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Dynamics of Hypoxia-Induced Factor Hif-1α in Children with Congenital Heart Defects

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ABSTRACT

HIF-1α has both neuroprotective and neurotoxic effects during hypoxia due to the specificity for the cell type of markers associated with the severity of hypoxia. Uncovering the complex functions of HIF-1α is important in the development of protective therapy for hypoxic-ischemic damage to the body.

KEYWORDS:hypoxia-induced factor HIF-1α, congenital heart disease.

INTRODUCTION

Most of the defects disrupt the blood flow inside the heart or through the large and small circles of blood circulation. Heart defects are the most common birth defects and are the leading cause of infant mortality [3,10, 14].The diagnosis of congenital heart defects (CHD) is currently based on clinical, instrumental and laboratory data. To prevent adverse effects, early diagnosis and the timing of initiation of therapy are of great importance [2, 8. 9]. Of course, CHD therapy can in principle be divided into surgical (in most cases it is the only radical) and therapeutic (more often auxiliary). In our study, we diagnosed laboratory parameters of hypoxia before and after surgery using combined inhalation anesthesia. In this regard, it is worth noting that hypoxia biomarkers can detect damage at the stage when its clinical picture has not yet been formed. Among potential markers of hypoxia resulting from impaired blood flow, HIF-1α (hypoxia-induced factor-1 alpha) is of interest [7, 10, 12, 15].

HIF-1α has an anti-apoptotic effect, increasing the expression of anti-apoptotic factors such as EPO during mild hypoxia. The neurotoxic effects of HIF-1α are represented by its participation in the apoptotic process by increasing the resistance of the p53 tumor suppressor protein during severe hypoxia. Moreover, HIF-1α plays a role in cell necrosis by interacting with calcium and calpain [1, 5, 7]. HIF-1α can also aggravate cerebral edema by increasing the permeability of the blood-brain barrier [4, 6, 16]. Given these properties, it can be said that HIF-1α has both neuroprotective and neurotoxic effects after hypoxia-ischemia. According to the authors, these events are specific for the cell type and are associated with the severity of hypoxia. Uncovering the complex functions of HIF-1α may be important in the development of protective therapy for hypoxic-ischemic damage to the body.

Purpose of the study was to determine the level of HIF-1α in blood serum in children with CHD, depending on the various techniques of anesthesia.

MATERIAL AND METHODS

We examined 65 children with CHD who were in the cardiac surgery department of the clinic of the Tashkent pediatric medical institute.

Inclusion criteria: established diagnosis of CHD.

Exclusion criteria: children with severe genetic diseases and stigmas of

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dysembryogenesis, the presence of infectious and inflammatory diseases.

The control group consisted of 20 (23.6%) practically healthy children.

The main group consisted of 65 (76.4%) patients with a verified diagnosis of CHD, including: ventricular septal defect - 16 (23%), atrial septal defect - 12 children (12%), ventricular septal defect with high pulmonary hypertension - 9 (13.8%), pulmonary artery stenosis - 11 (17%), Fallot's tetrad - 8 (12.3%), patent ductus arteriosus - 9 (13.8%).

Subsequently, the main group was divided into 2 groups, depending on the anesthesia performed: group 1 included 34 children who received combined general anesthesia with sevoflurane; Group 2 consisted of 31 children who underwent combined inhalation anesthesia with isoflurane.

Anesthetic risk was assessed using the ASA. Pre-operative premedication included atropine sulfate 0.1% - 0.01 mg / kg, sibazone 0.5% - 0.3 mg / kg, ketamine 5% - 3-5 mg / kg. Anesthesia was induced by sibazone 0.25 mg / kg, fentanyl 5-7 μg / kg. Muscle relaxation was carried out using pipcuronium bromide 0.1 mg / kg and further supported by bolus administration of 0.015 mg / kg. Maintenance of anesthesia was provided by inhalation anesthetic sevoflurane 2-3% of the volume in the first group and isoflurane 2-3% of the volume in the second group and fractional administration of fentanyl.

All patients underwent an enzyme-linked immunosorbent assay before surgery, during surgery and on the 3rd day after surgery with the determination of the HIF1-α level. The set "Vector-Best", Russia) was used on the apparatus "LUSURITE" (USA).

The material for the enzyme-linked immunosorbent assay was blood serum, which was collected in vacuum tubes. The tubes contain a clotting activator and a gel. After blood sampling, the tube was carefully inverted 5-6 times to ensure good mixing. Within 20 minutes, it was infused at room temperature, then centrifuged (1000 rpm for 3 minutes).

It was frozen in a freezer at a temperature (up to -20 C). According to the instructions, the serum can be stored for up to 2 months.

RESULTS

The study showed that the level of HIF-1α was different in patients of both groups. Thus, in patients of group 1, the level of HIF-1α was 12.65 ng / ml before surgery, 14.28 ng / ml during surgery, and 8.44 ng / ml on day 3 after surgery (P <0.001). In group 2 patients, the level of HIF-1α before surgery was 11.19 ng / ml, during surgery - 30.42 ng / ml, on day 3 after surgery – 21.76 ng / ml (P <0.001) (Table 1)

Table 1. HIF-1α level, ng / ml in patients with CHD, depending on the performed anesthesia

HIF-1α index, ng / ml	Control group (n=20)	1st group(n=34)	2nd group(n=31)
before surgery	1,98±0,53	12,65±0,71***	11,19±0,18***
during surgery		14,28±0,66***	30,42±0,82***
3 days after surgery		8,44±0,35***	21,76±0,95***

Note: *- differences relative to control group data are significant (* - P<0,05, ** - P<0,01, *** - P<0,001)*

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In children of group 1, the level of HIF-1α before the operation exceeded the control value by 6.38 times, during the operation - 7.2 times, on the 3rd day after the operation - 4.3 times, respectively. In patients of group 2, it was 5.6 times higher than in the control group before surgery, 15.7 times during surgery, and 10.9 times on day 3 after surgery, respectively.

Drugs for inhalation anesthesia and intravenous ultrashort anesthetics have changed the attitude of cardiac anesthesiologists to the postoperative period [8]. Postmedication concomitant with total intravenous anesthesia has ceased to be an obstacle for early activation of patients undergoing heart surgery with artificial circulation [3]. In turn, the reduction in the time of postoperative artificial ventilation of the lungs, and early activation of patients can reduce to a minimum the number of respiratory complications, which lengthen the hospitalization of patients in the intensive care unit [2].

CONCLUSION

Taking into account the increase in the level of HIF-1α, depending on various methods of inhalation anesthesia, it can be used as a biomarker, an increase in which will indicate an aggravation of the child's condition. Thus, HIF-1α mediates critical physiological responses to hypoxia, and the identification of this homeostatic mechanism may lead to improved treatment.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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