Federal State Budget Institution
«National Medical Research Center for Obstetrics, Gynecology and Perinatology named after Academician V.I. Kulakov»
Ministry of Healthcare of the Russian Federation

Institute of Neonatology and Pediatrics
Department of neonatal surgery

THE EXPERIENCE OF USING LEVOSIMENDAN IN THE TREATMENT OF PULMONARY HYPERTENSION IN NEWBORNS WITH CONGENITAL DIAPHRAGMATIC HERNIA

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4th European conference on Neonatal and Pediatric Pulmonary vascular disease
09 – 11 October 2019 года

The new concept of treating infants with congenital malformations on the basis of the largest perinatal center in Russian Federation

Prenatal diagnosis of malformation

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Transportation in the perinatal center «in utero»

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Surgical treatment of a newborn with a congenital malformation at birth or in the first days/weeks of life

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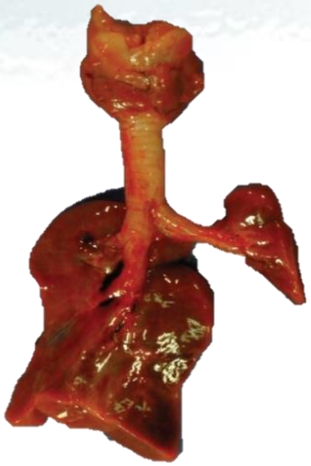
Intensive care and nursing of the child until discharge home

Purpose of the study

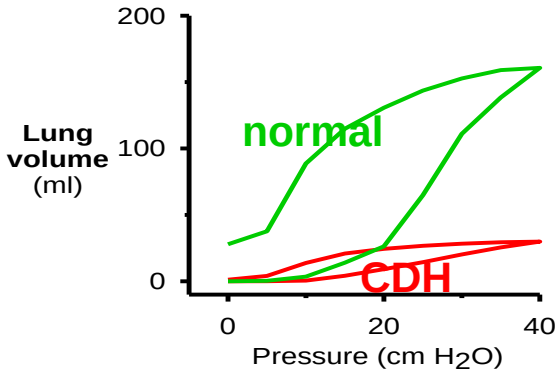
- The search for optimal hemodynamic support, including the prevention and treatment of pulmonary hypertensive crises, as one of the fundamental points in the complex treatment of newborns with CDH
- To study of the effectiveness and safety of the use of levosimendan in the treatment of pulmonary hypertension in newborns with CDH in the perioperative period.

Pathophysiology of CDH

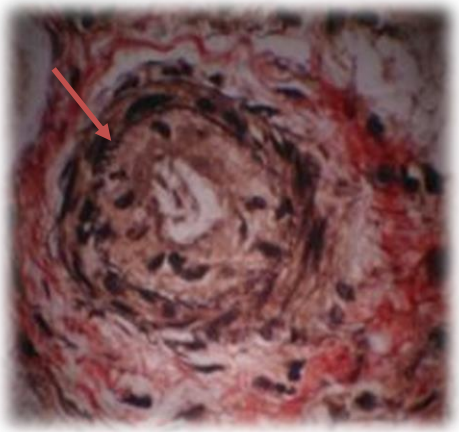
Lung hypoplasia → Pulmonary hypertension



Lung hypoplasia



Abnormal compliance



Decrease in number and change in vascular morphology

High vascular resistance in the lungs +
Right-left shunting of blood through the ductus arteriosus

