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EFFECT OF GENERAL ANESTHETICS ON SURFACE ACTIVITY OF THE LUNG ALVEOLAR SURFACTANT

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UDC 615.212.7.015.4:612.212.014.1.014.462.8

The surface properties of the lung surfactant were studied with a modified Wilhelmy's apparatus after general anesthesia. Halothane and, to a lesser degree, pentobarbital, were shown to inhibit the surface activity of the surfactant. This phenomenon was observed only after prolonged (4-6 h) general anesthesia.

KEY WORDS: surface activity of the lung surfactant; general anesthetics.

After long operations under general anesthesia pulmonary complications often arise. In particular, the elasticity of the lung diminishes and atelectasis is observed [1, 3, 4, 7, 8]. These pulmonary disorders have been shown to be largely due to disturbance of the state of the surfactants which form the inner lining of the alveolar surface [10]. It has therefore naturally been suggested that under the influence of general anesthetics the properties of the surfactant are inhibited. It must be remembered that the possible mechanisms of disturbance of the surface activity of surfactants may be connected either with a direct disturbance of the surfactant activity by general anesthetics and with the "elution" of the surfactant from the alveoli as a result of unsuitable conditions of artificial ventilation of the lungs [13].

In this investigation the effect of general anesthetics on the surface activity of the surfactant was studied in rats breathing spontaneously.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred rats weighing 130-180 g. The animals were kept in an airtight chamber into which halothane was supplied in the proportion of 1-2 vol. % in a current of oxygen through a Ftorotek vaporizer. The halothane concentration at the outlet of the vaporizer was chosen so that the response of the rats to nociceptive stimulation (pricking with an injection needle) was suppressed. After halothane anesthesia for 2-6 h the heart–lung preparation of the rats was removed. A solution of surfactant was obtained by tracheal irrigation. For this purpose, 7-10 ml of physiological saline was injected from a syringe through the trachea into the lungs. After the lung had been filled, the washings were aspirated and the procedure repeated

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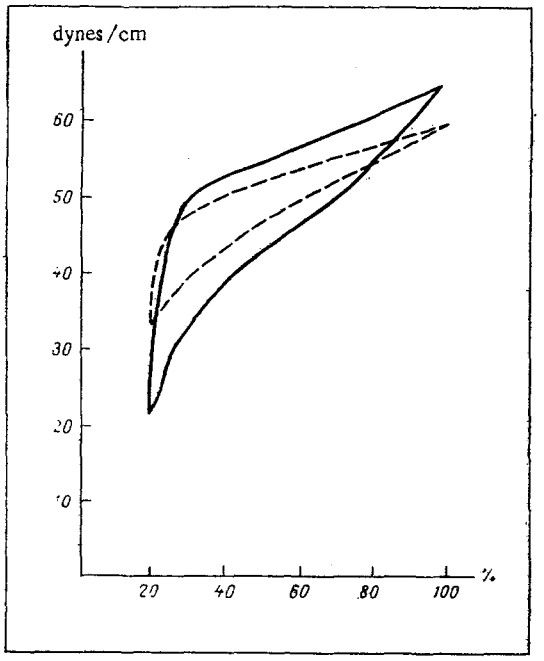

Fig. 1. Hysteresis of surface tension of lung surfactant. Continuous line represents normal lung; broken line, after general halothane anesthesia for 6 h. Abscissa, area of surface (in %); ordinate, surface tension (in dynes/cm).

seven times with the same volume of fluid. As a result, a slightly turbid, frothy fluid, the volume of which was 80-90% of the initial volume, was obtained. Contaminating cells were sedimented by gentle centrifugation (at 300g for 10 min).

The resulting solution of surfactant was tested with a modified Wilhelmy's apparatus [1] and the relationship between the surface tension of the solution of surfactant and the area of surface occupied by the monolayer in the course of its cyclic changes (Fig. 1) was expressed graphically. The surface activity of the washings was judged from the value of the minimal surface tension (γ_{min}) achieved by compressing the surface from 100 to 20%.

