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Afferent Activity in Pulmonary Stretch Receptors Before and After Lung Injury

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ABSTRACT

This study was undertaken to determine the effect of a lung-injury on the activity of slowly adapting pulmonary stretch receptors. Comparisons of receptor activity were made at inhibition of inspiratory (phrenic nerve) activity. The inspiratory activity of these receptors was found to be decreased after lung-injury.

INTRODUCTION

We have previously studied the effects of ventilatory variables in cats at inhibition of inspiratory activity (4,5,7). Comparisons of the effects of different changes in ventilatory variables were made at inhibition of inspiratory activity, i.e. when the sum of afferent inputs (e.g. from chemo-receptors and mechano-receptors) inhibits inspiratory activity. We consider a ventilatory setting that barely inhibits inspiratory activity to be a useful biological reference point for comparisons ("inhibition of inspiratory activity"). We found that inhibition of inspiratory activity occurred at a somewhat lower arterial PCO2 after lung injury

(5), which would lead to correspondingly lower chemoreceptor activity. This implies that the activity of other afferents changes after lung injury if inhibition of inspiratory activity is maintained. The present investigation was undertaken to determine whether the activity of the slowly adapting pulmonary stretch receptors (PSR) was altered after a lung injury that included a reduction of pulmonary compliance. Changes in pulmonary compliance alone are known to lead to changes in the activity of rapidly adapting pulmonary stretch receptors (3,9).

The aim of the present study was to determine whether the PSR changes its over-all activity or its phasic activity after lung injury.

METHODS

In five cats (2.2-3.5 kg), general anaesthesia was induced with chloroform and maintained with intermittent infusions of chloralose (7.2 g/l) as required. After endotracheal intubation a ligature was tied around the endotracheal tube to prevent air leakage. A catheter was inserted through femoral artery until its tip lay in the thoracic aorta, and another catheter was introduced through the femoral vein until its tip lay in or near the right atrium. A mixture of glucose and sodium bicarbonate (two-thirds 5.5% glucose + one-third 0.6 M $NaHCO_3$) was given intravenously throughout the experiment at a rate of 2 ml/kg b.w./h. Body temperature was maintained in the normal range with use of a heating pad.

Arterial samples were taken at intervals throughout the experiment via the femoral artery catheter. Acid-base imbalances were corrected by administration of $NaHCO_3$ or respirator adjustments. Arterial blood pressure and intratracheal pressure were measured with transducers (Druck Ag, GFR) placed at the level of the tips of the respective catheters. Signals were amplified (Hellige AG GFR) and recorded (Recorder 330-P, Hellige AG, GFR) and in addition intratracheal pressure and vagal impulses were recorded on an oscillograph (Oscillograph 6608, SE Labs, UK). The cats were ventilated with a volume-controlled ventilator (Siemens-Elema 900C). Positive end-expiratory pressure (PEEP) of 4-5 cm H_2O was used at a respirator rate of 60 breaths/minute. FIO_2 was increased to 0.5 after lung injury (see below). Spontaneous breathing activity could be inhibited by increasing pre-set tidal volume until the phrenic nerve activity ceased (inhibition of inspiratory activity).

A medial frontal incision was made in the pre-tracheal region, permitting exposure and dissection of vagal and phrenic nerves. These were immersed in mineral oil to prevent drying of the nerve and for electrical insulation.

After dissection and removal of connective tissue, the left phrenic nerve was placed on two hook electrodes. Phrenic nerve activity was amplified with the use of one channel of a Neurolog system (NL 100; NL 103; NL 105; NL 115; NL 200), and was fed through an integrator and recorded on the recorder (Recorder 330-P, Hellige AG, GFR).

