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HEMODYNAMIC EFFECTS OF XENON ANESTHESIA IN CHILDREN

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The study was aimed at *hemodynamic effects of xenon on operative interventions in children.* ***Patients and methods:*** *the study involved 30 5-17-year-old children – 10 (33.3%) girls and 20 (66.7%) boys with ASA score 1-3 admitted for surgical treatment. The children underwent endotracheal anesthesia with xenon-oxygen mixture (Xe:O2 = 60-65:30%) and fentanyl (2.5-3.5 mcg/kg per hour) for the following operations: appendectomy – 10 (33.3%) patients, herniotomy – 8 (26.7%) patients, Ivanissevich procedure – 6 (20.0%) patients, plastic surgery of posttraumatic defects of skin and soft tissues – 4 (13.3%) patients, abdominal adhesiotomy – 2 (6.7%) patients. Central hemodynamics was studied echocardiographically (Philips HD 11, the Netherlands) using the Teichholz technique along the cephalocaudal axis (parasternal access).* ***Results:*** *the anesthesia was notable for hemodynamic stability during the operation: as a result, a statistically significant ($p < 0.05$) increase in systolic, diastolic and mean arterial pressure by 10, 18 and 17%, respectively, was observed.* ***Conclusion:*** *the analysis demonstrated that xenon anesthesia improves lusitropic myocardial function statistically significantly increasing cardiac output by 12% by way of increasing stroke volume by 30%.*
Keywords: *xenon, inhalation anesthesia, hemodynamics at xenon, children.*

Introduction

Xenon (Xe) anesthesia is becoming the most widely used in modern anesthesiology due to manageability and capability not to enter metabolic processes or cause allergic reactions [1-4]. Hemodynamic properties of xenon are of doubtless interest: it does not directly affect myocardial contractility, vascular tone, maintains mean arterial pressure and left ventricular ejection fraction [5-8]. This favorably sets xenon apart from other known anesthetics and makes its use both in general surgery and cardiosurgery and in the event of emergency conditions requiring intensive therapy justified [9-12]. Apart from cardiac stimulant activity, Xe also produced cardioprotective effect [13].

Given positive impact of Xe on hemodynamics in adult patients and lack of such studies in children, a study of impact of this inert anesthetic on hemodynamics during operative interventions in children was performed at the Research institute of pediatric surgery and traumatology.

The study was aimed at analyzing hemodynamic effects of xenon during operative interventions in children.

PATIENTS AND METHODS

The study involved 30 children aged from 5 to 17 years – 10 (33.3%) girls and 20 (66.7%) boys admitted to the clinic for surgical treatment. Physical status of the children was assessed on the basis of the scale suggested by the American Society of Anesthesiologists (ASA) and conformed to class 1-3; all the children underwent endotracheal balanced anesthesia with medical Xe. Premedication of the patients involved a cholinolytic (0.01% atropine sulfate solution in the dose of 0.01 mg/kg) and antihistamines (if indicated); induction was performed intravenously (1% propofol in the dose of 3 mg/kg); children were intubated and placed on artificial pulmonary ventilation after analgesia (0.005% fentanyl in the dose of 3 mcg/kg) and myoplegia (rocuronium bromide in the dose of 0.6 mg/kg). The process of denitrogenation and Xe saturation did not exceed 12-15 minutes. Anesthesia was maintained with gas mixture Xe:O_2 = 60-65:30% and bolus analgesic administration (0.005% fentanyl in the dose of 2.5-3.5 mcg/kg per hour). Preoperative preparation included crystalloid infusion (Sterofundin, saline solution) in the dose of 8-10 ml/kg and preventive administration of antibiotics (amoxicillin and clavulanic acid in the dose of 10 mg/kg [amoxicillin]) in 14 (46.6%) emergency patients. Intraoperative infusion was performed with crystalloids in all the patients in the dose of 5-10 ml/kg per hour. Xe anesthesia was performed at the following operative interventions: appendectomy (10 patients; 33.3%), herniotomy (8 patients; 26.7%), Ivanissevich procedure (6 patients; 20.0%), plastic surgery of posttraumatic defects of skin and soft tissues (4 patients; 13.3%) and abdominal adhesiotomy (2 patients; 6.7%). Anesthesia was performed with apparatus Siesta i Whispa (Dameca, Denmark) adjusted with anesthetic machine KNP-01 (Akela-N, LLC, Russia). System MP 60 (Philips, Germany) was used to monitor vital functions: systolic (SAP), diastolic (DAP) and mean (MAP), heart rate (HR) and perfusion index (PI). Gases (In/EtO_2, EtCO_2, InXe) were monitored with gas analyzers M1026B (Philips, Germany) and GKM-03-INSOVT (Akela, Russia). Central hemodynamics was studied echocardiographically (Philips HD 11, the Netherlands) using the Teichholz technique along the long axis (parasternal access); this process involved determining left ventricular internal diastolic dimension (IDD), left ventricular internal systolic dimension (ISD), ventricular ejection (VE), cardiac minute output (CMO) and left ventricular fraction ejection (FE). The study consisted of 3 stages: before anesthesia, during Xe anesthesia and after Xe anesthesia.

