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

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Abstract

Congenital diaphragmatic hernia (CDH) is a complex congenital malformation with high mortality (up to 50%) due to lung hypoplasia with congenital pulmonary hypertension with severe pulmonary hypertensive crises (PHC).

The search for optimal hemodynamic support, including the prevention and treatment of PHC, is one of the fundamental points in the complex treatment of newborns with CDH.

Purpose

The study of the effectiveness and safety of the use of levosimendan in the treatment of pulmonary hypertension (PH) in newborns with congenital diaphragmatic hernia (CDH) in the perioperative period.

Materials and Methods

We compared two time intervals equal in time and number of patients with CDH with a change in the time and duration of use of levosimendan in therapy.

Group 1 - Levosimendan was used in the recommended doses: at a 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 after reaching the maximum doses of traditional inotropic and vasopressor drugs.

Group 2 - Levosimendan was used at the beginning of therapy at a support dose of 0.1-0.25 μg/kg/ min for more than 24 hours simultaneously with dopamine.

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%)
Types of CDH		
Left-side	32 (91,4%)	31 (88,5%)
Right-side	2 (5,7%)	3 (8,6%)
Bilateral	1 (2,9%)	1 (2,9%)

Results

Standardized therapy in neonates with CDH 2018 *vs* 2019

1. Therapeutic protective regime

Prevention of pulmonary hypertensive crises

Comfortable environment, appropriate sedation, adequate anesthesia, high thoracic epidural analgesia - was the same.

2. Maintenance therapy

* *Respiratory therapy*

IVL → HFV → ECMO (not used since 2018) - was the same.

* *Maintaining systemic blood pressure*

adequate fluid therapy and use of inotropic agents:

Group 1 «2018»: Dopamine → Dobutamine → Epinephrine → Norepinephrine → Levosimendan

Group 2 «2019»: Dopamine + Levosimendan → Epinephrine → Norepinephrine

3. Reduction in pulmonary vascular tone

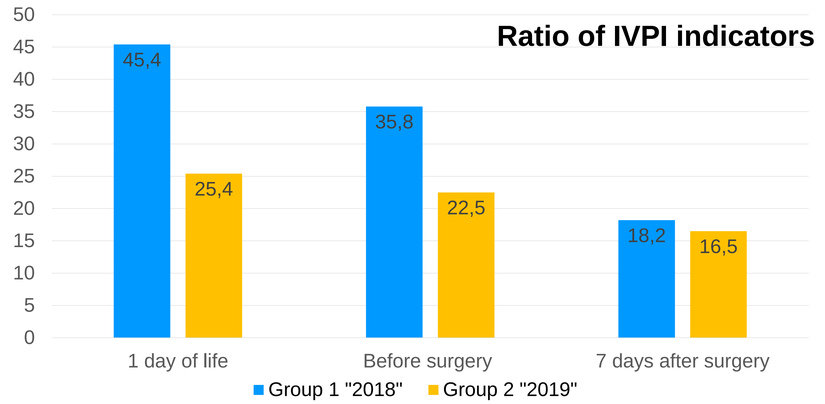
iNO → Sildenafil → Alprostadil → Bosentan

We used in the treatment of pulmonary hypertension a first-line drug nitric oxide (iNO) and subsequent titration of oral sildenafil. Duration of inhalation iNO 5.8±1.4 days, dose 18.5±3.5 ppm, sildenafil length - 36.5±9.8 days, dose 2.5±0.6 mg/kg/day. Also in newborns with resistance to treatment with iNO we used early administration of bosentan at 100%, intravenous alprostadil at 67%.

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, while 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 or Levosimendan dose (μg/kg/min) x 100.



In Group 2 "2019" IVPI significantly decreased at all stages of therapy. And the dose of epinephrine in complex therapy was significantly reduced.

Dose of Epinephrine in complex therapy		
	Group 1 “2018”	Group 2 “2019”
Epinephrine dose (μg/kg/min)	0,83±0,53	0,21±0,08
MAX Epinephrine dose (μg/kg/min)	2,5	1,0

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 adrenaline.

Side effects were noted only in 2 cases - signs of liver failure, after cancellation of levosimendan, relief of these effects was noted.

We noted a decrease in the frequency and duration of pulmonary hypertensive crises by 45% despite a decrease in the maximum dose of epinephrine to an average of 0.5 μg/kg/min.

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 form of CDH.

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