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Impact of short term forced oral breathing induced by nasal occlusion on respiratory function in mice

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ABSTRACT

Inconsistent findings regarding the experimental nasal obstruction on respiratory functions in small animals have been reported. The purpose of this study was to investigate the impact of short term forced oral breathing on respiratory functions as well as the therapeutic implication of esophageal intubation in BALB/c mice. Thirty BALB/c mice were randomized equally to two groups: an experimental group and control group. Oral breathing was induced by applying petrolatum ointment in nostrils for occlusion both nasal cavities. Esophageal tube was inserted to enlarge the oropharyngeal airway in the experimental mice. Respiratory parameters were measured by barometric whole-body plethysmography (WBP) in the following condition: normal nasal breathing; nasal breathing loading in a soft bag; forced oral breathing loading in a soft bag; forced oral breathing loading in a soft bag after undergoing esophageal intubation. After applying petrolatum ointment of nostrils, all the mice switch to oral breathing with apparent discomfort (bradypnea). Nasal occlusion was associated with a decrease in the average respiratory rate (268 ± 36 vs. 90 ± 10 breaths/min; $P < 0.01$) and an increase in Penh (0.67 ± 0.14 vs. 19.23 ± 2.12; $P < 0.01$). After undergoing esophagus intubation, these mice switched to oral breathing with less discomfort. Compared with the control mice, respiratory rate (175 ± 25 vs. 90 ± 10) was higher; the Penh (8.84 ± 1.05 vs. 18.09 ± 2.03; $P < 0.01$) was lower. Short term forced oral breathing induced by nasal occlusion caused respiratory insufficiency in mice. Stenotic oropharyngeal airway was supposed to be one of the most important factors. Enlarging oropharyngeal airway by esophagus intubation could improve the respiratory insufficiency under nasal occlusion.

1. Introduction

Allergic rhinitis (AR) is the most prevalent allergy disease in the world (Asher et al., 2006). The most common clinical manifestations of AR are nasal obstruction, rhinorrhea, sneezing and nasal pruritus. Impaired nasal breathing results in forced oral breathing, one of the most frequent complaint from patients with AR (Bekes et al., 2011; Patou et al., 2006). Nasal obstruction is also commonly observed in many other pathological conditions, such as rhinosinusitis, adenoid hypertrophy and nasal polyps. Forced oral breathing inhales gas by-pass the nasal mucosa and increased levels of inhaled aeroallergens may reach the lower airways (Rimmer and Ruhno, 2006). Transition from nasal to oral breathing is easily accomplished in awake adults. This is not the case however with infants, in whom the close approximation of the soft palate, tongue and epiglottis makes oral breathing difficult (Bergeson and Shaw, 2001; Harding, 1986; Polgar and Kong, 1965; Shaw, 1968; Stocks and Godfrey, 1978; Swift and Emery, 1973; Trabalon and Schaal, 2012). Consequently, in children, forced oral breathing, whether or not caused by nasal obstruction, can be associated with both social and physical stress (Fensterseifer et al., 2013; Hitos et al., 2013; Jefferson, 2010).

Mouse allergic airway models have been extensively employed. A previous study conducted in the authors' laboratory showed that airway resistance (RNA) increased in the allergic rhinitis (AR) mouse model, however the phenomenon of transition from nasal to oral breathing after nasal challenge appeared to be rare (Xie et al., 2010). These results consequently posed the question of whether or not it is inherently difficult for mice to breath through the mouth. Several studies have investigated the impact of early nasal obstruction in mice. Niaki et al. (2008) found that mice with nasal occlusion that were switched to oral breathing suffered from apparent bradypnea, higher PCO_2 levels, and decreased arterial

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blood pH levels. Nakajima and Ohi (1977) found that obstructing nasal passages in small animals (including mice) induced excessive accumulation of gas in the gastrointestinal tracts. Not all studies however report consistent results. Agrawal et al. (2008) reported that mice were preferential but not obligate nasal breathers with the majority of mice that switched to oral breathing in the study presenting with no apparent discomfort after nasal occlusion.

A previous study has conducted invasive lower airway resistance experiments in mice (Zhang et al., 2009). In this study, the mice were inserted with esophagus intubation to induce intrapleural pressure. On several occasions, it was found that if lavage fluid from the trachea to the upper airway directed towards the nasopharynx, the fluid almost always effused from the mouth. However, if mice did not undergo esophagus intubation, the fluid outflow from the nose was equivalent to that of the infusion rate. These results indicated that mice may have an inherent stenotic oropharyngeal airway and that esophagus intubation in mice can enlarge the oropharyngeal airway.

The impact of oral breathing induced by nasal occlusion on respiratory function in mice remains controversial. The aim of this study was to evaluate the impact of short term forced oral breathing, induced by nasal occlusion, on respiratory functions in conjunction with the therapeutic implication of esophageal intubation in BALB/c mice.