Statistical manipulation

Statistical data manipulation was performed using software package Statistica 6.0. We used repeated measures analysis of variance and compared mean values by means of Lilliefors test. Statistical connection between the attributes was assessed using Spearman's rank correlation coefficient. In order to determine correlation ratio between ranked attributes (random amount), we employed Kendall's multiple rank correlation coefficient (coefficient of concordance). The data are reported in terms of mean values ± standard deviation. $P < 0.05$ was considered a statistical significance criterion.

STUDY RESULTS AND DISCUSSION

Data of study stage 1 corresponded to the initial hemodynamic parameters at the child's admission to the pre-operating room for premedication. At study stage 2, data of the central hemodynamics were registered in the period of maximum Xe saturation of the body (60-65%) and in the most traumatic moment of the operative intervention. The last stage, i.e. stage 3, designated the period of the child's complete recovery: parameters were registered at least 30-40 minutes after the patient's intubation.

Data on the changes of hemodynamic parameters in the course of Xe anesthesia are given in tb. 1.

Table 1. ***Results of analysis of hemodynamics at xenon anesthesia in children***

Central hemodynamic parameters	Study stages		
	Stage 1	**Stage 2**	**Stage 3**
HR (per minute)	105±16	93±18	98±11
SAP	110.6±10.7	122.2±12.9*	119.8±10.0*
DAP	60.6±9.2	74.7±14.4*	69.9±10.1*
MAP	72.8±9.4	85.5±9.7**	80.2±8.1**
PI	0.95±0.4	4.4±2.1**	1.6±0.7**
FE (%)	64.9±11.8	69.3±8.09.7	65.0±7.2*
VE (cm^3)	44.9±17.8	58.6±20.4**	50.9±15.8**
CMO (l/min)	4.7±2.0	5.4±1.9*	5.6 ±1.5
IDD (cm)	3.9±0.6*	4.3±0.6*	4.1± 0.6*
ISD (cm)	2.6±0.5	2.6±0.4	2.5±0.4

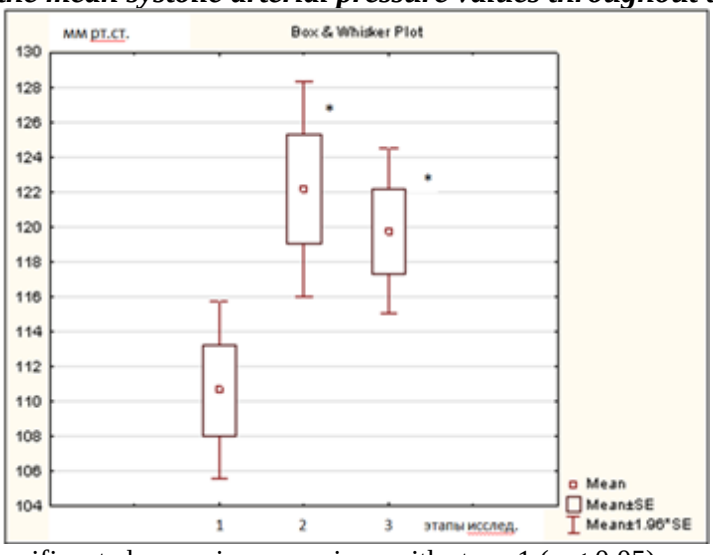
Note. SAP/DAP – systolic/diastolic arterial pressure, MAP – mean arterial pressure, PI – perfusion index, FE – fraction ejection, VE – ventricular ejection, CMO – cardiac minute output, IDD/ISD – left ventricular internal diastolic/systolic dimension; * $p < 0.05$ and ** $p < 0.001$ – statistically significant changes in comparison with stage 1.

