

Effect of surfactant inhalation on allergic bronchoconstriction in guinea pigs

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Summary

Background In the small airway, surfactant reduces surface tension, prevents liquid filling of bronchioles, thereby maintaining patency in the small airways. Recent reports demonstrated that surfactant dysfunction develops in experimental asthma in immunized guinea pigs. However, there are few reports concerning surfactant and lung function in an experimental asthma model.

Objective To examine whether inhaled surfactant improves lung mechanics in antigen-induced bronchoconstriction in guinea pigs.

Method We developed a passively immunized guinea pig model for allergic bronchoconstriction induced by antigen inhalation. Using this model, we investigated the effect of inhaled exogenous surfactant, surfactant TA, on the airway opening pressure (Pao) after antigen challenge.

Results Aerosol antigen challenge produced a gradual and long-lasting increase in Pao. Twenty minutes after antigen challenge, aerosolized surfactant TA, 20 mg/ml, was inhaled for 90 s, and it significantly reduced the Pao by 32.8% in 12 min, while a 10.2% reduction was observed in a control group in the same period. When surfactant TA was administered by 90-s inhalation before antigen challenge, it inhibited the Pao increase in a dose-dependent manner: mean inhibitory rates of Pao were 33.6% in surfactant TA 10 mg/ml and 61.9% in surfactant TA 20 mg/ml, respectively.

Conclusion Inhaled surfactant showed preventive and recovery effects on antigen-induced bronchoconstriction in an immunized guinea pig model.

Keywords: surfactant, bronchial asthma, aerosol, inhalation, guinea pig

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Introduction

It is generally realized that asthma is a very complex syndrome with different causes and a variation of the dominating clinical symptoms. However, one symptom seems to stand out: the patient has a feeling of an increased airway resistance, particularly during expiration. Since there is no reason for the spasm increase during that phase of the respiratory cycle, it remains to be answered why the resistance is so much greater during expiration.

G. Enhörning presented the hypothetical roles of surfactant in asthma [1], and recent experimental studies suggest the surfactant functions need to be considered in the interpretation of pathological mechanisms of asthma. Recently, Liu *et al.* demonstrated that a rapid inactivation of surfactant develops when the immunized guinea pig is challenged with antigen [2]. Drazen *et al.* suggested that surfactant normally counteracts any bronchoconstriction response by preventing fluid filling in ridges and folds of the epithelial surface [3]. Due to the collapse in the respiratory bronchioles and resulting compression of slightly larger airways, expiration meets considerable resistance. Thus, several signs typical for asthma may be due to a relative surfactant deficiency.

While in an experimental ARDS the inhibitory effect

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surfactant in the small airway should not be ignored in diseases such as COPD and bronchial asthma.

To examine whether airway surfactant has a significant effect if any in asthmatic attack, it is essential to examine the effect of surfactant administration or surfactant depletion on lung function in an asthma model. For example, future studies, e.g. on inhalation of SP-B antibody, may or may not support the results of this experiment. In a previous report by Becher [22], intra-tracheal instillation of natural surfactant prevented allergic bronchoconstriction. However, as an asthma model, an instillation procedure may not be adequate because it might change bronchial responsiveness and cause local airway liquid filling that may make it difficult to assess the data.

In our asthma model, particular efforts were made to produce reproducibility, such as 'vital capacity manoeuvre' to unify the volume history, blocking the effect of histamine, timing of sensitization, and so on. Another reason for choosing an inhalation method was that, in the clinical situation of an asthmatic attack, aerosol inhalation will be preferable because it is a more safe and easier mode of administration.

In this study, the effect of surfactant pre-inhalation was much more significant than that post-inhalation. There are several possible reasons for this explanation. Firstly, distribution of administered surfactant may be different before and after challenge. It is known that in constricted airways deposition of aerosol shifts to the proximal side [23]. Secondly, once airway oedema occurs, exudated protein or liquid causes surfactant inhibition that may not be overcome completely by exogenous surfactant.

The doses of surfactant inhaled in this study were approximately 0.46 or 0.90 mg which means about 1.2 or 2.3 mg/kg. The endogenous surfactant pool size is not known for guinea pig, but for sheep it has been reported to be 15 mg/kg [24]. If it is of a similar size in the guinea pig, approximately one-tenth of the volume of endogenous surfactant was administered in this study. It is a considerably small amount of surfactant compared to that used in RDS [25].

In future studies, each surfactant biophysical property should be examined in more detail with relevance to bronchial asthma. For example, surface spreading force of surfactant [26] may be important for the delivery of inhaled surfactant. Because of this spreading force surfactant may spread uniformly over the airway when we use exogenous surfactant as a possible treatment for pulmonary diseases. In our preliminary study, DPPC pre-inhalation alone could not inhibit the Pao increase in antigen-induced bronchoconstriction (data not shown). However, the effects of other components of surfactant,

such as other lipids, SP-A, B and C remains to be explained.

Although the mechanism of administered surfactant in an asthma model should be identified in more detail, the results of this study may support the possible effect of aerosol surfactant in clinical asthma.

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