2. Materials and methods

2.1. Animals

Thirty female BALB/c mice weighing 18–20 g (6–8 weeks of age) were obtained from the Guangdong Laboratory Animal Center (Guangzhou, China). All animals were housed in a specific pathogen-free animal facility with a repeating 12:12 h light:dark cycle at a constant temperature of 22 °C ± 1 °C. Mice were randomly assigned to either the control or experimental groups.(Fig 1) Fig. 1 showed schematically protocol of a different condition. The experimental group was then subdivided into four condition groups namely: condition (1) normal nasal breathing; condition (2) nasal breathing loading in a soft bag; condition (3) oral breathing induced by nasal occlusion loading in a soft bag and condition (4) oral breathing induced by nasal occlusion loading in a soft bag after esophageal intubation. Both the control group and the experimental group underwent nasal occlusion, but the experimental group was treated with esophageal intubation to enlarge the oropharyngeal airway.

2.2. Nasal obstruction procedure

This study was conducted in conformity with the American Physiological Society's Guiding Principles in the Care and Use of Animals. All experimental procedures were approved by the Animal Ethics Committee of the First Affiliated Hospital, Guangzhou Medical College. After mice were restrained in a soft bag (Fig. 2), petrolatum ointment was applied to the nostrils of mice for the purpose of total occlusion in both nasal cavities. Completely sealing both nostrils resulted in immediate oral respiration and obvious bradypnea. If compensatory oropharyngeal breathing with swallowing was absent, petrolatum ointment was carefully applied to the nostrils of mice again.

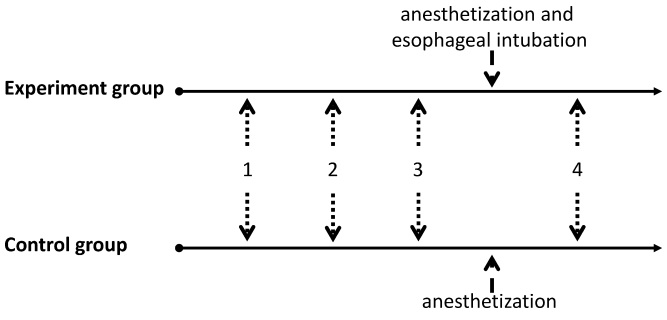

Fig. 1. Schematic experimental protocol of different experimental conditions.

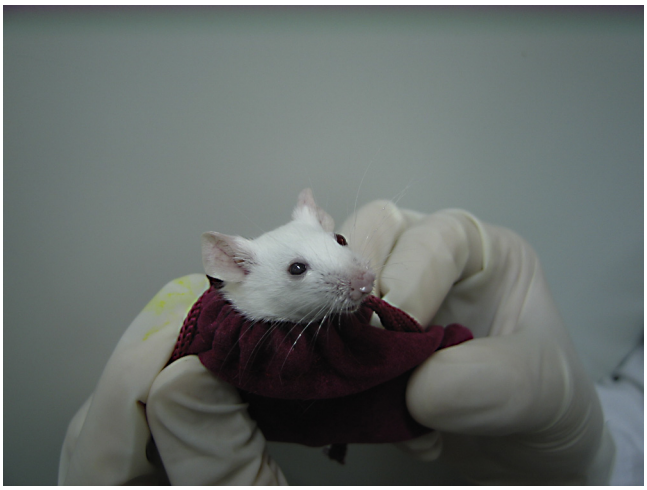

Fig. 2. A small soft bag (10 cm × 5 cm) was used to restrain the limbs of mice.

2.3. Esophageal intubation

All mice after condition 3 were anesthetized with intraperitoneal (i.p) injections of 90 mg/kg body weight sodium pentobarbital. In experimental group, the esophageal tube (RC Mouse Esophageal Kit-CNS1010, Buxco, USA) carefully inserted. The approximate depth where the esophageal tube would reach the esophagus was marked and the esophageal tube slowly removed. Mice in the control group underwent i.p injections of sodium pentobarbital alone after condition 3.

2.4. Measurement of respiratory parameters by barometric whole-body plethysmography (WBP)

Breathing parameters were measured using a single-chamber WBP (Buxco, NY, US) (Miyahara et al., 2005). Spontaneous breathing mice were placed into a small soft bag (10 cm × 5 cm), so that their limbs were restrained in the bag. The mice were then placed into the main chamber of the plethysmograph. Mice remained in the main chamber of the plethysmograph for 10 min, with constant airflow, before the respiratory parameters were measured. The airway inspiratory and expiratory times and respiratory frequency (RF) were recorded automatically and then averaged. From the box flow signal, RF, inspiratory time (TI), expiratory time (TE), tidal volume (VT), minute ventilation (MV), and Penh (pause × PEF/PIF) were recorded. Enhanced pause (Penh) values were measured during each 3-min sequence as previously described (Zhang et al., 2009).

2.5. Statistical analysis

All data are expressed as means ± standard deviation (SD). The multiple comparisons were conducted while comparing multiple variables between the control group and the experimental groups. The paired-samples *t* test was used to compare the means of two variables for a single group. All statistical analyses was performed