# EFFECT OF HYPERBARIC OXYGENATION ON BLOOD CORTICOSTERONE LEVEL IN EXPERIMENTAL RESPIRATORY DISTRESS SYNDROME

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Considering the possible toxic effect of high oxygen concentrations on lung tissue [2, 5, 7, 12] and data in the literature on the stressor effect of hyperbaric oxygenation (HBO) on the intact organism [4, 8, 15], the need for corresponding research on hypoxic states will be evident. In particular, data on the functional state of the adrenal cortex during the use of HBO to treat one of the most serious and wisespread forms of hypoxia, namely the acute respiratory distress syndrome (ARDS), may be of great theoretical and practical importance.

In the investigation described below, in order to clarify the mechanism of action of HBO in acute oxygen deficiency, changes in the endogenous corticosterone concentration were studied in rats during correction of a model of ARDS by means of HBO.

## EXPERIMENTAL METHOD

A model of the syndrome was reproduced in 139 Wistar rats weighing 150-350 g by intrapleural injection of oleic acid (OA) in a dose of 0.27 ml/100 g body weight. Animals of series I (54 rats) were the controls, and animals of series II (34 rats) and III (51 rats) were subjected to a single session of HBO, under a pressure of 3 atm for 2 h, after 4 and 12 h respectively. Before and 4, 12, 24, 36, 48, 60, and 240 h after injection of OA the corticosterone (CS) concentration was determined in plasma from arterial blood, a sample of which was taken by puncture from the femoral artery or abdominal aorta. The partial pressure of oxygen ($p_aO_2$) in the same blood samples was measured by means of a model M-165 blood gas microanalyzer ("Cording," England). At the time of injection of OA and taking the blood samples the animals were anesthetized by open inhalation of ether. The plasma CS level was determined by radioimmunoassay using kits from "Sorin." The results were subjected to statistical analysis.

## EXPERIMENTAL RESULTS

Intrapleural injection of OA caused the development of rapidly progressive arterial hypoxemia (Table 1), characteristic of ARDS, in the experiments of series I, leading to death of the majority (up to 80%) of the rats by the end of the first 24 h and of 96% of the rats by the end of the 3rd day of observation.

This rapid and severe course of the experimental syndrome was accompanied by marked changes in the blood CS concentration, which were biphasic in character. In the first place (the first few hours of the process) the hormone concentration was raised. Because of this, the mean CS concentration by the 4th hour of observation was twice as high as initially (Fig. 1). During the next few hours there was a marked tendency for the blood CS concentration to fall, and by the end of the period of observation the mean hormone level was the same as initially.

After the session of HBO the course of the experimental syndrome in the animals in the experiments of series II and III was more favorable. The mortality of the animals in the experiments fell on average by 75%, and the peak of the number of deaths was shifted from the first 18-24 h to later times (3rd-7th days). Thus the duration of survival of the experimental

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TABLE 1. Time Course of $p_aO_2$ (in mm Hg) in Arterial Blood of Rats during Correction of ARDS by HBO (M ± m)

| Series of experiments | Time elapsing after beginning of process, h | | | | | | |
|---|---|---|---|---|---|---|---|
| | initial data | 4 | 12 | 24 | 48 | 60 | 200–240 |
| I | 93,3±4,2 | 84,5±6,6 | 56,4±3,4 | 40,2±1,6 | — | — | — |
| II | — | 74,7±8,9 | 86,8±5,5* | 63,6±6,9* | 85,3±12,7 | — | 70,1±10,7 |
| III | — | — | 70,3±11,7 | 58,7±7,1* | 55,2±10,2 | 59,3±7,7 | 67,2±4,6 |

Legend. Asterisk indicates significant ($p < 0.05$) differences compared with control (I) series.

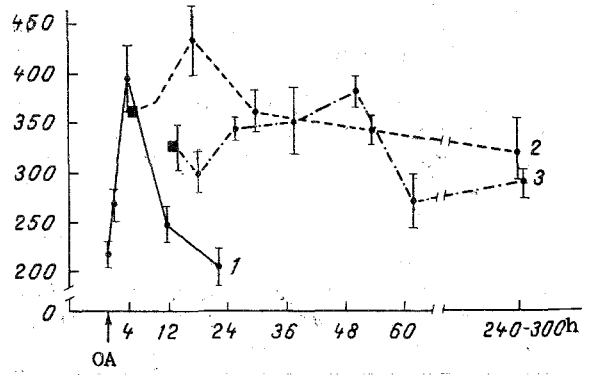


Fig. 1. Time course of blood CS concentration in rats after intrapleural injection of OA. Abscissa, time (in h): ordinate, CS (in nmoles/liter). 1) Control series (I); 2 and 3) series of experiments with HBO (II and III), conducted 4 and 12 h respectively after injection of OA. Filled squares indicate period of HBO session. Arrows indicate time of injection of OA.

animals was increased by many times. The fall of $p_aO_2$ observed in these experiments could not reach the degree observed in the control (I) series, even in the experiments of series III. When arterial hypoxemia reached its minimal level (50.0 ± 10.2 mm Hg), $p_aO_2$ had a tendency to recover.

Measurement of the blood CS concentration showed that in the animals in the experiments of series II it was 1.5-2 times higher than initially throughout the period of observation (Fig. 1). A similar but weaker tendency for the CS concentration to rise was observed in the experiments of series III, in which HBO was applied when the syndrome was in an advanced stage. HBO applied 12 h after injection of OA apparently prevented the sharp fall in the CS level observed during this period in the control. In the next 2 days a relatively high plasma concentration of the hormone was maintained. The normalization of the blood CS level, or even small rise above the normal level, are evidence that the HBO session achieved a sufficiently lasting effect of maintenance of adrenocortical function.

Comparison of the results reveals a manifestation of one of the most important mechanisms of the adaptive effect of HBO on the body: it prevented or delayed the critical reduction of the secretory function of the adrenal cortex, induced by progressive hypoxemia, in the period of emergency mobilization of protective and adaptive reactions to acute hypoxia that is vital for survival.

Maintenance of the necessary level of corticosteroid synthesis in the situation under examination is important not only from the point of view of formation of an adequate level of development of the general adaptation (or stress) syndrome [8], but also from the standpoint of organization of "local" mechanisms of defense. Considering data in the literature on the

role of glucocorticoids in the synthesis of lung surfactant [2, 13, 14], the results enable HBO to be regarded as an active means of prevention and correction of nonspecific changes in the lungs connected with the development of ARDS. Since weakening of surfactant synthesis in this pathology is regarded as a direct cause of the depression of the pulmonary gas exchange function [2], it can be tentatively suggested that HBO, by stimulating synthesis of surfactant lipids, can contribute to the restoration of the pulmonary gas exchange. Evidence in support of this suggestion was obtained in our own experiments and also in those in [11].

The result of application of a single session of HBO can be understood in the light of data in the literature, indicating the possibility of a marked metabolic after-effect of HBO [3, 6, 8], including after a single exposure to the conditions of HBO [10]. Since the metabolic activity of lung surfactant is relatively high [1], there are grounds for considering that the after-effect of a session of HBO ensured metabolic activity essential for surfactant synthesis by the specialized apparatus of the type 2 alveolocytes.

Thus the use of HBO on a model of development of ARDS, by maintaining a stable increase in the blood CS concentration, creates the conditions for the development of an adequate defensive reaction of the body to acute progressive hypoxia, resulting in a marked reduction of mortality among the animals.

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