Pollutant exposure during postnatal development induced differential gender susceptibility to lung inflammation: evidence for defective antioxidant response.

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INTRODUCTION: Epidemiological evidence suggests that early life exposure to pollutant can significantly determine later impairment of respiratory function and / or exacerbate lung inflammatory diseases (e.g. asthma; Colais et al., 2012). Moreover, asthma that often takes root in early development, displays some degree of sex bias and is highly associated with increased oxidative stress and altered antioxidant defenses (Celik et al., 2012). This study uses both male and female C57Bl/6 mouse model to test the hypothesis, that neonatal exposure to the pollutant 1,2-naphthoquinone (1,2-NQ) will alter lung development and antioxidant defenses to allergic inflammation at a juvenile age.

METHODS: Under approval of the Institute of Biomedical Sciences Ethics Committee of University of São Paulo (113/07/CEEA), neonate male and female C57Bl/6 mice (2-5 g) were used and nebulized with 1,2-NQ (100 nM; 10 mL) or corresponding vehicle for three alternate days during 15 min. Seventeen and twenty four days later, animals were sensitized via subcutaneous (s.c.) route with a single dose of ovalbumin (OVA; 10 µg 0.2 ml^{-1} PBS) or vehicle. On days 40 and 42, animals were challenged with 100 µl of OVA 1% or its vehicle. Following 24 h, both *in vivo* airways hyperresponsiveness (Penh) assessment and *in vitro* inflammatory/biochemical parameters (e.g. leukocytes counts, cytokines, antioxidants enzymes) in lungs were assessed. Data are presented as mean ± SEM. Stats were performed by ANOVA followed by Bonferroni's test. $P<0.05$ was taken as significant.

RESULTS: The OVA treatment in prior exposed 1,2-NQ male mice markedly increased eosinophil counts in the BALF ($6 \pm 1.5 \times 10^4$ cells $BALF^{-1}$) and peripheral blood ($7 \pm 2 \times 10^5$ cells $blood^{-1}$) as compared to BALF ($3 \pm 1 \times 10^4$ cells $BALF^{-1}$) and peripheral blood ($0.5 \pm 0.1 \times 10^5$ cells $blood^{-1}$) of female mice. Likewise, the BALF concentration of Th1/Th2 cytokines (IL-4, IL-5, IL-13, INF-γ) were significantly higher in male than in female mice. In contrast, antioxidant enzyme activity (e.g. catalase, glutathione peroxidase and reductase) and Penh values measured in female lung were greater ($P<0.05$) compared to male mice.

DISCUSSION: We show, for the first time, that brief exposure to the pollutant 1,2-NQ during postnatal development induced increased susceptibility to allergic inflammation and differential impairment of lung antioxidant defenses in male but not in female mice gender throughout puberty, thus suggesting that males are at greater risk. The potential applications of inhaled antioxidants might be of potential interest in the additional therapy available to the anti-inflammatory treatments for lung diseases such as asthma.

References:

Celik et al., 2012. Pediatr Allergy Immunol. Mar 22. doi: 10.1111/j.1399-3038.2012.01294

Colais et al., 2012. Epidemiology 23(3):473-481.

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