Allergy 2018 : Obesity enhances allergen-induced airway inflammation in murine model of asthma - Rehab Bagadood – Cordula Stover and Yassine Amrani University of Leicester

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Abstract

Asthma is a chronic inflammatory disease of the lungs[1] affecting millions of people worldwide[2]. Obesity, on the other hand is considered as a low grade systemic inflammation that affects large number of individuals[3]. It is important to note that obesity has a significant impact on asthmatic patients as obese patients are mostly suffering from severe symptoms, frequent exacerbation, poor quality of life and poor response to anti-inflammatory therapies including corticosteroids[4,5], although the underlying mechanisms are still unknown. We here investigated whether obesity affects pro-asthmatic changes in the lung and immune cells in a murine model of allergic asthma.

Methodology: Splenocytes were isolated from ovalbumin (or saline as control) sensitized and challenged C57BL/6 mice that were fed with either low (LFD) or high-fat (HFD) diets. These splenocytes were treated with (1mg/ml ovalbumin) in the presence of dexamethasone and production of different cytokines was measured using ELISA. Inflammatory cytokines levels were also assessed in bronchoalveoral lavage fluids. To score the degree of inflammation and mucus secretion in the airways, mice lung sections were stained with haematoxylin & eosin (H&E) and periodic acid-Schiff (PAS) stains, respectively. **Results**: Production of TNFα and IL-6 levels by cultured splenocytes was greater in HFD-fed ovalbumin-challenged mice (148.5±13.4 and 597.9±136.5 pg/ml; P<0.0001 and P=0.01 respectively) when compared to that in cells from LFD-fed group. Interestingly, dexamethasone failed to inhibit the production of IL-6 by splenocytes from ovalbumin-challenge HFD-fed mice compared to LFD mice. Ovalbumin-challenged obese mice exhibit significant IL-6 secretion into BALF (P<0.05). H&E and PAS stains showed high levels of inflammatory cell infiltration and mucus secretion in the airways of ovalbumin-challenged mice. More importantly, HFD significantly increased lung inflammation in various compartments including peri-vascular, peri-bronchial and parenchyma areas in ovalbumin-challenged mice.

Conclusion and significance: HFD exacerbates allergen responses in vivo and dexamethasone sensitivity in vitro in cultured-splenocytes. Obesity induced by HFD augments allergen-induced airway inflammation possibly as a consequence of increased infiltration of immune cells in the lungs and release of pro-inflammatory cytokines. Asthma is a chronic inflammatory disease of the lungs affecting millions of people worldwide. Obesity, on the other hand is considered as a low-grade systemic inflammation that affects large number of individuals. It is important to note that obesity has a significant impact on asthmatic patients as obese patients are mostly suffering from severe symptoms, frequent exacerbation, poor quality of life and poor response to anti-inflammatory therapies including corticosteroids, although the underlying mechanisms are still unknown. We here investigated whether obesity affects pro-asthmatic changes in the lung and immune cells in a murine model of allergic asthma. Methodology: Splenocytes were isolated from ovalbumin (or saline as control) sensitized and challenged C57BL/6 mice that were fed with either Low (LFD) or High-Fat (HFD) diets. These splenocytes were treated with (1 mg/ml ovalbumin) in the presence of dexamethasone and production of different cytokines was measured using ELISA. Inflammatory cytokines levels were also assessed in bronchoalveolar lavage fluids. To score the degree of inflammation and mucus secretion in the airways, mice lung sections were stained with Haematoxylin & Eosin (H&E) and Periodic Acid-Schiff (PAS) stains respectively. Results: Production of TNF? and IL-6 levels by cultured splenocytes was greater in HFD-fed ovalbumin-challenged mice (148.5 13.4 and 597.9 136.5 pg/ml; P<0.0001 and P=0.01 respectively) when compared to that in cells from LFD-fed group. Interestingly, dexamethasone failed to inhibit the production of IL-6 by splenocytes from ovalbumin-challenge HFD-fed mice compared

to LFD mice. Ovalbumin-challenged obese mice exhibit significant IL-6 secretion into BALF ($P<0.05$). H&E and PAS stains showed high levels of inflammatory cell infiltration and mucus secretion in the airways of ovalbumin-challenged mice. More importantly, HFD significantly increased lung inflammation in various compartments including peri-vascular, peri-bronchial and parenchyma areas in ovalbumin-challenged mice. Conclusion & Significance: HFD exacerbate allergen responses in vivo and dexamethasone sensitivity in vitro in culturedsplenocytes. Obesity induced by HFD augments allergen-induced airway inflammation possibly as a consequence of increased infiltration of immune cells in the lungs and release of pro-inflammatory cytokines. Compared to ovalbumin-challenged lean mice, ovalbumin-challenged obese mice had higher levels of IL-6 into BALF by 79%, greater neutrophilic infiltration (by 35%, $P<0.05$), and higher histopathological changes specifically in peri-vascular, peri-bronchial and parenchyma areas by 27, 46 and 26%. Mucus secretion and eosinophilic infiltration were not affected. Allergen-induced TNFα and IL-6 production was greater by 37% and 68% and resistant to corticosteroid suppression in cultured splenocytes from obese mice compared to responses in cells from lean mice.

Recent Publications

1. **Increasedβ2-adrenoceptor phosphorylation in airway smooth muscle in severe asthma: possible role of mast cell-derived growth factors** Latifa Chachi, Abdulrahman Alzahrani, Cynthia Koziol-White, Michael Biddle, Rehab Bagadood, Reynold A. Panettieri, Jr., Peter Bradding, and Yassine Amrani

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2. Masjedi M, Ainy E, Zayeri F, Paydar R. Assessing the prevalence and incidence of asthma and chronic obstructive pulmonary disease in the eastern mediterranean region. Turkish Thoracic Journal. 2017; 19(2):56-60.
3. Shore SA. Obesity and asthma: Possible mechanisms. J Allergy Clin Immunol. 2008; 121(5):1087-1093.
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Biography

Rehab Bagadood is a lecturer in immunology at Umm-alqura Universityy, Saudi Arabia. She completed her Bachelor's degree in laboratory medicine from Umm-alqura University, SA in 2010. She later moved to University of Leicester where she earned a MSc degree in infection and immunity in 2014. Rehab is currently a third year PhD student at University of Leicester, UK. Her PhD thesis mostly focused around the mechanisms by which obesity exacerbates allergic asthma under the supervision of Drs. Amrani and Stover. Rehab has mastered different cellular and molecular techniques relevant to fundamental to preclinical research in asthma pathogenesis and has generated unique observations regarding the impact of obesity on allergen-induced airway inflammation. She is expecting to defend her PhD thesis in late 2019.

Bottom Note : This work is partly presented at 13th International Conference on