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INITIAL EXPERIENCE WITH HYBRID APPROACH FOR HYPOPLASTIC LEFT HEART SYNDROME

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With the purpose of assess the experience of off-pump hybrid approach for palliation of hypoplastic left heart syndrome 15 neonates included in the study. The mean diameter of the ascending aorta was 2.08±0.14mm. 6 (40 %) patients had concomitant large ventricular septum defect. Hybrid palliation surgery included bilateral banding of pulmonary artery branches to 2.5–3.5 mm in 15 patients, supplemented by endovascular stent implantation in the lumen of the patent ductus arteriosus in 15 patients; balloon atrial septostomy – in 6 (40 %) patients. In-hospital mortality comprised 60 % (n=9): 6 (66.7 %) – due to heart failure; 2 (22.2 %) – due to septic pneumonia; in 1 (11.1 %) – Rashkind procedure complicated with left atrium perforation. 4 (26.7 %) patients discharged with improvement. In neonates with extremely high risk of performing Norwood I-Blalock /Sano, the alternative is off-pump hybrid palliative intervention, serving like a life-supporting "bridge" either to Norwood–Glenn surgery, and/or subsequent heart transplantation.

Key words: hypoplastic left heart syndrome, hybrid palliation surgery, Norwood surgery, balloon atrial septostomy, neonates.

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ПЕРШИЙ ДОСВІД ГІБРИДНОГО ПІДХОДУ ПРИ СИНДРОМІ ГІПОПЛАЗІЇ ЛІВИХ ВІДДІЛІВ СЕРЦЯ

З метою оцінки досвіду застосування гібридного підходу без штучного кровообігу для паліативного лікування синдрому гіпоплазії лівих відділів серця до дослідження було включено 15 новонароджених. Середній діаметр висхідної аорти становив 2,08±0,14 мм. У 6 (40 %) пацієнтів був супутній великий дефект міжшлуночкової перегородки. Гібридна паліативна операція включала двостороннє лігування гілок легеневої артерії до 2,5–3,5 мм у 15 пацієнтів, доповнене імплантацією ендоваскулярного стенту у просвіт відкритої артеріальної протоки у 15 пацієнтів; балонну атріосептостомію – у 6 (40 %) пацієнтів. Госпітальна летальність становила 60 % (n=9): у 6 (66,7 %) – через серцеву недостатність; у 2 (22,2 %) – через септичну пневмонію; у 1 (11,1 %) – операція Рашкінда, ускладнена перфорацією лівого передсердя; 4 (26,7 %) пацієнти виписано з покращенням. У новонароджених з вкрай високим ризиком виконання операції Норвуда І-Блалока/Сано альтернативою є гібридне паліативне втручання без штучного кровообігу, яке служить життєзабезпечуючим «мостом» або до операції Норвуда-Гленна, або до подальшої трансплантації серця.

Ключові слова: синдром гіпоплазії лівих відділів серця, гібридна паліативна операція, операція Норвуда, балонна атріосептостомія, новонароджені.

The study is a fragment of the research project "To organize a system for providing emergency and uncomplicated cardiac surgical assistance to patients with critical congenital heart defects"; state registration No. 0120U102154.

Congenital atresia of the aortic and mitral valves is usually combined with underdilation of the left heart chambers and hypoplasia of the ascending aorta. He was the first to forward the concept of a complex congenital heart disease (CHD) representing the totality of multiple lesions of the anatomical structures of the left heart. The term "hypoplastic left heart syndrome" (HLHS) was proposed by JA.Noonan and AS.Nadas (1958) [10].

In the prenatal period, HLHS is not an obstacle to the normal development of the fetus. A characteristic feature of placental circulation is the flow of mixed arteriovenous blood with equal partial oxygen pressure into the aorta and pulmonary trunk, which results in almost identical oxygen saturation in the right and left ventricles. In hypoplasia of the left ventricle with dysfunction of the aortic and mitral valves, systemic circulation is maintained by the single (right) ventricle and the patent ductus arteriosus (PDA) [12].