From one of the cervical vagus nerves fine slips were dissected from the intact nerve after removal of the connective tissue. Nerve activity was recorded between a single electrode and ground. Filaments were split from the slip of the vagus nerve and impulse activity was analysed until the signal from a single slowly adapting PSR was found. This receptor was recognized by its characteristic respiration-synchronized activity and by the occurrence of enhanced activity on airway occlusion of the expiratory tube, leading to an increased lung volume. Impulses were processed by the other channel of the Neurolog system, and a spike processor (Digitimer, UK) counted the impulses within the range of a window discriminator. This range could be adjusted to accept potentials of desired amplitude. The impulses were displayed on an oscilloscope and recorded on the oscillograph, together with the intratracheal pressure. Thus PSR impulses could be counted for inspiratory and expiratory phases or for shorter intervals of individual respiratory cycles. The remaining part of the vagus nerve was left intact, as well as the contralateral vagus.

Protocol

All observations were made at inhibition of inspiratory activity and at a constant minute volume and ventilation frequency. When a PSR was found, the acid-base status was checked and a baseline recording, at inhibition of inspiratory activity, was made after i.v. administration of 2 ml of pancuroniumbromide (Pavulon) for muscle relaxation, so as to prevent disturbing muscle reflexes. Recording was repeated

after lung injury induced by administration of xanthine oxidase, (50 units/ml, 0.2 ml/kg b.w.). This was given through a thin catheter into the distal part of the endotracheal tube. Recordings were made at steady state and at inhibition of inspiratory activity, usually 10-15 minutes after administration of xanthine oxidase.

In one animal, recordings were made after a single dose of xanthine oxidase and again after a second dose. In another animal the protocol was followed twice on two different, separately isolated PSR fibers.

Analysis of Data

Afferent vagal nerve activity was computed as the **mean impulse rate** (impulses/s) recorded for inspiratory and expiratory phases over a period of ten respiratory cycles. Mean values for the six fibers are presented in the figures. In some experiments the afferent activity was also computed for intervals of 100 ms. Inspiratory and expiratory phases were determined from simultaneous recording of intratracheal pressure. Mean peak and end-expiratory pressures were calculated analogously.

RESULTS

This study shows that the overall and phasic activity of PSRs is altered after lung injury induced by xanthine oxidase. Before lunginjury the PSR activity was proportional to the

airway pressure, with lower activity during the expiratory phase and higher activity during the inspiratory phase (Fig.1). After lung injury the PSR activity was less pronounced at the peak of inspiration than before the lung injury (Fig.2).

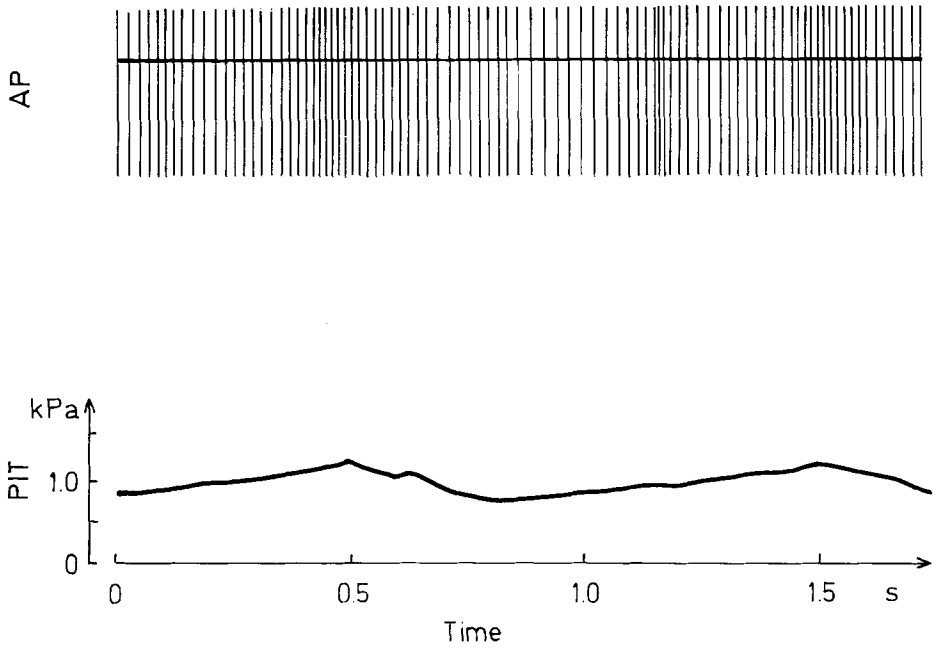

Fig.1. Intratracheal pressure (PIT, lower panel) and activity (action potential, AP) from one slowly adapting pulmonary stretch receptor during mechanical ventilation before lung injury.

