MORPHOFUNCTIONAL CHANGES IN THE BRAIN BLOOD LOSS ON THE BACKGROUND OF ALCOHOL INTOXICATION

The application of histological and morphometric methods allowed to determine significant changes of brain structures in people who died from traumatic hemorrhage in the condition of alcohol intoxication of mild and moderate degree. A marked spasm of large pial arteries has been revealed. Dystonia with a predominance of spasms is typical for intracerebral arteries, and dilatation for the veins. Spasm of the arteries leads to a significant increase in perivascular spaces. The density of glial component in the gray substance of the brain is sharply reduced, and in the white substance it does not change significantly. The total area of the microcirculatory bloodstream vessels reduces significantly. Marked changes in the structure of neurons suggest that these disorders are caused not only by anemia, dissociation of vessels with neuroglia, but by direct influence of ethanol on nerve cells as well.

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Introduction

Need for a detailed microscopic study of the brain in alcohol intoxication as a target organ, is recognized by many researchers (Permyakov and Viter, 2002). Studies have established that acute alcohol intoxication causes marked changes of the vascular system of the brain in a person with the disorder of arterial and venous tonus of their blood, plasmatic soaking of the walls have been established. Alcohol has also a damaging effect on nerve cells, neuroglia, and white substance (Zoroastrov, 2005; Shormanov and Shormanova, 2005). In chronic alcoholism rough organic changes take place in the brain: multiple sclerosis and hyalinosis of arteries at different levels of branching of veins and capillaries. Specific gravity of nerve cells in all studied areas of this organ decreases due to progressive atrophy and loss of neurons, while glial component of the brain increases (Shormanov, 2006, Shormanov and Shormanova, 2006). Most researches are devoted to the study of the brain in case of poisoning by high doses of ethanol. Structural changes in blood vessels and nerve elements of the brain in alcoholemia of mild and moderate degree are studied much less. Study of the reactive changes of the brain tissue structures in deaths from acute hemorrhage on the background of alcohol intoxication has a practical significance (Dolzhansky and Borlakova 2006).

Our study investigates the state of pial and intracerebral vessels and nerve tissue of the human brain in acute anemia on the background of alcohol intoxication of mild and moderate degree.

Materials and methods

Materials for our study were pia mater and areas of the brain (Brodmann area 6, area III of the ventricle and the hypothalamus, and area IV of the ventricle and medulla oblongata). The material was taken from people who died of traumatic blood loss without alcohol intoxication (17 cases), and people who died from acute blood loss in the condition of alcohol intoxication of mild and moderate degree(18 cases) aged 18 to 60 years. Alcohol content in blood ranges from 0.4 to 2.4% of . The material in all cases was
taken in the same periods (up to 12-16 hours) after death. Material fixation and filling in paraffin were performed by standard methods. Histological sections were stained with hematoxylin and eosin, using the methods of van Gieson, Mallory and Nissl. The linear dimensions of blood vessels using an ocular ruler were determined. Vascular-perivascular ratio was calculated by measuring the diameter of blood vessel and the diameter of surrounding area. Nuclear-cytoplasmic ratio in neurons, density of the neuroglia, as well as the overall total area of microcirculatory blood stream (MCBS), were determined by a point method. Measurements were carried out in all investigated parts of the brain in the same proportion to a certain area of the slice. Processing of figures was carried out by variation statistics, the coefficient of reliability of values of comparable groups was determined according to Student.

Results and their discussion

In deaths from traumatic blood loss (group 1) large and medium arteries of pia mater have a narrow lumen and contain a small amount of units of red blood cells. The lumen of the majority of small pial arteries is round and is filled with aggregates of red blood cells. Diameters of large, medium and small arteries are respectively 518±19.81, 179±12.17, 71.93±6.71 µm. Pial veins have thin walls, they are collapsed, anemic. The average diameter of intracranial arteries is 30.43±3.06 µm. Around intracerebral arteries, both in gray and white medullary substance of the brain a narrow perivascular (periarterial) space is determined because of the small vascular spasm. Vascular-perivascular ratio is equal to 3.1±0.38. Almost all arteries contain a small quantity of blood cells, and a certain part does not contain them at all. On the longitudinal sections along the arteries marked unevenness of their diameters is noted. Intracerebral veins are differ by hyperemia, their diameter is 71.52±6.24 µm. The overall total area of the MCBS vessels is 9.48 ± 0.27. Neurons of studied divisions of the brain in traumatic hemorrhage are differ by staining by the Nissl method. Chromatophilic substance in the body of neurons in the nuclei of cranial nerves is represented by big lumps. While in the cytoplasm of neurons in the olivary nucleus it is fine grained and has pulverized feature of distribution. The degree of staining of the cytoplasm of nerve cells is diverse, sometimes tigrolysis occurs. Perineural space is represented by a narrow bright rim around the neurons. Nuclear-cytoplasmic ratio in neurons equals to 0.19±0.02. The density of neuroglia in the gray substance is less (6.91±0.27), than in the white one(10.38±0.51). Gliocytes are located around the neurons and interneuronal space, some of them are located in close proximity to nerve cells.

