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Ariway Pressures During Positive Pressure Ventilation with Superimposed Oscillations Before and After Lung Injury in the Cat

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ABSTRACT

This study was made to determine how oscillations superimposed on intermittent positive pressure ventilation (IPPV) influence the arterial blood gases, pH and the airway pressures during adequate alveolar ventilation i.e. at inhibition of inspiratory activity, before and after experimentally induced lung injury in the anaesthetized cat. Two IPPV frequencies were studied. The lung was injured by instillation of xanthine oxidase into the upper airways during IPPV. The peak, mean and end-expiratory intrapleural and airway (intratracheal) pressures at two levels were measured and the arterial blood gases and pH were determined at inhibition of inspiratory activity with and without superimposition of oscillations on the ventilatory pattern. Before lung injury, superimposed oscillations lowered the airway pressures only at an IPPV rate of 15 breaths per minute (b.p.m.). After lung injury, such oscillations increased the airway pressures only at 15 b.p.m. The airway pressures were always lower at 60 than at 15 b.p.m.

INTRODUCTION

We have previously shown that superimposition of oscillations on intermittent positive pressure ventilation (IPPV) lowers the mean intratracheal airway pressure at IPPV frequencies of 15 breaths per minute (b.p.m.) but not at 100 b.p.m. (3). The pressure reduction with superimposed oscillations may be of value during ventilation of newborn infants, since high airway pressures during IPPV together with oxygen administration are considered to play an important pathogenetic role in bronchopulmonary dysplasia (5). In infants with interstitial emphysema, superimposed oscillations are of advantage in most cases (4,8).

Experimental studies of the effects of ventilatory patterns on the airway pressures and arterial blood gases in the presence of a lung disease require a good and stable experimental model which allows repeated measurements under standardized conditions. Recently Saugstad et al (7) demonstrated that injection of xanthine oxidase into the trachea results in lung damage with formation of perivascular oedema, dilatation of lymph vessels and infiltration of neutrophils with reduced lung compliance. The lung damage in this experimental model has some histopathological characteristics in common with that which may be seen in prolonged neonatal ventilation (> 5 days). The model could therefore be applicable in studies of the way in which IPPV with and without superimposed oscillations influences the airway pressures and arterial blood gases after lung injury.

The present study was undertaken to determine whether pressure

oscillations superimposed on IPPV influence the arterial blood gases and pH and the airway pressures differently at inhibition of inspiratory activity in cats with normal and injured lungs.

METHODS

Subjects and preparation

Seven cats, weighing between 2.5 and 4.7 kg, were studied. Anaesthesia was induced with chloroform and maintained with intermittent injections of chloralose (Merck AG, GFR). Catheters were introduced through the femoral vein and artery into the inferior vena cava and aorta. The left phrenic nerve was exposed through a frontal, medial incision in the neck. An endotracheal tube was inserted just below the larynx and a ligature was placed so that no air could leak between the endotracheal tube and the tracheal wall. Two equally long catheters had previously been attached to the endotracheal tube so that one had its tip 1 cm above the carina and the other had its tip 5 cm further down. To measure the pleural pressure, another catheter was inserted through the rib cage, without letting any air into the pleural space.

Measurements

Airway pressures were measured at the tip of the endotracheal tube ("tip pressure") and also about 1 cm above the carina and 5 cm below the tip of the endotracheal tube ("distal pressure"). Pleural pressure was measured through a catheter

inserted into the pleural space. Arterial blood pressure was measured through a catheter placed in the abdominal aorta. All catheters were connected to identical transducers (Druck AG, GFR) and amplifiers (Hellige AG, GFR). All signals were amplified with an 8-channelled medical amplifier system (Hellige AG, GFR) and fed to a recorder (Recorder 330-P, Hellige AG, GFR). Measurements of arterial blood gases and pH were made with an automatic acid-base analyser (Radiometer, Denmark).

The phrenic nerve activity was recorded by placing the left phrenic nerve on bipolar hook electrodes. The nerve and electrodes were immersed in mineral oil. For amplification a Neurolog system (Digitimer, U.K.) was used.