Right ventricular dysfunction

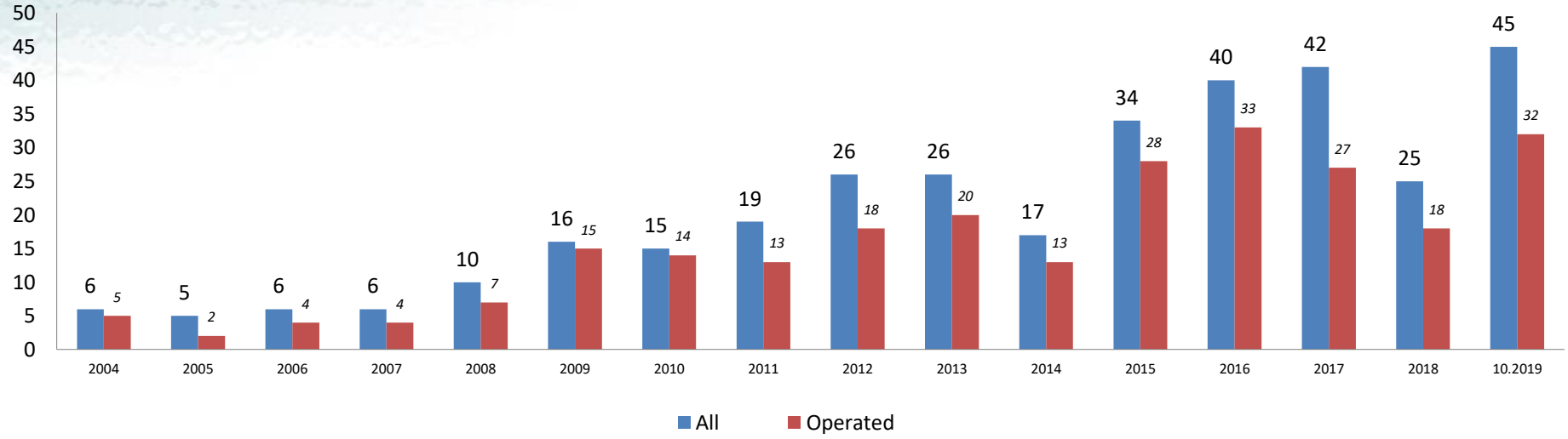
Left ventricular dysfunction

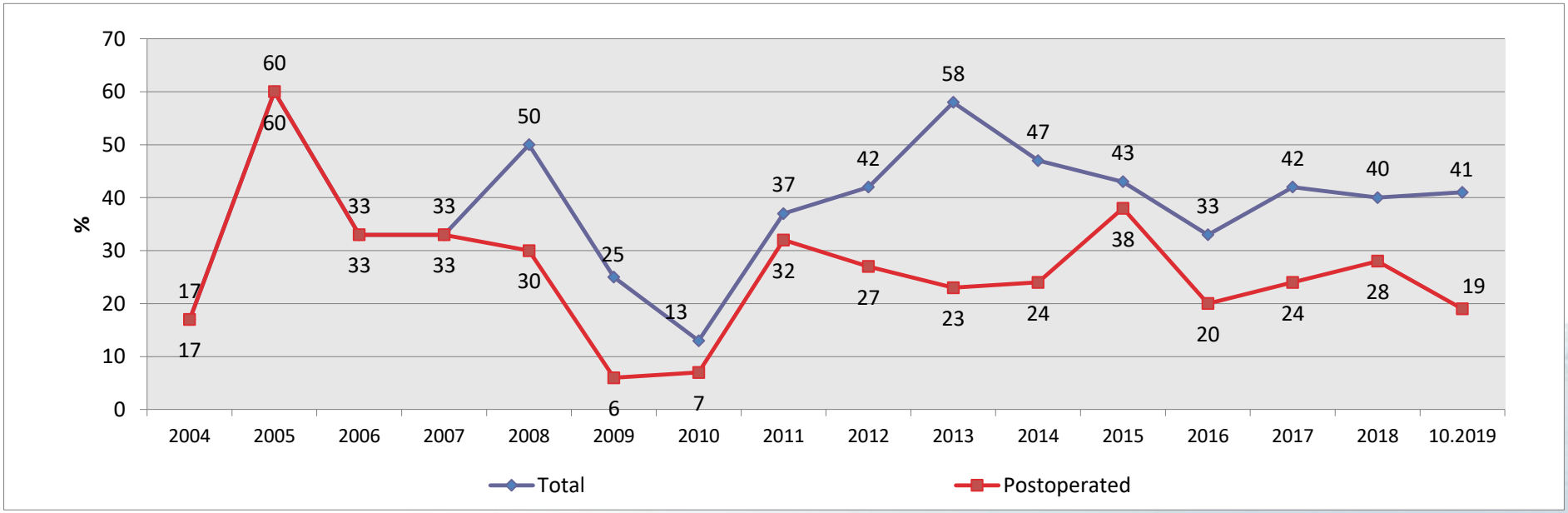
"Prefect storm"

"Volumetric" hypoplasia of the left ventricle in CDH

Congenital diaphragmatic hernia

All – 338 Operated on – 253 (75,1%)





Inodilator - Levosimendan

Cardiotonic drug, increases the sensitivity of contractile proteins to Ca2 + by binding to the myocardium troponin C in the calcium-dependent phase, increases the strength of heart contractions, does not affect ventricular relaxation.
It opens ATP-sensitive K + channels in the smooth muscles of blood vessels, and thus causes relaxation of the systemic and coronary arteries and veins.

Selective inhibitor of phosphodiesterase 3.