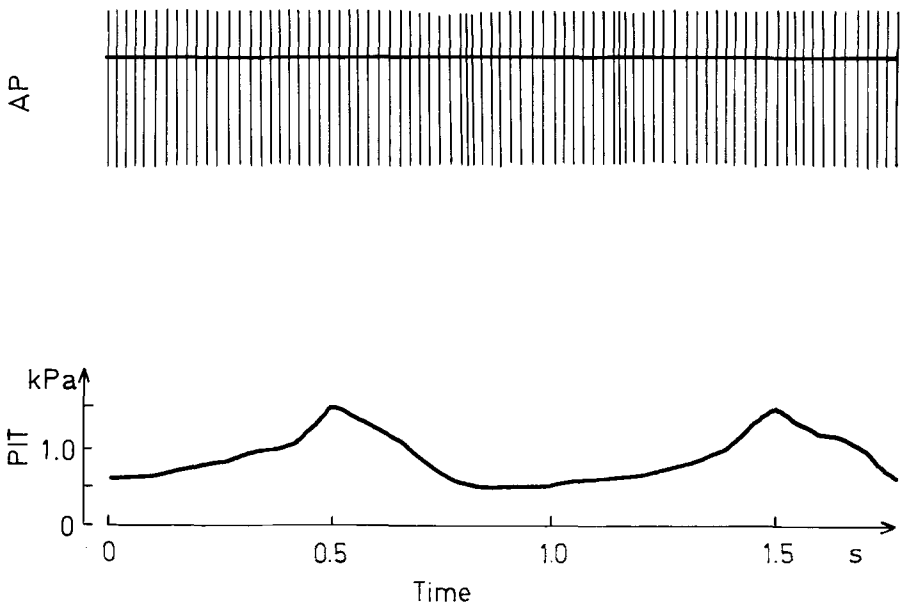

Fig.2. Intratracheal pressure (PIT, lower panel) and activity (action potential, AP) from the same slowly adapting pulmonary stretch receptor as in Fig.1 during mechanical ventilation after lung injury.

The average impulse activity was calculated both for whole respiratory cycles and for inspiratory and expiratory phases. The total mean activity of six fibers before lung injury was 89 impulses per second and after lung injury 74 impulses per second. The inspiratory activity before lung injury was 56 impulses per second and after lung injury 45 impulses per second, ($p<0.05$), whereas the corresponding values for expiratory activity were 33 and 30 impulses per second respectively (difference non-significant) (Fig.3).

