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Foramen ovale (FO) – The underestimated sibling of ductus arteriosus (DA): Relevance during neonatal transition

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1. Introduction

The immediate transition from intra-uterine to extra-uterine life causes complex changes affecting all vital organ systems, especially the cardiovascular system [1]. During the pregnancy the low-resistance placenta supplies the fetus with oxygenated and with nutrient enriched blood. During fetal development pulmonary vascular resistance remains high and the majority of the right ventricular output (RVO) bypasses the lung. Venous blood coming to the heart follows the physiological right-to-left shunt through the foramen ovale and the ductus arteriosus into the systemic circulation. Whereas the majority of the left ventricular output (LVO) supplies the brain and the upper body [2]. With the first breath, immediately after birth, the pulmonary vascular resistance decreases rapidly and RVO is redirected through the lung [3]. Recently, there is a growing interest to evaluate the cardio-circulatory changes during the immediate transition, especially the shunt behavior via DA. Several animal and human studies have investigated the shunt via DA after birth, showing the DA shunt changes from predominantly right to left into left to right during the first 15 min after birth [2,4,5].

The brain is one of the most vulnerable organs during fetal to neonatal transition. In recent years, interest has grown to monitor the brain after birth [6]. Measurement of regional oxygen saturation parameters using near infrared spectroscopy (NIRS) has been demonstrated to be feasible even during immediate transition period [7–10] and a recent review summarized the NIRS measurements during immediate transition [11]. Oxygen delivery to the brain is dependent on cardiac output and arterial oxygen content [12]. As the ductal blood flow is an important component of cardio-circulatory adaptation during neonatal transition, its influence on cerebral oxygen saturation is still not completely clear. Recently, our study group showed that the presence of left-to-right shunting via the DA was associated with higher cerebral tissue oxygenation values compared to infants without left-to-right shunting [5]. All studies have focused on the left to right shunting through the DA, whereas shunting via the foramen ovale (FO) and its potential impact on cardiocirculatory adaptation during transition was not investigated so far.

The aim of the present study was to investigate the presence of left-to-right shunting via FO, and furthermore, its potential influence on cardio-circulatory adaptation, and on the cerebral tissue oxygenation. As we did show, that presence of DA shunting had improved cerebral oxygen saturation, therefore we concentrated our observational focus on the neonates with left to right shunt via DA as well as via FO. In this study we tried to differentiate the influence of shunting for each of the two (FO, DA) on cerebral oxygen saturation. We hypothesized, that due to steal phenomenon of L to R shunting via FO the positive haemodynamic effects of L to R shunting via DA might be reduced, resulting in changes in cerebral oxygen saturation.

2. Methods

This prospective observational study was carried out at the Division of Neonatology, Department of Pediatrics, Medical University of Graz. The study was approved by the Regional Committee on Biomedical Research Ethics/Medical University of Graz. We included term infants with a gestational age of >37 weeks, fulfilling following criteria: i)

Abbreviations: TOI, tissue oxygenation index; SpO_2, arterial oxygen saturation; HR, heart rate; FO, foramen ovale; DA, ductus arteriosus; CBF, cerebral blood flow; CBV, cerebral blood volume; NIRS, near-infrared spectroscopy; LR shunting, left to right shunting.

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uncomplicated neonatal transition of 15 min, ii) no requirement of respiratory or medical support iii) written informed consent by the parents prior to birth and iv) delivery through caesarean section. All infants with major congenital malformation were excluded.

The antepartum medical history was collected before birth and demographics (gestational age, birth weight, gender, pH of umbilical artery, Apgar score and cord clamping time) were documented in each neonate.

A stopwatch was started when the neonate was fully delivered. After cord clamping neonates were brought to the resuscitation table and were placed under an overhead heater in supine position. The neonates were dried and stimulated.