Before analyzing the obtained study results (see tb. 1), we performed verification of the normal law of data distribution. Given the absence of the normal law of distribution, we used non-parametric tests (Friedman tests) for further statistical analysis, as they do not depend on the data distribution forms.

Tb. 1 demonstrates that HR decreased from 105±16 bpm at stage 1 down to 93±18 bpm at stage 2 without any statistically significant difference. The tendency to HR decrease during Xe anesthesia in adult patients is associated with parasympathetic system's activation with xenon along with decrease in activity of the sympathetic system; in literature, this is defined as sympatholytic action of Xe [7, 8].

In order to analyze effect of Xe on myocardial contractility, we analyzed SAP changes throughout stages of the study, the results whereof are given in pic. 1.

Pic. 1. ***Dynamics of the mean systolic arterial pressure values throughout the study stages***



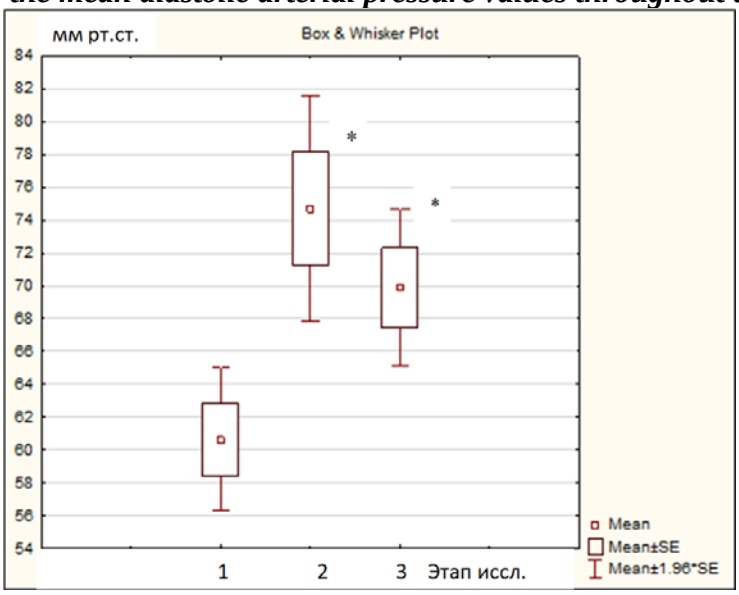
Note. * - statistically significant changes in comparison with stage 1 ($p < 0.05$).

High-low chart (see pic. 1) demonstrates a statistically significant ($p < 0.05$) increase in the mean SAP by 10% at study stage 2 in comparison with stage 1: stage 1 – 110.6±10.7 mm Hg, stage 2 –

122.2±12.9 mm Hg. At stage 3, after xenon anesthesia completion, SAP had a tendency to statistically insignificantly decrease by 2.5% (down to 119.8±10.0 mm Hg) in comparison with stage 2. Statistically significant SAP increase at study stage 2 corresponded to 60-65% Xe concentration in the ABM; this confirmed the studies conducted previously in adult patients indicating positive effect of the anesthetic on myocardial contractility. Absence of cardiodepressant effect favorably sets Xe apart from all the known inhalation anesthetics and contributes to its application not only in cardiothoracic anesthesiology, but also in the event of myocardial depression in medical patients [9, 11, 12].

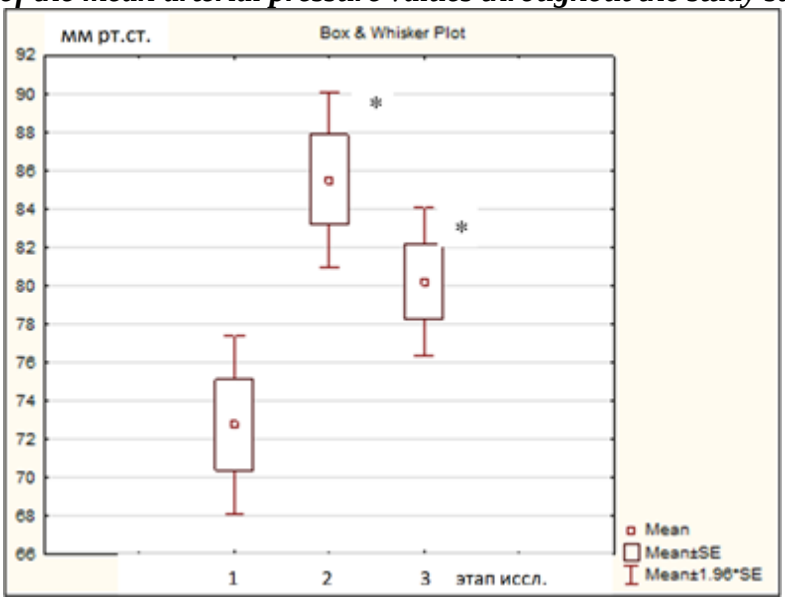
We performed a non-parametric data variance analysis in order to analyze impact of Xe anesthesia on DAP (pic. 2).