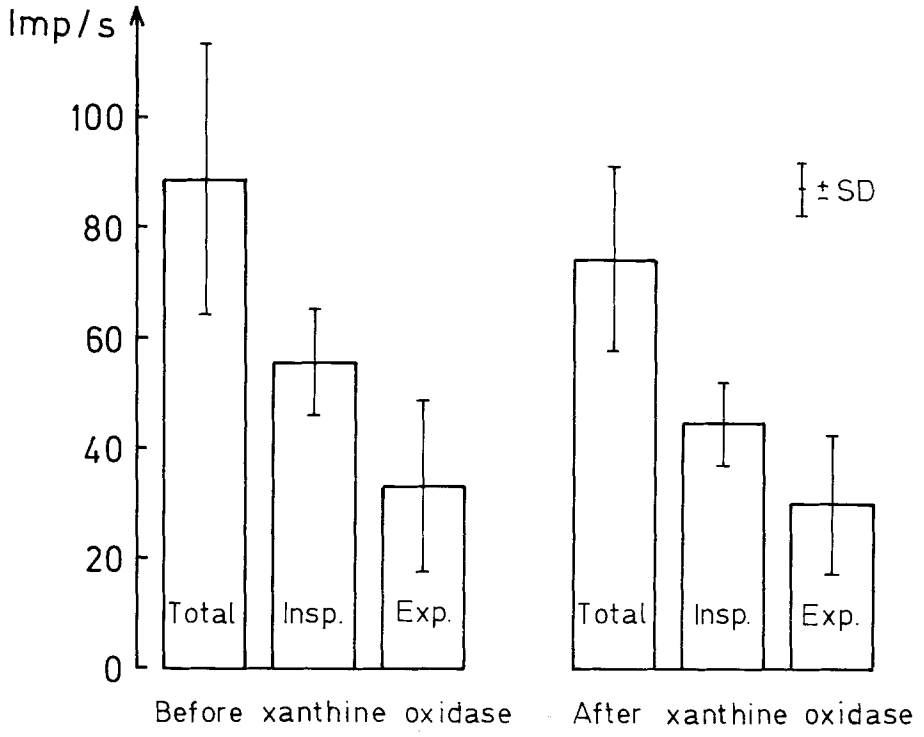

Fig.3. Mean impulse frequency of six different slowly adapting pulmonary stretch receptors. The impulse frequency has been calculated for the whole respiratory cycle and for the inspiratory and expiratory phases before and after lung injury.

When the PSR activity was further subdivided into periods of 100 ms, this pattern became more pronounced. This was done for two fibers and representative curves are shown in Fig.4. Thus, the results in Figures 3 and 4 demonstrate that instillation of xanthine oxidase into the airways reduces the total number of impulses per respiratory cycle and that the reduction in impulse frequency is most marked during inspiration.

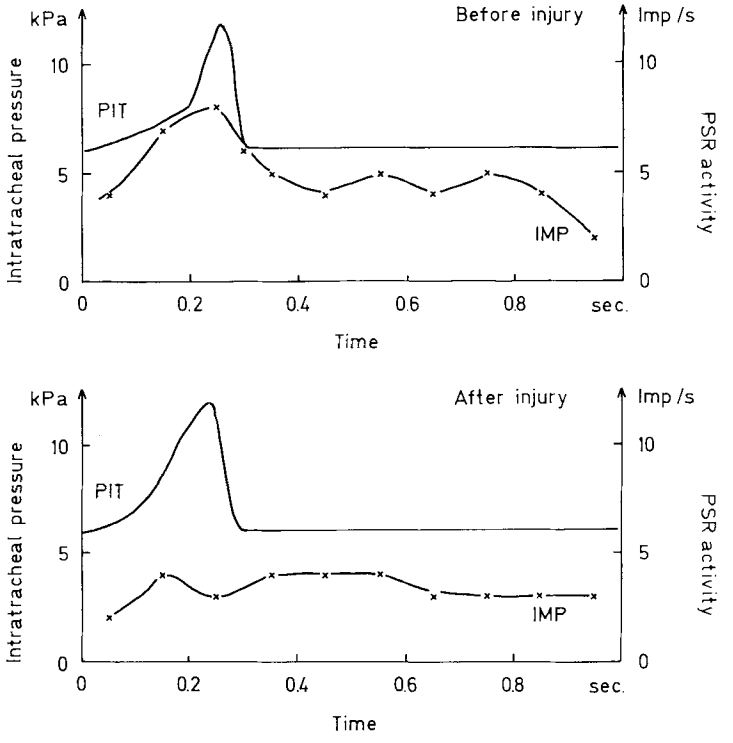

Fig.4. Impulse frequency in one slowly adapting pulmonary stretch receptor before and after lung injury. The impulse frequency has been calculated for 100 ms intervals during one respiratory cycle.

Before lung injury the airway pressure at inhibition of inspiratory activity was 1.3 kPa at the peak of inspiration and the end-expiratory pressure 0.6 kPa. After lung injury the corresponding values were 1.5 and 0.6 kPa respectively (Fig.5). Thus the difference in peak pressure was significant-

ly higher after lung injury ($p<0.025$).