In newborns with HLHS, postnatal circulatory remodeling is fatal on the first six weeks of life and is the most common cause of neonatal mortality. Newborns with HLHS usually manifested with severe heart failure on the first week of life and leads to mortality in majority of newborns on the first two weeks of life (~25 % of cardiac deaths during the first week of life are due to HLHS). Without in-time surgical intervention, mortality reaches 100 % on six months of life [2, 9].

The leading predictors of mortality in newborns and infants with natural history of HLHS includes rapid closure of PDA, and concomitant lesions of the tricuspid, and pulmonary valves; coarctation of the aorta [11].

In the case of fetal Echo-verification of HLHS, the examining cardiologist strongly recommends termination of pregnancy. HLHS cannot be repaired by conventional surgery. The management of HLHS continues today as one of the major challenges in pediatric cardiac surgery [8, 13, 14].

Surgical treatment of HLHS is based on two principles: reconstructive interventions and heart transplantation. Reconstructive interventions are represented by Norwood I–Blalock/Sano; Norwood II–Glenn; Norwood III–Fontan, or hybrid interventions. It should be emphasized that while the tactics of surgical intervention is determined by the surgeon's preference, the appropriateness of the intervention itself depends on the child's parents [2, 7].

In recent years, the introduction of prenatal endovascular interventions has led to the delineation of pre-stage I: fetal [5], where prenatal endovascular perforation of the aortic valve, or dilatation of the restrictive interatrial communication done. The first stage of hemodynamic intervention (Norwood I–Blalock/Sano) performed on the first 4–10 days of the newborn's life. The optimal time for the first stage of surgical intervention in HLHS recognized as the 2–5 day of the newborn's life. As the first stage of surgical intervention, Norwood I–Blalock or Norwood I–Sano procedures performed [2, 3, 7].

Recently, survivals have vastly improved, and large numbers of these patients survive. As this population grows, it becomes increasingly important to understand the outcomes, and modify the approaches.

The purpose of the study was to assess the experience of off-pump hybrid approach for palliation of hypoplastic left heart syndrome

Materials and methods. The study was conducted at the basis of National Amosov Institution of Cardio-Vascular Surgery (Kyiv, Ukraine) in the period of 2018–2020.

The inclusion criteria of our 15 HLHS patients for hybrid treatment were ascending aortic diameter less than 2 mm, and low body weight. Enrolled group included 11(73.3 %) boys and 4 (26.7 %) girls. Prematurity (gestational age less than 32 weeks) and birth weight <1500g both were not considered contraindications for hybrid endovascular and surgical intervention. The exclusion criteria: patients with ascending aortic diameter more than 2 mm.

The age of newborns at surgery ranged from 4 to 13 days of life (9.1±2.4 days). The body weight ranged from 2.1–4.3 kg (2.24±0.14 kg). Ascending aorta diameter comprised 1.5–3.5 mm (2.08±0.14 mm). In 7 (46.7 %) patients, ascending aorta was less than 2 mm. In 6 (40 %) cases revealed concomitant large ventricular septal defect (VSD).

HLHS was diagnosed prenatally in 11 (73.3 %) patients and verified by Echo-exam after birth. In 4 (26.7 %) patients HLHS was verified at birth.

All patients underwent initial medication on 1–10 days to correct systemic and pulmonary vascular resistance and increase SO_2 level to 80 %. Before interventions, prostaglandin E_1 infusion was performed to prevent closure of patent ductus arteriosus (PDA), which supplemented by inotropic drugs and repair of metabolic acidosis.

Initially, both branches of the pulmonary artery were banded to 2.5–3.5 mm. Thereafter, combination of two endovascular procedures was performed: a) stent implantation in PDA by catheter inserted through the PA trunk. In 13 patients stent implantation was performed on a balloon; in two cases we used self-expandable stent implantation; b) balloon atrial septostomy. The aim of hybrid interventions was to achieve a balance between systemic arterial pressure and SO_2: stabilization of systolic pressure ≥70–80 mmHg, and SO_2 up to 85–90 %. If SO_2 value was higher, and systemic pressure was lower, the pulmonary artery branches banding was continued until the set parameters were achieved.

Results of the study and their discussion. In all 15 infants, off-pump hybrid intervention included bilateral pulmonary artery branch banding in 15 patients, supplemented by endovascular stenting of the PDA in 15 patients, and balloon atrial septostomy in 6 (40 %) patients. One patient underwent pacemaker implantation due to the development of complete A-V heart block after the intervention.