Ventilators

A Siemens Elema Servo Ventilator (SV 900C) was used in the experiments. A positive end-expiratory pressure (PEEP) of 0.5 kPa was applied. The set PEEP was not altered when oscillatory ventilation was superimposed. Oscillations of the ventilation gas were accomplished by attaching metal bellows to the tubing between the ventilator and the endotracheal tube. The bellows were controlled by a motor on which the stroke volume and the number of strokes per minute could be set independently. The stroke volume of the bellows in these experiments was 19 ml. The number of strokes was 570-600/minute.

Experimental procedure

Before any measurements were made a check was made to see that all airway pressures were at zero during expiratory rest with the cat breathing spontaneously and also that the acid-base status was normal and that the base excess (BE) was above -5 mEg/l. The experiments were performed during ventilation with 15 or 60 breaths per minute with the ventilator in volume-controlled mode. The inspiratory time was always 33% of the cycle and a plateau of 10 % was used.

First the cat was ventilated at a frequency of 15 or 60 per minute, and the minute ventilation was slowly increased until the phrenic nerve activity was inhibited. About 20 seconds after inhibition of inspiratory activity, measurements of the peak, mean and end-expiratory airway and pleural pressures were made. A blood sample was drawn for determination of arterial blood gases and pH. Oscillations were then superimposed and the tidal volume of the ventilator was reduced until the phrenic nerve activity reappeared; it was then again slowly increased until the phrenic nerve activity was inhibited and the same measurements were repeated. Subsequently 10 U/kg b.w. of xanthine oxidase was injected into the airways and the fraction of inspired oxygen (FIO_2) was increased to 0.4. After 30 minutes the same procedure was repeated, with ventilation to inhibition without and with superimposed oscillation.

Histopathology of the lungs

After the experiment the lungs were perfused with a mixture of formaldehyde (10%) and glutaraldehyde (4%) through a catheter inserted into the pulmonary artery. The lungs were then removed and placed in a 4% solution of formaldehyde. Histological examination revealed a non-homogeneous distribution of atelectatic areas with capillary dilatation, oedema, and fluid accumulation in the alveolar spaces. In some animals there was also local infiltration of leucocytes in the atelectatic areas.

RESULTS

Before lung injury, without oscillations, at inhibition

At inhibition of inspiratory activity, without oscillations the arterial PO_2, PCO_2, pH and BE were the same at 15 and 60 b.p.m. The peak and mean airway pressures were lower at 60 than at 15 b.p.m. ($p<0.01$).

Before lung injury, with oscillations, at inhibition

When oscillations were superimposed the arterial blood gases and pH were the same as without superimposed oscillations at inhibition of inspiratory activity. With oscillations, as without the peak and mean airway pressures were lower at 60 than at 15 b.p.m. ($p<0.01$). At 15 b.p.m. the peak and mean airway pressures were lower with than without superimposed oscillations ($p<0.01$).