Replacement is not available Milrinone

Russia - Off label in newborns

Levosimendan in Two Neonates with Ischemic Heart Failure and Pulmonary Hypertension

Maria Pia De Carolis[a] Marco Piastra[b] Iliana Bersani[a] Manuela Pardeo[c] Eleonora Stival[b] Alessia Tempera[d] Costantino Romagnoli[a] Giorgio Conti[b] Gabriella De Rosa[c]

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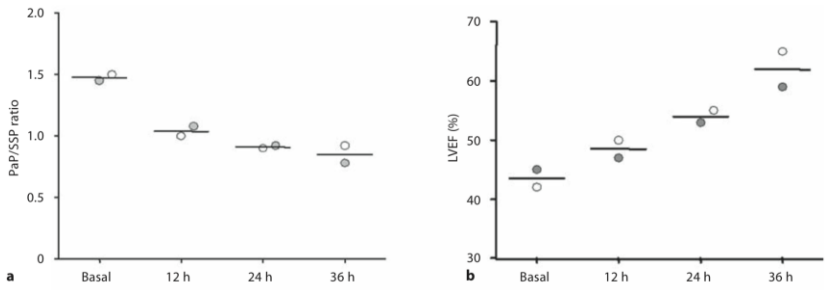

Maria Pia De Carolis at al. Levosimendan in Two Neonates with Ischemic Heart Failure and Pulmonary Hypertension. Neonatology 2012;101:201–205

Case Report

Levosimendan in a neonate with severe coarctation of aorta and low cardiac output syndrome

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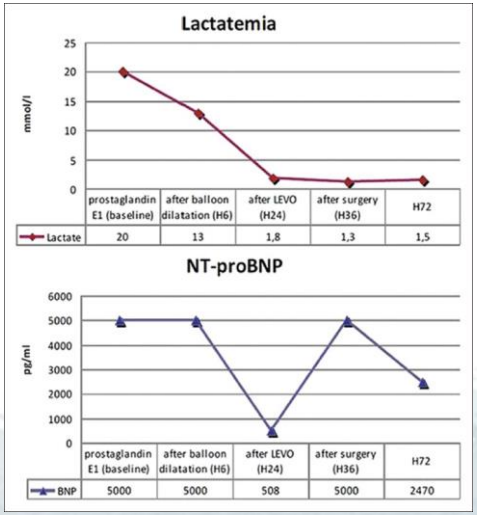
ABSTRACT

We report successful use of levosimendan after failed balloon angioplasty in a critically ill neonate with coarctation of aorta (CoA) and severe low cardiac output syndrome (LCOS). Treatment with levosimendan improved left heart function, and decreased lactate and brain natriuretic peptide levels. To our knowledge, this is the first report on the safe and successful use of levosimendan in the management of LCOS due to severe CoA in a neonate awaiting surgical repair.



Boegli YO, Gioanni S, van Steenberghe M, Pouard P. Levosimendan in a neonate with severe coarctation of aorta and low cardiac output syndrome. Ann Card Anaesth 2013;16:212-4.

Materials and Methods

	Group 1 “2018”	Group 2 “2019”
Time period	**08.2017 – 08.2018**	**08.2018 – 06.2019**
Number	**35**	**35**
Prenatal indicators of the degree of pulmonary hypoplasia		
o/e LHR (the index of pulmonary hypoplasia), %	48±18	45±15
CCI (cardiac compression index)	1,45±1,7	1,38±1,8
Liver in the pleural cavity	27 (77,1%)	28 (80,0%)
Type of using levosimendan		
Doses	Saturation dose of 10 µg/kg iv in 15 min and then at a support dose of 0.1-0.25 µg/kg/min for only 24 hours	Support dose of 0.1-0.25 µg/kg/ min for more than 24 hours
Appointment sequence	***Dopamine → Dobutamine → Epinephrine → Norepinephrine → Levosimendan***	***Dopamine + Levosimendan → Epinephrine → Norepinephrine***

Standard guidelines in neonates with CDH

1. Therapeutic protective regime

Prevention of pulmonary hypertensive crises

Comfortable environment, appropriate sedation, adequate anesthesia, high thoracic epidural analgesia

2. Maintenance therapy

Respiratory therapy

IVL → HFV → ECMO (not used since 2018)

Maintaining systemic blood pressure

Adequate fluid therapy and use of inotropic and vasopressor therapy:

3. Reduction in pulmonary vascular tone

iNO → Sildenafil → Alprostadil → Bosentan

4. Surgical intervention is carried out only when the stabilization of patient was achieved.

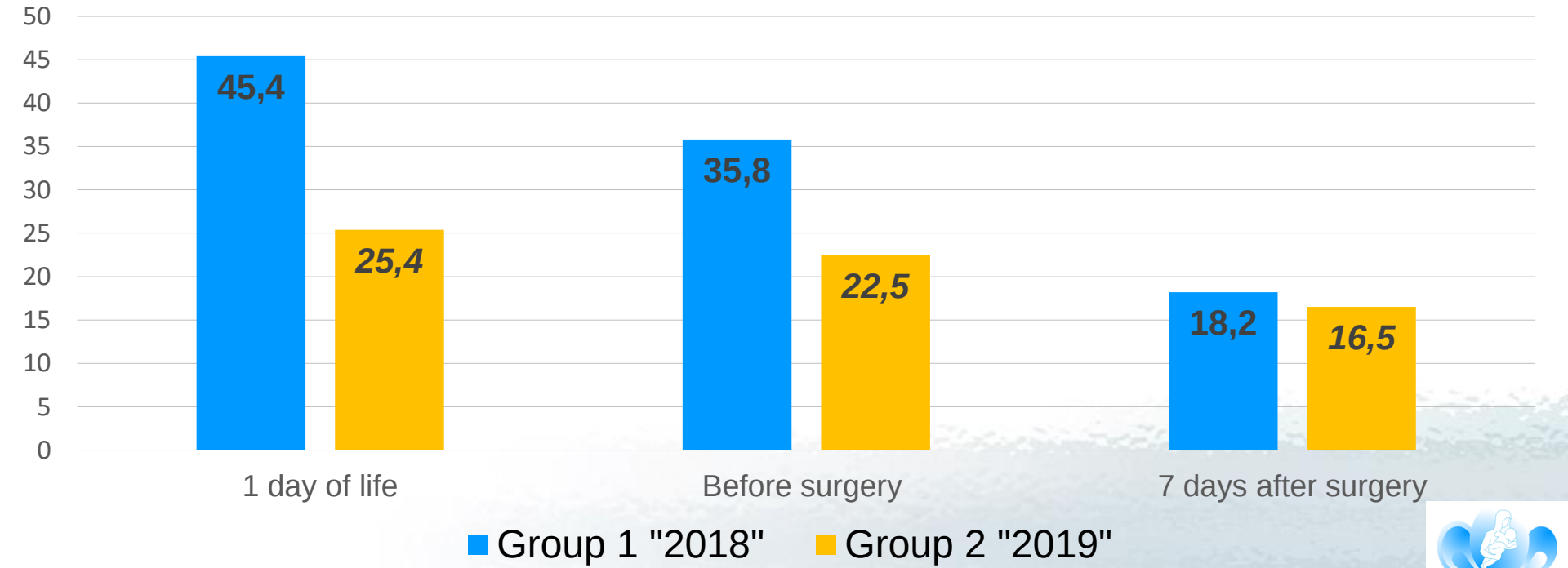
In Group 1 «2018», 22 (62,8%) children were operated on, of which 4 (18,1%) died in the postoperative period

In Group 2 «2019» 27 (77,1%) children were operated on and 2 (7,4%) died in the postoperative period.

For description and evaluation of hemodynamic disturbances we used **vasopressor-inotropic support index (IVPI),** which was calculated by the formula:

Dopamine dose (μg/kg/min) x 1 +
Dobutamine dose (μg/kg/min) x 1 +
Epinephrine dose (μg/kg/min) x 100 +
Norepinephrine dose (μg/kg/min) x 100 +
Levosimendan dose (μg/kg/min) x 100.

Ratio of average values IVPI indicators



Results

- The infusion duration of levosimendan in Group 2 “2019” was 14.5±5.6 days, cancellation was performed in the postoperative period after the cancellation of epinephrine.
- Decrease in the frequency and duration of pulmonary hypertensive crises by 45%
- Decrease in the maximum dose of epinephrine to an average of 0.5 μg/kg/min.
  Group 1 “2018” - 0,83±0,53 μg/kg/min vs Group 2 “2019” 0,21±0,08 μg/kg/min
- Decreased use of dobutamine and norepinephrine/
- Side effects were noted only in 2 cases - signs of liver failure, after cancellation of levosimendan, relief of these effects was noted.

Conclusions

The use of levosimendan as a standard hemodynamic support in newborns with CDH allowed to reduce the incidence of PHC, reduce the dose of epinephrine to an acceptable level in therapy, prepare more children for surgery and improve survival in the group of children with severe forms of CDH.

THANKS FOR YOUR ATTENTION!

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