In 9 (60 %) patients, balloon atrial septostomy was either not possible or not necessary: in two cases the Rashkind procedure was not performed due to the presence of a large atrial septal defect (ASD); in 5 patients, ASD was absent; in 2 patients, after banding of the pulmonary artery branches and implantation of a stent in PDA, the planned balloon atrial septostomy was not performed due to the development of hemodynamically significant cardiac rhythm disturbances that required cardioversion and termination of the operation.

The following 2 case reports illustrates hybrid intervention (successful and interrupted, respectively).

Case 1. Newborn A., aged 21 days of life was admitted to the center on 27.01.2016. Echo-exam on 27.01.2016: A large (0.6 cm.) VSD at the border of membranous and muscular part of the septum with

cross-discharge was found. Underdeveloped left ventricular outflow tract and aortic valve ring were revealed. The aortic diameter was 0.4 cm. There was more evidence for aortic arch interruption. The descending aorta supplied by PDA 0.3–0.4 cm. An open oval window ~0.35 cm was found. Spontaneous Positive Airway Pressure (SPAP) was equal to the systemic pressure, comprising 60 mmHg. LVEF was 42 %. The diagnosis was HLHS.

On 01.02.2016, a hybrid operation was performed – bilateral banding of pulmonary artery branches, endovascular stent implantation in PDA, and balloon atrial septostomy. The initial left and right atrial pressures were 160 and 80 mmH_2O, accordingly; following Rashkind procedure the left and right atrial pressures equaled: 120 mm H_2O both. SO_2, on oxygen background, was 98 % in the arm; 95 % in the leg. On 10.02.2016 due to decreased SO_2 the patient underwent re-banding of the pulmonary artery branches. SO_2 increased from 60 % to 85 %. The postoperative period manifested by cardiopulmonary and hepatic insufficiency. On 13.07.2016 the child was discharged from the clinic in satisfactory condition. The length of hospital stay comprised 169 days.

Case 2. Newborn B., aged on the first day of life was admitted to the cardiac center on 07.12.2017. Echo-exam on 07.12.2017 verified HLHS. Severe hypoplasia of the left ventricular and mitral valve was found. There was an aortic valve atresia. The ascending aorta diameter comprised 0.25 cm; the segment "C" of aortic arch – 0.3cm; the segment "B" of aorta – 0.4cm; the segment "A" – hypoplasia of the aorta to 0.2 cm. Retrograde filling of the ascending aorta and coronary arteries was found. A wide PDA (5 mm) was noted. The systolic pressure in the right ventricle was 55 mmHg.

On 14.12.2017, a newborn underwent a hybrid intervention: bilateral pulmonary artery branch banding was performed as the first stage. Systemic pressure increased from initial 53/40 mmHg to 63/40 mmHg. SO_2 **(**on lower extremities) decreased from 94 % to 87 %. The next stage of hybrid intervention was planned stent implantation in the PDA and balloon atrial septostomy. Using introducer, inserted in pulmonary artery (PA) trunk, stent was implanted in PDA. The control angiography verified the adequate position of the stent. After stent implantation in PDA, a paroxysm of supraventricular tachycardia was developed. The patient underwent cardioversion with restoration of sinus rhythm. However, subsequent hemodynamic instability forced to postpone atrioseptostomy and to complete the operation. The intensive care unit (ICU) – stay manifested by low cardiac output syndrome, which could not be controlled. The patient died on 15.12.2017.

The postoperative period was complicated by fatal outcomes in 9 (60 %) infants. Heart failure dominated in 6 (66.7 %) cases. Development of heart failure following interventions tied with thrombosis of the stent implanted in PDA, which caused obstruction of the aortic arch and ascending aorta with secondary compromise coronary blood flow. In 2 (22.2 %) patients, death following intervention tied with septic pneumonia; in 1 (11.1 %) patient perforation of the left atrium occurred during balloon atrial septostomy. After the intervention, 4 (26.7 %) patients were discharged to inpatient hospitals for further follow-up. All four survived patients had concomitant large VSD. Six months after the hybrid intervention, one patient underwent re-stenting of PDA (stent-in-stent), accompanied by a clinical improvement.