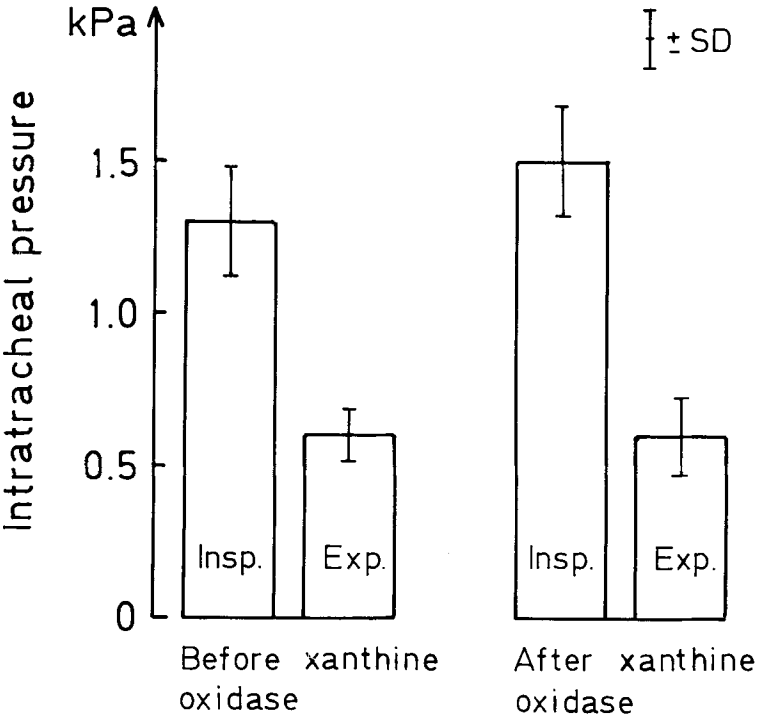

Fig.5. Peak and end-expiratory intratracheal pressure before and after lung injury at inhibition of inspiratory activity. Measurements were made simultaneously with the receptor activity presented in Fig.3

DISCUSSION

The results of this study show that the activity of the slowly adapting pulmonary stretch receptors decreases after lung injury induced by instillation of xanthine oxidase into the airways. The inspiratory activity was lower after lung injury,

although the airway pressure was higher. This led to a shift in the receptor activity from a phasic pattern to a more continuous one.

Saugstad el al (10) reported that instillation of xanthine oxidase into the airways produced a lung injury characterized by perivascular oedema, dilatation of lymph vessels, infiltration of neutrophils and filling of the alveoli with amorphous material, resulting in a reduction of lung compliance. We did not measure lung compliance in our experiments, but the tidal volume and consequently the airway pressure had to be increased after the lung injury in order to maintain inhibition of inspiratory activity, which probably reflects a decrease in lung compliance.

Reductions in lung compliance have been shown to increase the activity of rapidly adapting pulmonary mechano-receptors (3,8). These receptors are thought to stimulate inspiratory activity, possibly as sighs, in response to changes in lung compliance and/or functional residual capacity. It is difficult to determine their role in the present experiments.

The slowly adapting pulmonary stretch receptors are thought to be involved in the control of the depth and rate of breathing (2); their major function may be to interrupt inspiration. Thus, a change from phasic to continuous activity of these receptors could be of great importance in the control of breathing. A continuous discharge from PSRs results in inhibition of inspiratory activity (1,6,9).

In newborn infants with severe respiratory distress requiring respirator treatment it is often seen that inhibition of spontaneous breathing requires that the arterial blood gases are within the normal range. During recovery, when the lung attains better compliance, while still mechanically ventilated, spontaneous breathing usually reappears and may interfere with the mechanical ventilation. These observations might be explained by the findings in this study that the activity of the slowly adapting pulmonary stretch receptors was continuous after lung injury, when compliance was low, but phasic before lung injury, when compliance was high.

CONCLUSIONS

It is concluded that the inspiratory activity of slowly adapting pulmonary stretch receptors is reduced after lung injury.

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