Pic. 2. ***Dynamics of the mean diastolic arterial pressure values throughout the study stages***



Note. * - statistically significant changes in comparison with stage 1 ($p < 0.05$).

Pic. 3. ***Dynamics of the mean arterial pressure values throughout the study stages***



Note. * - statistically significant changes in comparison with stage 1 ($p < 0.05$).

As we see in pic. 2, DAP statistically significantly increased by 18% at study stage 2 in comparison with stage 1 ($p < 0.05$): 74.7±14.4 and 60.6±9.2 mm Hg. However, by anesthesia completion at study stage 3, DAP had a tendency to decrease in comparison with stage 2 (down to 69.9±10.1 mm Hg). The resultant mean DAP remained 13% higher (i.e. statistically

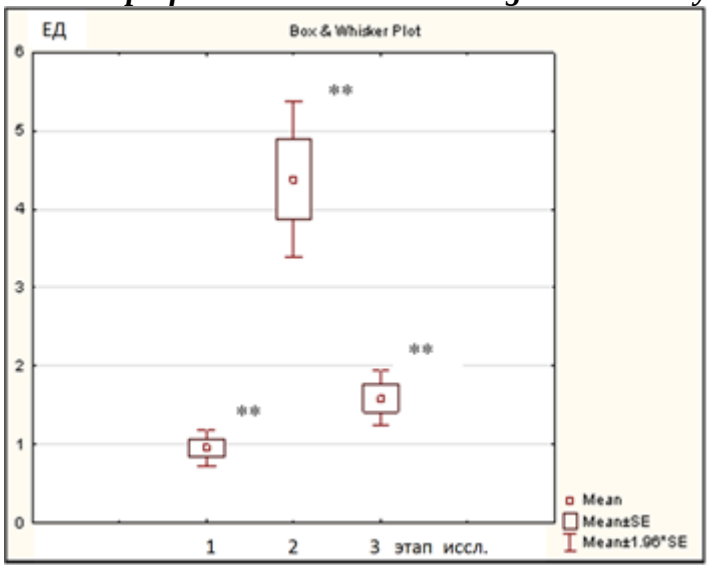
significantly higher [$p < 0.05$]) than the mean DAP at stage 1. Unlike the initial data, the increase in the mean DAP both during anesthesia and immediately after it indicates absence of vasodepressor effect of Xe. Moderate diastolic pressure increase during Xe anesthesia in adult patients was reported in the earlier publications by N.E. Burov et al., who observed absence of both cardiodepressant and vasodepressor effects of Xe [14, 15].

Friedman's non-parametric variance repeated measures analysis also demonstrated the increase in systolic and diastolic pressure is accompanied by MAP increase (pic. 3).

It ought to be mentioned (see pic. 3) that the mean MAP statistically significantly ($p < 0.001$) increased by 17% at study stage 2 (during anesthesia): from 72.8±9.4 to 85.5±9.7 mm Hg. Comparison of stages 3 and 2 helped to reveal a tendency to decrease by 9% of the mean MAP (85.5±9.7 and 80.2±8.1 mm Hg), which was not statistically significant. Comparison of the mean MAP at study stage 3 with the initial data yielded a statistically significant ($p < 0.001$) 10% increase of this parameter: 80.2±8.1 and 72.8±9.4 mm Hg. Statistically significant increase of the mean MAP during Xe anesthesia and immediately after it in comparison with the initial data indicates positive impact of Xe in the 60-65% concentration on systemic hemodynamics and the capability to improve organ and tissue blood flow not only during Xe anesthesia, but also after it. This property of Xe makes it useful for anesthesia in transplantology, cardiac operations in adult patients and opens prospects for its application in these spheres of pediatric surgery [16].

In order to analyze tissue perfusion at Xe anesthesia, we analyzed PI dynamics at all the study stages (pic. 4).

Pic. 4. ***Dynamics of the mean perfusion index values throughout the study stages***



Note. * - statistically significant ($p < 0.001$) changes (all stages).