Analyzing the hospital outcomes for Norwood I–Blalock and Norwood I–Sano performed over 14 days of life in 35 neonates and infants, Andronache AA et al. (2024) noted a 25.7 % hospital mortality, highlighting that 89 % of patients (of the 9 postoperative deaths) underwent surgery on over 15 days of life. The mean age of patients at surgery was 27 days (6–259 days). The maximum age at the first stage of surgery was 259 days of life only in one patient. In 71 % of patients, Norwood I was performed on >14 days of life. Additional predictors of high hospital mortality were the presence of a restrictive ASD in 82.6 % of patients; the initial need for ventilator support, and systemic infection in 45.7 % and 42.9 % of infants, respectively. The HLHS subtype with aortic and mitral valve atresia was observed in 52.1 % of patients [1].

Despite the technically successful Norwood I–Blalock-Taussig operation, hospital mortality remained high until 2000. The majority of fatal outcomes on 24–48 hours following surgery were due to hemodynamic instability tied with unpredictably rapid decrease of pulmonary vascular resistance. The leading option for stabilization of hemodynamic in the postoperative period was the banding of systemic-pulmonary shunt. By 2000, some centers had achieved 63–94 % hospital survival rate after Norwood I–Blalock, however, this operation is still accompanied by a high mortality rate in most centers with low surgical activity [6, 11]. In our work the percentage of survivals and those who were discharged to inpatient hospitals for further follow-up was 26.7 %.

Initially, the frequency of operations in the Norwood I–Blalock and Norwood–Sano variants was mixed. Thus, using databases from 52 centers, 13 (25.5 %) clinics performed a randomized comparison

of both Norwood procedures; 18 centers tended to perform Norwood-Sano; 14 centers performed Norwood I–Blalock; in 6 centers the choice of intervention was based on surgeon and/or cardiologist preference [8]. A number of surgeons explain their reticence to the Norwood-Sano procedure by the necessity of right ventriculotomy, with the potential risk of its dysfunction and rhythm disturbances (Ohye RG, et al., 2016) [11].

Currently, at the first stage of hemodynamic repair of HLHS, the Norwood I–Sano operation favorable (Andronache AA, et al., 2024) [1]. Analyzing the outcomes of the first stage of repair in 35 newborns and infants with HLHS, the authors applied Norwood I–Sano correction in 97.1 % of patients (n=34), whereas Norwood I-Blalock surgery was performed in only one (2.9 %) patient. The second and third stages of interventions presented with Norwood II–Glenn, and Norwood III–Fontan procedures. Our hybrid palliation surgery included bilateral banding of pulmonary artery branches to 2.5–3.5 mm in 15 patients, supplemented by endovascular stent implantation in the lumen of the patent ductus arteriosus and additional balloon atrial septostomy – in 6 patients [1].

Hospital mortality after Norwood II–Glenn comprises from 5 % to 20 %. Hospital mortality following Norwood III-Fontan ranges from 5% to 23%. The long-term survival on 4 years monitoring comprised 52 %. After completion of three-stage hemodynamic correction of HLHS, the survival rate is 62 % [6]. In our study in-hospital mortality was 60 %.

Hemodynamic palliation for HLHS with Norwood I–III, and subsequent monitoring of such patients is a privilege of high-budget countries. Taking in account that treatment of complex congenital heart disease is not available everywhere, the need for joint projects to ensure timely transfer of such patients to countries with appropriate cardiac centers is pointed out.

Hybrid approach includes bilateral banding of pulmonary artery branches (from the midline sternotomy) with simultaneous two endovascular interventions, including stent implantation in PDA, and Rashkind procedure. Indications for such hybrid intervention include prematurity, low birth weight, concomitant genetic pathology, severe tricuspid valve insufficiency, low right ventricular ejection fraction, intact atrial septum or restrictive interatrial communication, and minimal diameter of the ascending aorta. When performing hybrid endovascular and surgical intervention, before stent implantation, a careful angiographic assessment of the anatomy and size of the PDA is necessary, followed by control angiography to verify the position of the implanted stent. Mismatch in the size of the implanted stent may lead to narrowing of the duct diameter, creating an obstruction to the systemic blood flow. If the stent is overextended, it may block the pulmonary artery branch orifices or retrograde blood flow into the proximal segment of the aortic arch and ascending aorta, leading to catastrophic consequences in group of patients with aortic atresia [12, 14].

