Re-establishing idiopathic diminished allergic responses to ovalbumin challenge in sensitised guinea-pigs

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The inhalation of antigen in atopic asthma can induce early (EAR) and late asthmatic responses (LAR), inflammatory cell infiltration and airways hyperresponsiveness (AHR) (Robinson et al, 1993). We have established a protocol of sensitisation and subsequent ovalbumin (OVA) challenge in guinea pigs which induced these 4 features (Smith & Broadley, 2007). Recently the responses of guinea pigs to OVA challenge have declined, therefore this study was undertaken to modify the protocol in an attempt to restore the responses.

Guinea pigs (200-250g, male, Harlan) were sensitised with a suspension of OVA (100 or 150 µg) and aluminium hydroxide (AlOH₃) (100 or 150 mg) by either 2 or 3 injections (days 1 and 5 or days 1, 4 and 7). Airway responses to inhaled OVA (10 µg or 30 µg) of sensitised, conscious guinea pigs were determined by whole body plethysmography (Buxco Systems, USA) as the change in specific airways conductance (sGₘᵦ), compared to baseline values over a 12 hour period and at 24 hours. AHR was investigated from the bronchoconstrictor response to inhaled histamine (0.3 mM) both 24 hours pre- and 24 hours post-OVA challenge. Inflammatory cell influx was determined by bronchoalveolar lavage (BAL) at 24 hours post challenge. Modifications were made to the protocol, accumulatively, one change at a time.

Animals sensitised with 2 injections of 100 µg OVA and 100 mg of AlOH₃ and challenged with 10 µg OVA displayed an EAR (-45.6± 6.2%) but no LAR, AHR or significantly increased cell numbers, as compared to saline challenged animals. This was the original protocol of Smith and Broadley (2007). An increased OVA challenge from 10 to 30 µg increased the peak bronchoconstriction during the EAR (-60.9±2.1%) and produced AHR (-4.1±2.3% pre- ; -38.5±7.9% post-OVA challenge). The addition of a 3rd sensitisation injection (OVA 100 µg, AlOH₃ 100 mg) in addition to previous changes did not significantly impact any variable measured. However, increasing the OVA sensitisation concentration to 150 µg produced a significant increase in total cell numbers and particularly eosinophils, when compared to previous protocols. The inclusion of an increased concentration of alum (150 mg), in addition to all previous changes revealed a LAR (-17.6±4.6%), in addition to an EAR, AHR and inflammatory cell influx. Eosinophil, macrophage and lymphocyte numbers were all significantly increased compared to all other protocols. Thus, 3 sensitisation injections with 150 µg OVA and 150 µg AlOH₃ and subsequent challenge with 30 µg OVA restored the EAR, LAR, AHR and cellular inflammation. This study has shown that a time-dependent loss of allergic responses to OVA can be restored by increasing the sensitisation and challenge conditions. It also indicates dissociation between AHR and LAR and between cell influx and LAR.

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