PHRENIC NERVE ACTIVITY AND VENTILATION DURING LUNG OEDEMA IN RABBITS

Maria GŁOGOWSKA

Department of Neurophysiology, Medical Research Centre, Polish Academy of Sciences, Warsaw, Poland

Abstract. Single fibre and "integrated" phrenic nerve activity was recorded in anaesthetized spontaneously breathing rabbits during experimentally induced lung oedema. Tidal volume, blood pressure, end-tidal CO₂ were monitored. In oedema the number of impulses in each volley slightly decreased while the discharge frequency was increased relatively to control values. The latter effect was due to the increased respiratory rate. "Integrated" phrenic nerve activity was also increased, contrary to tidal volume which was diminished. Minute ventilation obtained from pneumotachograph records \((f \times V_T)\) was compared to the neural output in terms of tidal phrenic amplitude times frequency \((f \times V_T\) eq). The minute ventilation rose insignificantly by \(45 \pm 40\%\) and neural output was increased on the average by \(150\%\).

INTRODUCTION

It has been shown that in pulmonary oedema lung compliance is markedly decreased while airway resistance and respiratory work are increased (2, 5, 13). The changes of mechanical properties of the lung are accompanied by changes in the pattern of respiratory rhythm. The reflexes involved in the neural control of breathing during pulmonary oedema have been studied by several authors. The results have shown that mainly the pulmonary stretch receptors (3) and myelinated fibres of the vagal nerves (6) initiate the tachypnoeic reflex. Also extra pulmonary and extra vagal sources participate in the excitation of respiration during
oedema since after vagotomy a small response is still present (3, 8). In the present study the effect of reflexes arising peripherally on the brainstem respiratory complex has been studied by recording the phrenic nerve activity. The evaluation of the phrenic nerve activity was made from the records from single fibres and the whole C3 root.

MATERIAL AND METHODS

Experiments were performed on 18 male rabbits weighing 2.5-3.7 kg anaesthetized with urethane-chloralose 0.8 g/kg and 35 mg/kg respectively. Tracheotomy, femoral artery and vein catherization were performed. Blood pressure (strain-gauge manometer) end-tidal CO₂ (capnograph KK, Godart) and tidal volume (pneumotachograph Godart) were recorded. Lung oedema was induced by intravenous injection of capric and caprilic acids mixture in olive oil in proportion 1:1:1 (1). In all rabbits C3 root of the phrenic nerve was cut and desheathed. In nine of them action potentials from single motor fibres were recorded using bipolar platinum electrodes. In the remaining rabbits the action potentials from C3 root were "integrated" with a leaky integrator. All variables were displayed on an oscilloscope (Tektronix 565) and filmed. The following variables were analysed in detail: number of impulses in one volley, frequency of discharges, amplitude of the "integrated" phrenic nerve activity, respiratory rate, tidal volume and minute ventilation. The latter was obtained from tidal volume record times frequency and compared to its neural output (tidal phrenic amplitude times frequency). Results were analysed by measuring three breaths before the intervention and three breaths 10 min after the inducement of lung oedema. Student's T test was used for calculation of means and standard deviations.

RESULTS

The activity of single phrenic motoneurones. The mean number of impulses in one volley changed insignificantly (18 ± 5 in control and 16 ± 4 in lung oedema). The peak inspiratory frequency increased (Fig. 1). Mean frequency of discharges was 11 ± 3 before intervention and 16 ± 5 when lung oedema has been evoked. The increased number of impulses per second was due to the acceleration of breathing. Usually the development of lung oedema was followed by the recruitment of new units (silent in control) and often the previously inspiratory fibres became active in expiratory phase (inspiratory modulated) (Fig. 2).

"Integrated" phrenic nerve activity. The amplitude of phrenic nerve
Fig. 1. On the upper trace single phrenic fibre discharge on the lower trace respiratory curve. A control record; B–J, registered in 0.5, 1, 2, 5, 7, 10, 15, 20, 25, 30 min after lung oedema inducement.

Fig. 2. Single phrenic fibre activity; traces as for Fig. 1. A, control record; B–E, dynamic changes during lung oedema development.

activity was increased in all cases of lung oedema (Fig. 4). We observed that the expiratory level of the "integrated" phrenic nerve activity during lung oedema has never reached a control value. According to this observation we have measured the increase in total amplitude (from expiratory-iso-line in control to peak inspiratory level during lung oedema) and tidal phrenic amplitude which in oedematous conditions was calculated as the amplitude from expiratory level to peak inspiratory level (Fig. 3). The difference between expiratory level in control state
and expiratory level during oedema indicates a tonic activity of dia-
phragm. The total amplitude was increased by $27.2 \pm 8\%$ while the tidal
phrenic amplitude rose by $18.1 \pm 9\%$ on the average.