EXPERIMENTAL RESULTS

Unlike in the investigations of Miller and Thomas [9, 11], who found no changes in surface activity in homogenates of lung tissue after general anesthesia in patients without lung diseases, the results of the present experiments pointed reliably to a clear disturbance of surface activity of the surfactants after general halothane anesthesia. These changes appeared after the animals had been kept for a long period in an atmosphere containing 1-2 vol % of halothane.

In the rats of the control group γ_{min} was 21.6 ± 0.56 dynes/cm. In the experimental animals kept in an atmosphere of oxygen for 4-6 h under halothane anesthesia, γ_{min} rose considerably to reach 30 ± 1.4 dynes/cm ($P < 0.01$).

By the experimental conditions the anesthetized animals were kept in an atmosphere of oxygen, which corresponds to the clinical method of conducting general anesthesia. However, there is evidence in the literature of the toxic action of pure oxygen on the surfactant system in mammals [6]. In order, therefore, to differentiate between the action of halothane and that of oxygen on the lung surfactant an additional series of experiments was carried out in which, instead of oxygen, air was supplied into the chamber containing the animals in both the control series and the experiments with general anesthesia. In that case γ_{min} for the control animals, kept in an atmosphere of air, was 21.3 ± 2.1 dynes/cm, i.e., the same as in rats kept for 6 h in an atmosphere of oxygen. After anesthesia for 6 h, γ_{min} for animals kept in an atmosphere of air rose considerably to 32 ± 1.5 dynes/cm. The results of these experiments thus showed that keeping the animals in an atmosphere of oxygen for 6 h had no effect on their surfactant system and, consequently, the changes in that system could not be attributed to the action of oxygen.

This incease in γ_{min} likewise could not be attributed to secondary changes connected with inadvertent overdosage of the anesthetics, for the survival rate of the animals after the conditions of general anesthesia chosen was 100%.

A significant disturbance of the surface-active properties of the surfactant was observed only after long periods (4-6 h) of general anesthesia. In the early stages (under 2 h) no significant changes in the value of γ_{min} were found (after 2 h γ_{min} was 24 ± 1 dynes/cm, i.e., indistinguishable from the control, 22.7 ± 0.9 dynes/cm).

Additional data on the action of general anesthetics on surfactant activity were obtained for another substance used in anesthesia, namely pentobarbital. During prolonged (4-6 h) pentobarbital anesthesia (3 mg/100 g) some decrease in the surface activity of the surfactant also took place (γ_{min} increased to 24-27 dynes/cm; $P < 0.05$). However, this change was less marked than in halothane anesthesia.

As already stated, changes in the properties of the surfactant under the influence of halothane were observed only after prolonged anesthesia (4-6 h), i.e., much later than the manifestation of its depressant action on the CNS. This suggests that the effect of the general anesthetics on the surfactant is exerted not at the level of physicochemical conversions in the monolayer, (for which the time required is comparable with the time for saturation of the body with the anesthetic, i.e., about 10 min), but at the level of synthesis or of supply of the surfactant to the surface. The results of an investigation by Evans et al. [5], in which no changes were found as a result of exposure of a monolayer of lecithin to inhalation anesthetics in experiments in vitro, confirm this hypothesis.

This hypothesis regarding the mechanism of the disturbance of surface activity of the surfactant explains the negative results obtained in the investigations mentioned above [9, 11]. In fact, if during general halothane anesthesia the synthesis of surfactant or its supply to the surface of the alveolus is disturbed, a new redistribution of phospholipids takes place between the cells synthesizing the surfactant and the monolayer on the surface of the hypophase of the alveolus. Meanwhile the "total" phospholipid obtained by homogenization of lung tissue remains unchanged, as these authors observed.

The decrease in the surface activity of the surfactant discovered during general halothane anesthesia directly confirms the conclusions obtained by Woo et al. [12], who found a decrease in the elasticity of the isolated lungs of dogs during artificial ventilation with a gas mixture containing general anesthetics and who explained these changes by a disturbance of the properties of the surfactant.

This experimental investigation, in conjunction with data in the literature, thus shows that pulmonary complications arising after prolonged general anesthesia may be attributable to the inhibitory effect of the general anesthetics on the activity of the lung surfactant.

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