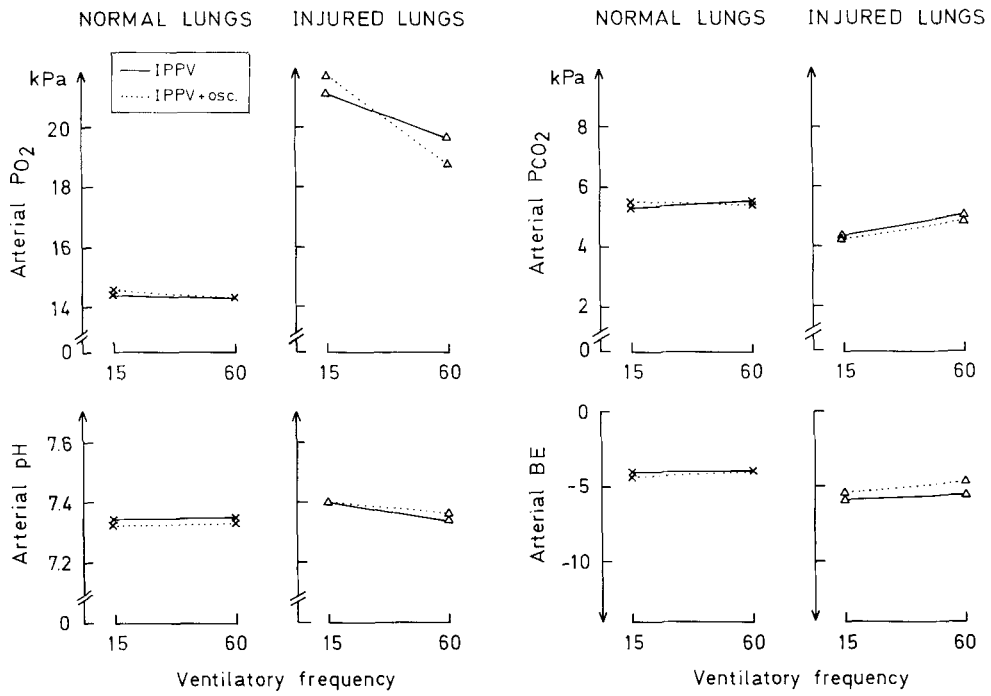

Fig. 1
Arterial PO_2 and PCO_2, pH and base excess (BE) during ventilation at 15 and 60 b.p.m. at inhibition of inspiratory activity without superimposed oscillations (whole lines) and with superimposed oscillations (dotted lines). Triangles represent experiments made after lung injury.

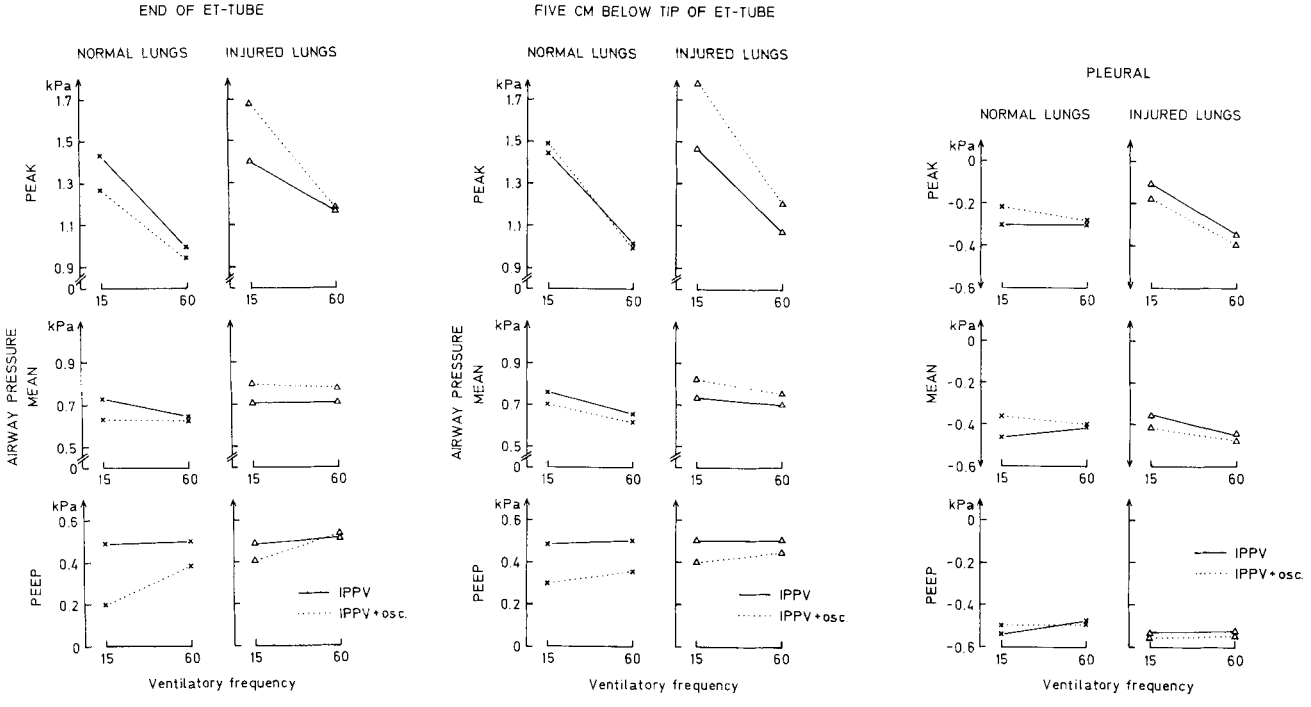

Fig. 2
Peak, mean and end-expiratory airway and pleural pressures during ventilation at 15 and 60 b.p.m., at inhibition of inspiratory activity without superimposed oscillations (whole lines) and with superimposed oscillations (dotted lines). The airway pressures are measured at the distal end of the endotracheal (ET) tube and 5 cm below the end of the ET tube. Triangles represent experiments made after lung injury.