Pic. 4 demonstrates that the mean PI at study stage 2 (4.4±2.1 U) was statistically significantly ($p < 0.001$) 4 times higher than at stage 1 (0.95±0.4 U). PI statistically significantly ($p < 0.001$) decreased 2.5 times at stage 3 in comparison with stage 2 (1.6±0.7 and 4.4±2.1 U). Statistically significant PI increase during Xe anesthesia in comparison with the initial data indicates improvement of tissue perfusion during Xe anesthesia. Positive impact of Xe anesthesia on tissue perfusion opens prospects of pediatric Xe use not only for anesthesia, but also for intensive therapy (shock management).

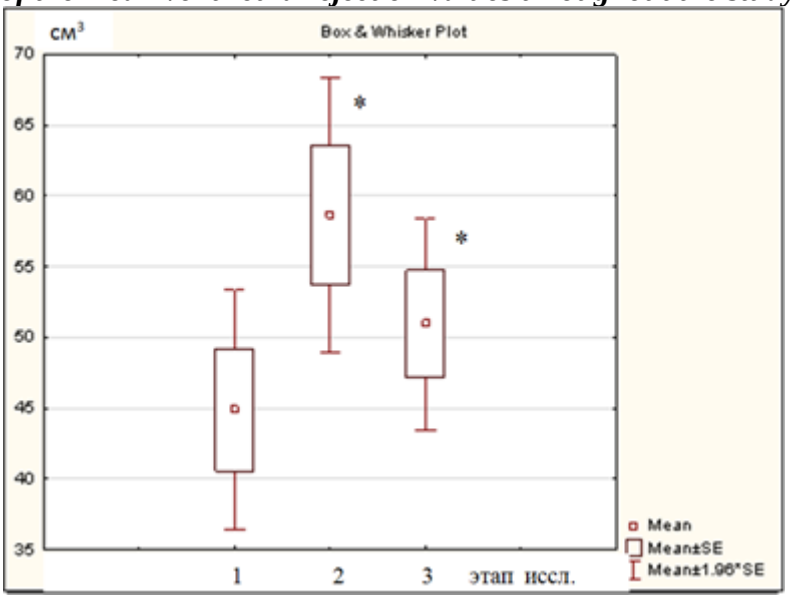
Thus, on the basis of the identified statistically significant increase in SAP, DAP, MAP and PI in the process of anesthesia maintenance in comparison with the initial data, we may assert that Xe in 60-65% concentration stabilizes systemic hemodynamics, improves tissue and peripheral blood flow during operative interventions in children.

In order to study impact of Xe on heart pump function, we analyzed the mean FE at different study stages. Tb. 1 demonstrates that the mean FE at study stage 1 was 64.9±11.8%, whereas at

stage 2 it showed a tendency to increase – up to 69.3±8%. We observed a statistically significant ($p < 0.05$) decrease in the mean FE down to 65.0+7.2% at study stage 3 in comparison with stage 2. Absence of statistically significant changes between the mean FE values at xenon anesthesia study stages indicates that Xe in 60-65% concentration does not depress heart function and satisfies body needs in effective blood supply.

As far as FE depends on VE, we analyzed the mean values of this parameter at different study stages (pic. 5).

Pic. 5. ***Dynamics of the mean ventricular ejection values throughout the study stages***

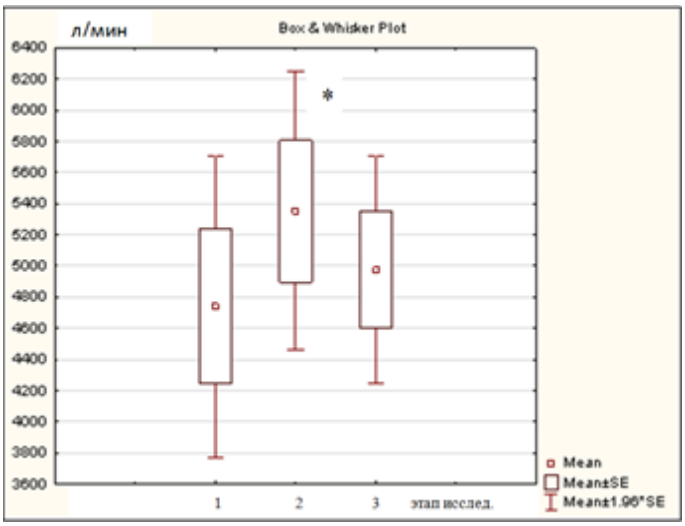


Note. * - statistically significant changes at stages 2 and 3 in comparison with stage 1 ($p < 0.001$).

