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THE DYNAMICS OF LUNG HISTOPATHOLOGY IN ACUTE BACLOFEN POISONING

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ABSTRACT — Baclofen (sold under the name Baclosan©, Lioresal©) is a muscle relaxant. This drug is chemically different from other muscle relaxants. Due to its pronounced psychotropic effect the drug is often a subject of abuse especially among young people. The article deals with the dynamics of lung histopathology in acute baclofen poisoning. Experimental studies were performed on 15 Wistar rats. The animals were divided into 3 groups (the controls and two experimental groups). The controls included 5 intact rats. Each experimental group included 5 animals. Both groups were treated with baclofen at a dosage of 85 mg/kg. The duration of the experiment was 3 and 24 hours, respectively. We revealed a complex of pathological changes in the lungs of the rats. There were circulatory disorders in all the elements of the microcirculatory bed, areas of emphysema, atelectasis and dystelectasis, WBC infiltration of intralveolar septa and their thickening due to edema. The changes were even more severe 24 hours after the drug administration. These results along with the results of chemical analysis will be useful in establishing the fact of baclofen intoxication and the exact moment of the intoxication.

KEYWORDS — Baclofen, poisoning, lungs, lung histopathology.

INTRODUCTION

Baclofen (sold under the name Baclosan©, Lioresal©) is a muscle relaxant. This drug is chemically different from other muscle relaxants and represents a beta-p-chlorophenyl derivative of an inhibitory neurotransmitter GABA (gammaaminobutyric acid) [1, 2].

Baclofen is presented in oral and intrathecal forms and is widely used in clinical practice [3]. Oral Baclofen is indicated for patients with multiple sclerosis, severe muscle spasticity, and various spinal cord diseases (including injuries, acute circulatory disorders, tumors and infections). The drug has been shown to be effective in the treatment of patients with alcoholism [4–6] and cerebral palsy [7–8]. The mechanism of baclofen action still remains unclear. The drug has been shown to inhibit monosynaptic and polysynaptic reflexes, reduce excitability of gamma-motoneurons, which underlies its myorelaxant effect [8].

Adverse effects when using baclofen may include drowsiness, headache, dizziness, weakness, fatigue, trouble sleeping, nausea and vomiting, urinary retention, constipation.

During treatment with baclofen, an increase in body weight may be observed. Baclofen has a hepatotoxic effect under prolonged use [1, 2]. Acute baclofen intoxication can result from an accidental overdose, criminal acts or suicidal behavior [9]. There is no specific antidote in acute baclofen poisoning. Symptomatic therapy (such as cardiovascular support, mechanical ventilation if needed) is recommended in such cases. Baclofen has a pronounced psychoactive effect and can be a subject to abuse by mostly young people [10, 11].

One of target organs in baclofen poisoning are lungs. As far as we know, no previous research has investigated lung histopathology in acute baclofen intoxication.

MATERIALS AND METHODS

The experiment was performed on 15 male Wistar rats weighing 290–350 g and aged 20 weeks.

The animals were kept and handled in accordance with the European Convention for the Protection of Vertebrate Animals used for experiments or other scientific purposes (Strasburg, March 18, 1986). Baclofen was administered under general anesthesia (chloralose) through a gastric tube.

The animals were divided into the following groups:

- control (n=5) which included animals that received normal saline 10 ml/kg;
- group 1 (n=5) comprising animals receiving baclofen 85 mg/kg in normal saline solution with the experiment duration of 3 hours;
- group 2 (n=5) which consisted of animals receiving baclofen 85 mg/kg in normal saline solution with the experiment duration of 24 hours.

After the experiment, the animals were euthanized by an overdose of anesthesia. The lungs were

fixated in 10% neutral formalin and embedded in paraffin. Histological sections of 5 μm thickness were prepared, placed on slides and stained with hematoxylin and eosin. Then the sections were examined by light microscopy using a Nikon Eclipse E-400 microscope with a video system based on a Watec 221S camera (Japan) at ×400 magnification.

The following signs were assessed: circulatory disorders (capillary and venous plethora, hemorrhages in interalveolar septa, hemorrhages in alveoli, sludge), atelectasis (complete and partial), emphysema, cellular response (increased WBCs in interalveolar septa), epithelial desquamation in the bronchial lumen.

Fisher criterion was used to assess the significance of a particular histological sign. The sign was considered significant if it was absent in one group and appeared in 4 or 5 cases in another group.

RESULTS

No pathologic changes were observed in the lungs of the controls.

Three hours after baclofen administration (85 mg/kg), we revealed circulatory disturbances (venous and capillary plethora, sludge), areas of emphysema, atelectasis (complete and incomplete), and cellular response (WBC infiltration of interalveolar septa). We also revealed areas of thickening of interalveolar septa due to edema. All the signs were considered significant.

24 hours after baclofen administration we also observed emphysema in the lungs of experimental animals. The presence of dystelectases, areas of thickening of the interalveolar septa (due to edema) was also significant, as well as circulatory disorders (capillary, venous plethora, a significant number of hemorrhages in the interalveolar septa). We revealed hemorrhages in the alveoli, which was not observed 3 hours after baclofen administration.

DISCUSSION

According to the literature [1, 2] baclofen has no direct toxic effect on the bronchi and lungs. However, the drug increases presynaptic blockade of nerve impulses originating in the spinal cord, which inhibits their transmission. The tone of the muscles (including the intercostal ones) decreases. Their excessive relaxation can cause breathing difficulties followed by hypoxia. GABA A receptor agonists are known to cause contraction of bronchial and bronchiolar smooth muscles accompanied by spasm and breathing difficulties [12, 13]. Baclofen is a selective agonist of GABA B receptors, but at high doses it can also stimulate GABA A receptors. This effect was observed in both experimental groups. Emphysema was observed in the lungs of the experimental animals in both groups.

CONCLUSION

Thus, we observed a complex of pathological changes in the lungs (disturbances of blood circulation — venous, capillary plethora, hemorrhages into intraaveolar septa; emphysema, dystelectasis, WBC infiltration of intraalveolar septa). The changes were more severe 24 hours after the drug administration. This results along with the chemical analysis will be useful in establishing the fact of baclofen intoxication and the exact moment of the intoxication.

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