggests that breastfeeding may be one mechanism for transmission of asthma risk. Given the absence of significant cytokine levels in breast milk in this study, future investigation is needed to identify the mediator(s) in breast milk that is responsible for increasing asthma risk.
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