After lung injury, without oscillations, at inhibition

The arterial PCO_2 was lower after than before lung injury ($p<0.01 - 0.05$). PO_2 was always higher after than before lung injury due to the higher FIO_2. Arterial pH and BE were the same as before lung injury. The peak and mean airway pressures were lower at 60 than at 15 b.p.m. ($p<0.01$). Pleural pressure was lower at 60 than at 15 b.p.m. ($p<0.05$).

After lung injury, with oscillations, at inhibition

The arterial PCO_2 was lower after than before lung injury ($p<0.01 - 0.05$). PO_2 was always higher after than before lung injury, because of the higher FIO_2. Arterial pH and BE were the same as before lung injury. The peak and mean airway pressures were lower at 60 than at 15 b.p.m. ($p<0.01$). Pleural pressure was lower at 60 than at 15 b.p.m. ($p<0.05$). The peak and mean airway pressures were higher with than without superimposed oscillations at 15 ($p<0.01$) but not at 60 b.p.m..

DISCUSSION

This study shows that airway pressures at inhibition of inspiratory activity differ before and after lung injury. Thus, the airway pressures were higher after than before lung injury at a ventilatory frequency of 60 b.p.m., but the same under both conditions at a ventilatory frequency of 15 b.p.m. Superimposition of oscillation lowered the airway pressures before but not after lung injury.

Attempts have been made to standardize animal models of bronchopulmonary dysplasia to be used in experimental studies (6). Of all species studied, only the newborn baboon has been kept on a ventilator long enough to mimic stages 2 and 4 of this condition (6). Even if damage caused by long-term ventilation may differ from that induced by chemical agents, the latter is the only alternative in most experimental situations. We therefore considered several alternatives such as oxygen injury, oleic acid injury and injury caused by xanthine oxidase.

Instillation of oleic acid into the lungs results in a very unstable condition, usually with progressive deterioration of lung function, and does not permit valid comparisons of different respirator settings. Administration of 100% oxygen needs 4 to 5 days to cause injury with pulmonary oedema and alveolar damage. We have therefore chosen the technique used by Saugstad et al (7) with instillation of xanthine oxidase into the airways. The adverse effect of xanthine oxidase may at least partly be explained by formation of superoxide radicals (2), and the amount of oxygen radicals formed is dependent on the hypoxanthine concentration, oxygen concentration and the presence of xanthine oxidase (1). We have made no attempt to characterize in detail the lung injury caused by instillation of xanthine oxidase into the airways, but have verified that the histopathological lung changes in our cats resemble those described by Saugstad et al (7). We have also considered it important to document the fact that during the period of the study there were no undue changes in acid-base status which could have influenced the inspiratory activity

and its inhibition.

We chose the model described by Saugstad et al (7) in our attempt to determine whether superimposed oscillations could be of advantage after a lung injury that has some features in common with a neonatal lung disease seen after some days of treatment. During this phase the lung disease may necessitate the use of high ventilatory pressures to achieve adequate alveolar ventilation. X-ray of the lung may then show variable aeration and sometimes localized densities.

Our results do not support the hypothesis that superimposed oscillations could be beneficial in reducing airway pressures after lung injury induced with xanthine oxidase. This injury is non homogenous with capillary dilatation, oedema and fluid accumulation in alveolar spaces and would probably cause localized densities on chest x-ray examination. Clinical results indicate, however, that superimposed oscillations are beneficial during ventilation of lungs (8) with interstitial emphysema without localized densities.

CONCLUSIONS

In cats with injured lungs:

1. Oscillations superimposed on IPPV do not lower the airway pressure at inhibition of inspiratory activity.
2. A low arterial PCO_2 is needed to inhibit inspiratory activity.

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