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The protective effect of fenretinide against allergic asthma

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Objective/purpose

Fenretinide [N-4-hydroxyphenyl, 4HPR] is a synthetic retinoid derived from vitamin A with pro-apoptotic and anti-inflammatory properties. Studies have shown that at high concentrations fenretinide is an effective anti-neoplastic agent, regulating cell growth and differentiation. We have recently demonstrated that fenretinide, at doses 5-10× lower than for cancer treatment, has protective effect against bacterial infection[1] and osteoporosis[2] in *Cftr*-knockout mice. The effect of fenretinide as a potential treatment for allergic asthma induced inflammation has not been evaluated in asthmatics. The goal of this study was to determine if, by normalizing inflammatory mediators, fenretinide would be able to alleviate the symptoms associated with allergic asthma.

Methods

Hyperresponsive to methacholine, mice of A/J strain were sensitized weekly using ovalbumin (OVA) for three consecutive weeks, then age-matched and separated into two study groups and two control groups. For a period of 4 weeks, the study groups were orally treated with fenretinide while the controls were treated with the drug vehicle. During the last week of treatment, the control and study groups were split into two additional groups and underwent allergen challenges for three consecutive days, with either an OVA solution or PBS. Forty-eight hours after the third challenge, resistance of the respiratory system of the mice in response to methacholine was measured using a Buxco plethysmograph. Total IgE in plasma was measured by ELISA. Lung histopathology was observed using H&E and PAS stains.

Findings

Vehicle treated OVA challenged mice exhibited high values of airway resistance, plasma IgE concentration, and immune cell infiltration into the airways compared to PBS challenged animals. Interestingly, fenretinide treated OVA challenged mice had a statistically lower respiratory resistance. In addition, fenretinide treatment abrogated the recruitment of eosinophils to the region surrounding the blood vessels and airways. Similarly, after drug treatment a decrease in goblet cell hyperplasia was also observed through histopathology. However, no difference was observed in the level of plasma IgE between the control and study groups.

Deliverables

Fenretinide has been demonstrated to have great potential as a therapeutic agent. Our findings provide a novel approach to treat allergen-induced asthma and will help us in pursuing these studies towards the use of this drug for patients suffering from allergic asthma.

Relevance

The data presented herein will facilitate the development of fenretinide as a therapeutic compound in the treatment of allergic asthma and provide the foundation for the identification of drug targets for the development of effective future drugs.

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