Fig. 3. Scheme of “integrated” phrenic nerve activity; A illustrates the control con-
dition, B, during lung oedema. The graph shows the method of measuring $V_T$ eq,
total phrenic amplitude and tonic activity (see text).

Tidal volume and minute ventilation. The tidal volume decreased
from $21.1 \pm 4.5$ ml to $14.3 \pm 4.6$ ($-31.6 \pm 20.5\%$). Fig. 4 shows the changes

![Graph](image)

Fig. 4. Graphic presentation of changes in “integrated”
phrenic activity (Int. phr. — $V_T$ eq, and tidal volume ($V_T$)
during lung oedema (mean and S.E.).

in $V_T$ and the amplitude of phrenic nerve activity during development
of pulmonary oedema. It should be noticed that the increase in amplitude
of phrenic nerve activity was associated with the decrease in tidal volu-
me. The differences between a central signal given to the respiratory
apparatus for tidal volume and its realization can be explained by pathol-
ogical changes in the lung parenchyma and the airways (f.e. oedematic
fluid). In this situation we can distinguish the “neural output” (meaning
a central demand for ventilation) and actual ventilation performed by
the respiratory apparatus. Consequently, we calculated both the central,
minute ventilation ($f \times V_T$ eq) and the ventilation obtained from pneu-
motachograph record. The central ventilation increased by $163.8 \pm 31.3\%$
while the actual ventilation increased only by $45 \pm 40\%$ on the average.

**DISCUSSION**

The lung oedema is the result of a very complicated pathological
process. Oedematic fluid in tissue and alveoli causes stiffness of the
lungs and thereby a decrease in compliance and an increase in respiratory
resistance. These changes are signaled to the respiratory complex mainly by pulmonary receptors and afferent pathways in the vagus nerve. In turn, the respiratory complex directs the work of respiratory muscles. According to Sant Ambrogio 75% of the respiratory work in rabbits is performed by the diaphragm (12). This fact allows us to assume that the phrenic nerve activity is an index of inspiratory excitation.

The increase in the phrenic nerve activity in lung oedema was expected since respiratory work is increased to overcome the enhanced respiratory resistance and diminished compliance (5). The results have shown that the increase in the phrenic nerve activity was mainly due to recruitment of high threshold units (10). Also the tonic activity (Fig. 2) contributes to the increase in amplitude of the "integrated" phrenic signal. The transition from phasic to tonic (inspiratory modulated) activity means that the diaphragm is not relaxed in the expiratory phase. This might be an electrophysiological index that expiratory resistance is increased (14). On the other hand expiratory resistance leads to increased FRC. We suggest that the proportional changes in FRC could be measured from the record of the "integrated" phrenic activity as it is shown in Fig. 3.

Minute ventilation values obtained in classical way and simultaneous calculation of "neural output" seems to be very useful in further consideration. Firstly, it has been shown that the changes in the integrated phrenic amplitude only in certain conditions may reflect the changes in $V_T$ (4, 9). It could be assumed that in lung pathology which is accompanied by changes in the mechanical properties of the lung $V_T$ is not adequate to $V_T$. On the other hand the estimation of "central ventilation" may be used as an index of the demand for ventilation in particular pathological conditions. The presented results have shown that in lung oedema minute ventilation should be increased by 150%. This could be obtained if an increase in the frequency of breathing was followed by increase in $V_T$. In the light of the presented data we claim that shallowing of breathing, even compensated by acceleration of the rate of breathing (rapid and shallow type), is disadvantageous from the physiological point of view. It is obvious that in the conditions of lowered tidal volume the larger proportion of that tidal volume is used for ventilation of the dead space. It must influence the alveolar ventilation, which is reflected by changes in the blood gases (1, 7, 11), mainly by hypoxia and acidosis. $PaCO_2$ is increased only in very severe lung oedema.

I express my thanks to Professor Witold Karczewski and to Professor Curt von Euler for their valuable comments to the manuscript of this paper. The tech-

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nical assistance of Mrs. Elżbieta Jędrychowska is gratefully acknowledged. This investigation was supported by Project 10.4.2 of the Polish Academy of Sciences.

REFERENCES


Accepted 15 November 1977

Maria GŁOGOWSKA, Medical Research Centre, Polish Academy of Sciences, Dworkowa 3, 00-784 Warsaw, Poland.