Initially, such hybrid endovascular and surgical intervention was not widespread. However, recently this technique has been used as an alternative to Norwood correction in extremely severe patients, eliminating the need of CPB, and serve like a “bridge” to Norwood II–Glenn, and subsequent heart transplantation [4, 5, 7].

Conclusions

1. In-hospital mortality in newborns with left heart hypoplasia syndrome underwent hybrid approach comprised 60 % (n=9).

2. Among patients underwent off-pump hybrid hemodynamic palliation 4 (26.7 %) patients discharged with improvement. All 4 survivals had concomitant large ventricular septal defect.

In newborns with an extremely high risk of performing the Norwood I–Blalock/Sano, an alternative is off-pump hybrid hemodynamic palliation serving like a “bridge” to either the Norwood–Glenn procedure and/or subsequent heart transplantation. However, comparison of the outcomes of hybrid intervention and Norwood variant correction is rather difficult due to the difference in the groups of operated patients, as hybrid intervention is usually performed in patients with an extremely high risk of on-pump operations.

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CHANGES OF MICROBIOTA-DERIVED SHORT-CHAIN FATTY ACID LEVELS IN CHILDREN WITH VIRAL DIARRHEA

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The purpose of the study was to assess the clinical and diagnostic significance of changes in short-chain fatty acids levels in children of the first year of life with viral diarrhea. The study was conducted in 94 children with diarrhea aged 0–1 year. The control group consisted of 30 healthy children. Determination of short-chain fatty acids levels was conducted, using gas-liquid chromatography. According to results, in the mono variant of viral diarrhea, acetic acid decreased by 1.5 times compared to the, in mixed variants – by 1.8 times ($p<0.001$); propionic acid in the mono variant decreased by 1.5 times, in the mixed variant it decreased by 2 times ($p<0.001$); butyric acid in the mono variant decrease of 2.5 times, in the mixed variant it was 3.6 times lower ($p<0.001$); isovaleric acid in the mono variant decreased by 1.2 times ($p<0.05$), while in the mixed course increased (14.1 %).

Key words: short-chain fatty acids, butyric acid, valerianic acid, microbiota, gastroenteritis.

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ЗМІНИ РІВНЯ КОРОТКОЛАНЦЮГОВИХ ЖИРНИХ КИСЛОТ, СИНТЕЗОВАНИХ МІКРОБІОТОЮ, У ДІТЕЙ З ВІРУСНОЮ ДІАРЕЄЮ

Метою дослідження була оцінка клініко-діагностичної значущості змін рівня коротколанцюгових жирних кислот у дітей першого року життя з вірусною діареєю. Дослідження проведено у 94 дітей з діареєю у віці від 0 до 1 року. Контрольну групу склали 30 здорових дітей. Визначення рівня коротколанцюгових жирних кислот проводилося методом газорідинної хроматографії. Згідно з результатами, при моно-варіанті вірусної діареї оцтова кислота знизилася в 1,5 рази в порівнянні з контролем, при змішаних варіантах – в 1,8 рази ($p<0,001$); пропіонова кислота при моно-варіанті знизилася в 1,5 рази, при змішаному варіанті – в 2 рази ($p<0,001$); масляна кислота при моно-варіанті знизилася в 2,5 рази, при змішаному варіанті була нижчою в 3,6 рази ($p<0,001$). Ізовалеріанова кислота при моно-варіанті знизилася в 1,2 рази ($p<0,05$), а при змішаному перебігу збільшилася (на 14,1 %).

Ключові слова: коротколанцюгові жирні кислоти, масляна кислота, валеріанова кислота, мікробіота, гастроентерит.

The term “microbiota” refers to the diverse ecosystem of bacteria, fungi, archaea, and viruses that inhabit the human gastrointestinal tract. These microbial communities are thought to exert a profound influence on the host’s physiological processes and pathological states [9]. Disruptions in the composition of the gut microbiota have been linked to a wide range of conditions, including gastrointestinal disorders as well as neurological, respiratory, metabolic, hepatic, and cardiovascular diseases [4].