The study of the same areas of the brain at the death of hemorrhage on the background of alcohol intoxication (cases of group 2) has shown that the large pial arteries are in spasm, their diameter is significantly lower than in group 1 (340 ±17.51 µm, p <0.001). Pial arteries of medium caliber are somewhat expanded (187.5±6.65 µm, p> 0.05), and small ones are in spasm (61.48±3.59 µm, p> 0.05), but the differences were not significant. Intracerebral arteries are in sharp spasm (Figure 1), their diameter is 21.77±0.82 µm, which is significantly less than in observations of group 1 (p <0.01). Perivascular space in the intracerebral arteries is extended in the majority of cases. Due to this, the vascular-perivascular ratio of intracerebral arteries of the brain is significantly lower than in those without alcohol intoxication and makes 1.9±0.30 µm (p <0.001). Dystonia of the blood vessels, is often marked that is why they have the wrong course and uneven diameter on longitudinal sections in different areas. On cross sections it can be seen that the lumen of some arteries has a star-like shape. Veins of the brain are full-blooded and become significantly wider. On average, their diameter is 92.83±9.94 µm (p<0.05). The overall total area of the MCBS vessels is decreased to 8.15±0.41 which is significantly different from group 1 (p <0.01).

In death from acute anemia on the background of acute alcohol intoxication the relative size of the nerve cell bodies is significantly reduced, and perineural space is dramatically expanded. Nuclear-cytoplasmic ratio in neurons increases dramatically by increasing the
size of their nucleus and reaches 0.61±0.06 (p <0.01). In the nuclei of almost all neurons there is a weakening pattern of chromatin, they lose their basophilia and look like white spots, in which the remnants of various configurations of chromatin are found only in some places. In the nuclei of cranial nerves sharp expansion of the boundaries of the nuclei of neurons, loosening of chromatin, vacuolization of the nuclei of some neurons are in the foreground. The phenomenon of tigrolysis, and in some neurons - a total dissolution of chromatophilic substance are observed. Consequently, in the nuclei of some neurons olives look like shadows. The density of the location of neuroglia in the gray substance is significantly (p <0.001) reduced compared with group 1 and is equal to 5.33 ± 0.20. At the same time there is an approximation of neuroglial cells to neurons. In the perivascular space a few cells of the neuroglia are occasionally found. The more glial cells are in this space, the smaller is the size of the neuron. Some of them are deeply pressed into the body of the neuron, i.e., a phenomenon of neurophagia takes place (Figure 2). There are not significant differences in density between the two observed groups of neuroglia in the white substance, as in a group of persons with alcohol intoxication density of the location of the neuroglia in the white substance are 10.10 ± 0.34 (p> 0.05).

**Figure 1. A sharp spasm of intracerebral arteries, dilatation of perivascular space. Ventricular wall III, alcholema. Hematoxylin and eosin staining. Vol. 10, circ.10**

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**Figure 2. Approximation of neuroglia to neurons, neuronophagia. Cortex of field 6, alcholema. Hematoxylin and eosin staining. Vol.40, circ.10**

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The study with employment of morphometric methods has made it possible to determine significant changes in the structures of the brain in people who died from traumatic hemorrhage in the condition of alcohol intoxication of mild and moderate degree. In this case, there is a damage of both the vascular system of the brain and the nervous tissue. In
the condition of acute anemia in the presence of alcoholemia a marked spasm of large pial arteries is observed, whereas medium and small arteries do not significantly change. Pial arteries are of great importance in providing an adequate blood supply to the brain in changing of its metabolic needs. In reducing the general blood pressure pial arteries naturally dilate (Mchedlishvili, 1968).

Dystonia is typical for the intracerebral arteries with a predominance of marked spasm, and dilatation of the veins. Spasm of the arteries leads to a significant expansion of perivascular space. Such reaction of intracerebral vessels, undoubtfully, leads to their dissociation with neuroglia. In alcoholemia the glial density in the gray substance is significantly reduced. At the same time, the density of the neuroglia in the white substance of the brain is not significantly altered. This presumably indicates, to a greater sensitivity of plasmatic astrocytes to ethanol than to fibrous and oligodendrocytes. In addition, blood supply to the gray substance is several times more extensive then to the white one, which makes it possible to damage ethanol, a larger number of cells of the neuroglia by ethanol. The death of astrocytes is associated with their hyperactivity, since they extensively convert ethanol into the spinal fluid. The block occurs at the level of astrocyte-neuron, neurocytes face substrate and oxygen deprivation, they develop dystrophic changes, some of them die, i.e., alcoholic encephalopathy is formed (Paukov et al., 2001). In mild and moderate alcoholemia the total area of the microvascular vessels is significantly reduced. Experimental studies have shown that even in single acute alcohol intoxication, changes in the vessels of the brain microcirculatory blood flow occur (Paukov et al., 2001). Damage of the neurons is shown by marked changes in nuclear-cytoplasmatic ratio. The structures associated with the genetic apparatus of cells change, which is manifested by a dislocation of chromatin and changes in its tinctorial properties.

With regard to the pathogenesis of structural damage of neurons in alcoholic intoxication, there is a widespread opinion about the effects on nervous cells, both of ethanol and severe disorders of cerebral blood circulation (Pigolkin et al., 2003). Our study has revealed the reported pathogenetic links of brain lesions even in a mild and moderate alcoholemia. Marked changes in neurons allow suggesting that these disorders are caused not only by anemia, dissociation of vessels with neuroglia, but by direct effect of ethanol on nerve cells as well.

References


