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HISTOMORPHOLOGICAL CHANGES IN THE LUNGS IN ACUTE BACLOFEN POISONING

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ABSTRACT — *Baclofen is a myorelaxant*, a derivative of gamma-aminobutyric acid. Due to its psychotropic effect the drug is often subject to abuse especially in young people. The article deals with histomorphological changes in the lungs in Baclofen poisoning.

KEYWORDS — Baclofen, poisoning, lungs, histomorphological changes.

INTRODUCTION

Baclofen is a beta-p-chlorophenyl derivative of one of the inhibitory neurotransmitters — gamma-aminobutyric acid [1, 2]. It is believed to work by agonizing GABA receptors (specifically the GABAB receptors) [3].

This drug is administrated orally or intrathecally (by delivery into the spinal canal) [3]. Oral Baclofen is indicated to patients with multiple sclerosis, muscular spasticity, some spinal cord diseases, such as tumors, infectious diseases, injuries, acute disorders of cerebral circulation, meningitis [4]. A number of studies have shown that Baclofen is effective in the treatment of alcohol addicts [5–10] and patients with cerebral palsy [11]. Adverse effects of Baclofen may include headache, drowsiness, dizziness, weakness, fatigue, nausea and vomiting, urinary retention, constipation [3].

This drug has a pronounced psychoactive effect and can be a subject to abuse in drug addicts, especially in young people [12]. Acute Baclofen poisoning, which is associated with high risk of death, can be resulted from an accidental overdose, criminal actions, or suicidal behavior. The pathogenesis of acute Baclofen poisoning and thanatogenesis in such cases remains unclear.

One of the target organs in Baclofen poisoning is the lung. At the same time, the data on morphological changes in such poisoning is limited.

The objective of the study was to assess histomorphological changes in the lungs in acute Baclofen poisoning 3 hours after its administration.

MATERIAL AND METHODS

Experimental studies were performed on 10 Wistar rats divided into 2 groups. The group of controls included 5 intact animals, experimental group was treated with Baclofen at a dosage of 85 mg/kg.

Keeping animals and working with them were carried out in accordance with the European Convention for the protection of vertebrates used for experiments or other scientific purposes (Strasbourg, 18.03.1986).

The lungs were fixed in 10% neutral formalin and immersed into paraffin. Histological sections were processed according to the standard method and stained with hematoxylin and eosin. The histological sections were examined by light microscopy using Nikon Eclipse E-400 microscope with a video system based on the Watec 221S camera (Japan) at 400× magnification.

The following signs were assessed: emphysema, atelectasis and dystelectasis, thickening of the interalveolar septi, WBC infiltration of the interalveolar septi, capillary and venous plethora, sludge, hemorrhages in the interalveolar septi and alveoli, the presence of secretion in the lumen of the bronchi.

In order to confirm the reliability of the appearance of a particular histological sign, we used the Fischer ratio. The presence of a histological sign was considered to be reliable if it did not appear in any cases in one group and appeared in 4 or 5 cases in the other.

RESULTS AND DISCUSSION

There were no pathological changes in the lungs of the controls. The alveoli were intact, airy. Small areas of subpleural dystelectasis were observed. There

were no signs of emphysema. There were no circulatory disorders (venous, capillary plethora, hemorrhages in the interalveolar septi and alveoli) either. The lumen of the bronchi was free.

In the lungs of animals treated with Baclofen at a dose of 85 mg/kg, plethora of venules and capillaries was observed. Sludge was observed in the pulmonary arteries. There was an expansion of the alveoli and pronounced emphysema (which was mainly subpleural). The interalveolar septi were thinned in the emphysema zone. There were subpleural atelectasis and dystelectasis. There were some areas of interalveolar septi thickening (due to edema). WBC infiltration of interalveolar septi was also detected. Macrophages were observed in the lumen of some alveoli.

The presence of plethora of venules and capillaries, sludge, emphysema, atelectasis and dystelectasis, and cellular reaction (WBC infiltration of the interalveolar partitions) can be considered reliable in this group.

According to literature, Baclofen does not have a direct toxic effect on the bronchi and lungs. However, it increases the presynaptic blockade of nerve impulses that are generated in the spinal cord. This leads to suppression of their transmission. As a result, muscular tone increases. Their excessive relaxation may lead to difficulty breathing and the development of hypoxia. The effects of GABA receptors stimulation on smooth muscles of the bronchi and on the lungs are also very important. GABAA receptor agonists are known to cause contraction of smooth muscles of the bronchi, bronchioles, which is accompanied by spasm and breathing difficulties [13, 14]. Although Baclofen is a selective agonist of GABAB receptors, in high doses it causes GABAA receptor stimulation as well. We observed this effect in the study group. Emphysema was observed in the lungs of the animals.

Under hypoxia vascular-tissue permeability increases. It was also shown that vascular-tissue permeability increased when GABA receptors were stimulated [15], which is also confirmed by the results of our experiments. Thickening of interalveolar partitions due to edema was observed in the experimental groups.

CONCLUSION

As a result of the study we identified a complex of pathological changes in the lungs of experimental animals in the early period after Baclofen administration, which included circulatory disorders in all the elements of the microcirculatory bed (plethora of capillaries, venules), emphysema, atelectasis and dystelectasis, WBC infiltration of intraalveolar septi and thickening of intraalveolar septi due to edema. In order to quantify the severity of histomorphological changes in the lungs a morphometric study is required.

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