Pic. 5 demonstrates that the mean VE was statistically significantly ($p < 0.001$) 30% higher at study stage 2 than at stage 1 (58.6±20.4 and 44.9±17.8 cm^3). We observed a statistically significant decrease in the mean VE down to 50.9±15.8 cm^3 at study stage 3, which is 13% lower than at stage 2 ($p < 0.001$). A statistically significant increase in the mean VE at Xe concentration peak and after Xe anesthesia in comparison with the initial data indicates positive impact of Xe on myocardial contractility not only during Xe anesthesia, but also after it.

In order to assess heart's functional condition during Xe anesthesia, we analyzed CMO at all the study stages (pic. 6).

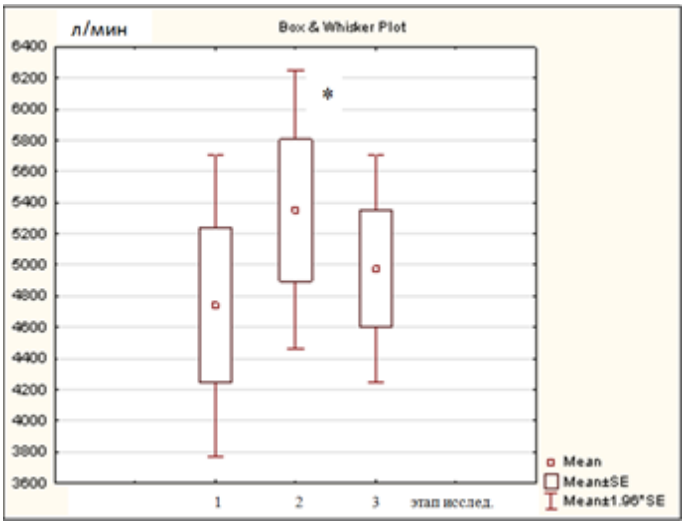
Pic. 6. ***Dynamics of the mean cardiac minute output values (l/min) throughout the study stages***



Note. * - statistically significant changes during anesthesia in comparison with stage 1 ($p < 0.05$).

Pic. 6 demonstrates a statistically significant increase in the CMO up to 5.4±1.9 l/min (12% higher than the initial data) at stage 2 from 4.7±2.0 l/min at stage 1 ($p < 0.05$). At stage 3, the CMO featured a tendency to decrease in comparison with stage 2 – 5.6±1.5 l/min – and had no statistically significant differences with stage 1. In order to clarify the cause of the CMO increase at xenon anesthesia, we analyzed VE and HR, as it depends on these parameters. As tb. 1 features no statistically significant changes in the HR throughout all the study stages, therefore, VE was the cause of CMO changes; pic. 5 demonstrates a statistically significant increase in the VE both during the Xe anesthesia and after it in comparison with the initial data. The study demonstrated that the VE increase was caused by the IDD increase, i.e. left ventricular myocardial distension in the diastolic phase. Results of the performed study are given in pic. 7.

Pic. 7. ***Dynamics of the mean left ventricular internal diastolic dimension values throughout the study stages***



Note. * - statistically significant changes during anesthesia in comparison with stage 1 ($p < 0.05$).

Pic. 7 demonstrates that the mean IDD statistically significantly ($p < 0.05$) increased by 10% up to 4.3±0.6 cm at study stage 2 in comparison with stage 1 (3.9±0.6 cm). The mean IDD statistically significantly ($p < 0.05$) decreased by 4% (down to 4.1±0.6 cm) at study stage 3 in comparison with study stage 2. Comparison of the mean IDD values did not yield any statistically significant differences between study stages 3 and 1. A statistically significant IDD increase during the anesthesia indicates that Xe in 60-65% concentration produces positive lusitropic effect in the myocardium – improvement of the diastolic heart compliance function. Improvement of the myocardial lusitropic function results in the VE increase by means of increased filling of the left ventricle in the diastolic phase and establishes favorable conditions for cardiac function [17]. No statistically significant changes in the mean ISD were being observed throughout the study (see tb. 1).

CONCLUSION

General balanced endotracheal xenon anesthesia in 60-65% concentration ensures hemodynamic stability during operative interventions in children by means of improving myocardial lusitropic function in the form of increase in the left ventricular fraction ejection, cardiac minute output and ventricular ejection without affecting myocardial contractility.

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