The study of behavior changes in growing rats under the conditions of halothane anesthesia and premedication with midazolam

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Abstract

Background: Cleft of lip and palate is widespread pathology of development. These malformations are repaired with surgery. Inhalation anesthetics, for example halothane, are widely used in pediatric orthognatic surgery, causes side effects. For preventing these complications benzodiazepines (e.g midazolam) are used, but based on last literature sources midazolam may cause long-lasted negative effects, such as high excitation and aggression. At same time, according to the literature, midazolam, which is used in sedation for infants, may have far-reaching adverse effects. For example, initiation of apoptosis in the developing brain, respiratory obstruction and other. The reverse data is obtained from adult white rats. It is determined that midazolam premedication does not react on behavioral characteristics and adaptation ability of experimental animals and reduces the halothane negative impact⁹. Relatively less is studied about far-reaching adverse effects of midazolam in growing organisms.

Aim of research: The effect of midazolam premedication (single injection) on behavior changes of growing rats under the conditions of halothane anesthesia after 1 week from the sham operation.

Methods: Open field test was used to assess behavior parameters and emotions in control and both test groups. We evaluated behavior changes in rats a week after the operation during 5 days. Each animal was explored during 5 minutes every day. There were registered following parameters: Vertical activity, sum of inner, external and center squares, time of staying in the center of the field, groomings, the grooming duration, defecation.

Results: It is shown that midazolam injections did not cause any negative effects on the growing rats’ behavior parameters. The adaptation to environment has been revealed in all three groups a day after. Similar results were shown in the third and fourth days. The high level research activity has been determined in control and third groups, in comparison with halothane group. This fact is related to adaptation to environment and it proves decreasing of tension and fear level. The adaptation to environment and high space orientation of growing rats in third group has to be caused by midazolam premedication.

Conclusions: The reason for weak adaptation to environment after halothane anesthesia compared to intact animals may be the reducing of dendrite growth by halothane in growing animals and thus the inhibition of brain development. The fact that these effects are not revealed after midazolam premedication allow us to think that reducing the anxiety activity of animals after midazolam premedication provides to avoid the inhibition of dendrite growth and brain development. On the bases of our results it is established that a week after operation in growing rats under the halothane anesthesia midazolam premedication (single injection) doesn’t cause any negative influence on behavior parameters of growing animals. (TCM-GMJ January 2016; 1:P8-P10)

Keywords: anesthesia, halothane, midazolam, premedication, behavior, rat.

Introduction

Inhaled anesthetics are widely used during surgical treatment of children with congenital defects of infants such as fissures of upper lip and palate. As it is known inhalation Anesthetic drugs are characterized by psyche damage impact.

In particular, it is determined that after their (e.g halothane, which is mainly used in the above mentioned congenital defects) usage patients suffer from post-operative complications, such as nausea, high anxiety, disorder of synaptogenesis, in the early stages of brain development, which directly revealed with the inhibition of behavioral activity and Other. The adverse effects of halothane on the responsible mechanisms of brain functioning is described also in experimental animals. In particular, it is shown that in the conditions of prolonged anesthesia, halothane causes inhibition of dendrites growth.¹²³⁴

For the prevention of complications caused by halothane, increasing of sedation is recommended. For this purpose benzodiazepines drugs including midazolam is widely used in maxillofacial Surgery. Midazolam is known to be associated with ionotropic GABAA receptor, which leads to the opening of the opening CI channels and transport of chloride ion from extra-cellular space to intracellular direction. Thus inhibitory postsynaptic potential is generated and sedation is increased.⁵⁶⁷

At the same time, according to the literature, midazolam, which is used in sedation for infants, may have far-reaching adverse effects. For example, initiation of apoptosis in the developing brain, respiratory obstruction and other.⁸

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The reverse data is obtained from adult white rats. It is determined that midazolam premedication does not react on behavioral characteristics and adaptation ability of experimental animals and reduces the halothane negative impact. Relatively less is studied about far-reaching adverse effects of midazolam in growing organisms. For example, it is shown that the usage of midazolam in spinal anesthesia leads to decrease in locomotion activity in experimental animal only the first 24 hours. The negative impacts of midazolam are not occurring for late period.

**Aim of research**

The effect of midazolam premedication (single injection) on behavior changes of growing rats under the conditions of halothane anesthesia after 1 week from the sham operation.

**Methods**

Experiments were carried out on growing (20 days, average mass 26 g) rats. Animals (48 white rats) were divided into three groups: 1. Control group. 2. First test group: This group includes animals, which has been operated (sham operation) under halothane anesthesia. 3. Second test group: This group includes rats, which has been operated (sham operation) under the conditions of halothane anesthesia and premedication with midazolam (midazolam injection- 200mg/kg, 30 minutes before surgery). Open field test was used to assess behavior parameters and emotions in control and both test groups. We evaluated behavior changes in rats a week after the operation. Research was lasted 5 days. Each animal was explored during 5 minutes every day. There were registered following parameters: Vertical activity, sum of inner, external and center squares, time of staying in the center of the field, groomings, the grooming duration, defecation.

**Results and discussion**

The high level research activity has been determined in all three groups in the first day of experiment (Vertical standing: the first group - 10,6±2,3; the second group - 7,6±3,3; third group - 15,1±2,7 (fig. 1.a). sum of external squares: first group-47,8±4,7; second group-45,6±5,8; third group- 50,9±4 (fig. 1.b). According to sum of inner (fig. 1.c) and center squares (fig. 1.d), and time of staying in the center of the field (fig. 2.a), revealed the higher level locomotion activity in the third group of animals, than in first and second groups (sum of inner squares: the first group - 4,8±1,3; II group - 4,3±1,2; III group- 9,2±1,7; sum of center squares: the first group- 0,3±0,1; the second group - 0,3±0,2; the third group - 1,3±0,3; time of staying in the center of the field: first group - 1±0,4; second group - 1,1±0,6; third group - 3,6±1,1), these results indicate decreasing of fear level (decreasing of fear in third group is connected to midazolam premedication).

Emotional tension disappeared in all three groups with short and seldom groomings (The first group (Fig. 2b) - 12±0,2; the second group 1,7±0,5; the third group-1±0,2). Grooming duration parameter showed following results: the first group-15,9±3,8; the second group-10,7±3,9; the third group-9,4±2,7 (Fig. 2.c). According to defecation (Fig 2.d) fear level was equal in all three groups of rats (1 group- 0,8±0,2; II group - 1,2±0,6; III group - 1,3±0,3).

The adaptation to environment has been revealed in all three groups a day after. Similar results were shown in the third and fourth days. The high level research activity has been determined in control and third groups, in comparison with halothane group. This fact is related to adaptation to environment and it proves decreasing of tension and fear level. The adaptation to environment and high space orientation of growing rats in third group has to be caused by midazolam premedication.

**Conclusions**

The reason for weak adaptation to environment after halothane anesthesia compared to intact animals may be the reducing of dendrite growth by halothane in growing animals and thus the inhibition of brain development. The fact that these effects are not revealed after midazolam premedication allow us to think that reducing the anxiety activity of animals after midazolam premedication provides to avoid the inhibition of dendrite growth and brain development. On the bases of our results it is established that a week after operation in growing rats under the halothane anesthesia midazolam premedication (single injection) doesn’t cause any negative influence on behavior parameters of growing animals.
**References**


