Chapter-1

Development of mouse model of asthma: Airway hyperresponsiveness
1.1 INTRODUCTION

Airway hyperresponsiveness (AHR) is one of the most important characteristics of asthma and one of its main causes is thought to be allergic inflammation (Chung., 1986, Barnes., 1989). The structural changes that lead to AHR have been modeled and studied in detail (Wiggs et al., 1992, Lambert et al., 1993, Pare and Bai., 1996). Several animal studies were performed to clarify the relationship between airway inflammation and remodeling, and furthermore their contribution to AHR in chronic asthma, despite the fact that the precise mechanisms and associations are unknown (Temelkovski et al., 1998, Blyth et al., 2000, Trifilieff et al., 2000, Leong and Huston., 2001, Kumar and Foster., 2001, 2002). Airway hyperresponsiveness (AHR) is a heritable polygenic trait and together with eosinophilic airway inflammation and IgE production, is a hallmark of human allergic asthma (Elena et al., 2003). Airway hyperresponsiveness (AHR) is a central feature of asthma (Busse and Lemanske., 2001). The analysis of responses associated with the clinical manifestation of respiratory allergy is based on the analysis of immediate- and/or delayed-onset of pulmonary sensitivity by pulmonary function tests. Measurements can be made during or after exposure in spontaneously breathing conscious animals using various types of plethysmograph (e.g. whole-body, bias-flow or barometric and nose-only, volume displacement).

The purpose of the present study was to study the breathing pattern of mouse sensitized and challenged with OVA. We intend to measure specific resistance of airways (sRaw) in mice with the help of a small animal plethysmograph.
1.2 MATERIALS AND METHODS

1.2.1 Animal groups and treatment

Female BALB/c mice were divided into two groups. Each group comprised 6 mice. Following groups were made;

Group I Control mice (SAL/SAL mice)
Group II Mice sensitized and challenged with OVA (OVA/OVA mice)

Animals were restrained into the plethysmograph and breathing patterns were monitored on day 28. Varying concentrations of Mch (0–40 mg/kg) induced AHR was measured by using a double-chambered whole-body plethysmograph (Buxco; model No. PLY 3351) in OVA/OVA and SAL/SAL mice. sRaw was monitored with the Acknowledge software program version 3.1 (Biopac, USA).

1.3 RESULTS

1.3.1 Induction of inflammatory and allergic airways in mice

We observed significant (p< 0.05) increase in sRaw in OVA/OVA mice in a dose dependent manner in comparison to the SAL/SAL treated mice. Mch induced increased sRaw in OVA sensitized and challenged mice is indicative of asthma pathogenesis. Saline sensitized and challenged mice showed average sRaw ranging from 1 to 5 cmH2O.s depending on the concentration of Mch (Fig. 1.1).
Fig. 1.1: Comparison of sRaw between SAL/SAL mice and OVA/OVA mice (mean ± SD, *P<0.05)
1.4 DISCUSSION

Increased sRaw is the measure of decreased lung function and forceful breathing (Simpson et al. 2007; Ranganathan et al., 2008; Paul et al. 2009). Our aim in the present study was to measure sRaw in Ovalbumin-induced asthmatic mice. Significant increase (P<0.05) in sRaw in OVA/OVA mice as compared to SAL/SAL indicated poor lung function as seen in asthma. The afferent innervation of the airways may play a role in the expression of airway hyperactivity. Reduction in the active respiratory parenchyma, airway remodeling and emphysema-like parenchyma changes may contribute to the airflow obstruction and AHR. Thus, the sensitization and challenge protocol adopted by us induced significant change in lung physiology in mice and mimics one of the feature of human asthma.