For monitoring of SpO_2 and HR, a pulse-oximetry was placed around the right wrist/hand (IntelliVue MP30 Monitor, Philips, Amsterdam, Netherlands). The blood pressure was measured non-invasively at the 15th minute of life using a neonatal cuff of appropriate size at the left upper arm (IntelliVue MP30 Monitor, Philips, Amsterdam, Netherlands). NIRS measurements were performed after uncomplicated neonatal transition 15 min after birth. The cerebral tissue oxygen index (cTOI) was measured for 60 s using an NIRO200NX monitor (Hamamatsu; Japan). The transducer was positioned on the right frontoparietal forehead in each infant. The sensor on the forehead was secured with cohesive conforming bandage (Peha-haft, Harmann, Heidenheim, Germany).

All variables were stored by using a multichannel system alpha-trace digital MM (BEST Medical Systems, Vienna, Austria) for subsequent analysis. Values of the SpO_2, and HR were stored every second, and the sample rate of cTOI was 2 Hz.

Immediately after the end of NIRS measurements (15 min after birth), an echocardiography was performed (Vivid 7 Pro, General Electric; USA) to evaluate the DA and FO. Echocardiography was always done by the same person.

After ruling out any form of structural heart disease, which automatically led to exclusion from the trial, we assessed ductal and FO patency. If there was a left to right flow through DA and FO was detectable, the diameter of DA and FO was measured. Ductal patency was directly assessed from left parasternal location in the parasternal short axis view. We measured the internal ductal diameter three times with pulsed Doppler echocardiography plus color flow mapping. Then we averaged the results of the measurements. Based on fulfilling the following echocardiographic criteria, a patency of ductus arteriosus was diagnosed as being haemodynamically important: a left atrium to aortic root diameter ratio of 1.4, internal ductal diameter > 1.4 mm/kg. None of our patients were diagnosed with such a haemodynamically significant DA. FO size and patency was using the subcostal 4-chamber view. We measured the FO diameter three times with pulsed Doppler echocardiography plus color flow mapping and averaged the results of the measurements.

3. Statistical analysis

Data are presented as mean and 95% CI for normally distributed continuous variables and median (interquartile range, IQR) when the distribution was skewed.

A correlation analysis was performed to investigate if there was a connection between cTOI and the diameter of DA and FO, individually. Furthermore to get the whole input of the left to right shunt on the cerebral tissue oxygenation, we added the diameter of PDA and FO, when there was a left-to-right shunt. As the next step we performed the correlation analyses between the sum of DA/FO diameters and the cerebral tissue oxygenation. Correlations were performed using Spearman's rank correlation coefficient or Pearson's correlation when appropriate. A p-value < 0.05 was considered statistical significant. The statistical analyses were performed using IBM SPSS Statistics 22.0.0 (IBM Corporation; Armonk, USA).

4. Results

Between July 2013 and October 2014, 780 term infants were eligible. Out of 780 eligible term neonates, 80 were enrolled and 60 neonates were included into final analyses. (Fig. 1.) The mean (SD) gestational age was 38.8 (0.9) weeks, birth weight 3320 (516) g and median (IQR) Apgar scores 9 (9-9) at 1 min, 10 (10-10) at 5 min and 10 (10-10) at 10 min. 35 neonates (44%) were male. All 80 neonates were delivered by caesarean section and underwent uncomplicated neonatal transition; none of them needed medical or respiratory support. 76 mothers received local anaesthesia, shortly before caesarean section and four mothers received general anaesthesia. After completion of study protocol all neonates were returned to their parents for kangaroo care. All infants received cord clamping within 30 s.

4.1. Arterial oxygen saturation, heart rate, blood pressure, and cerebral tissue oxygenation index (cTOI)

Arterial oxygen saturation was 95 (4) %, heart rate 154 (13) bpm, systolic blood pressure 64 (1) mm Hg, diastolic blood pressure 33 (1) mm Hg and mean blood pressure 43 (1) mm Hg 15 min after birth. Cerebral tissue oxygenation index (cTOI) was 74.1 (1.4) %.

4.2. DA and FO

73 neonates showed predominantly left-to-right shunt via DA with a mean diameter of 2.3 (0.4) mm. Seven neonates had bidirectional flow via DA. 60 neonates showed left-to-right shunt via FO with a mean diameter of 2.5 (0.3) mm.

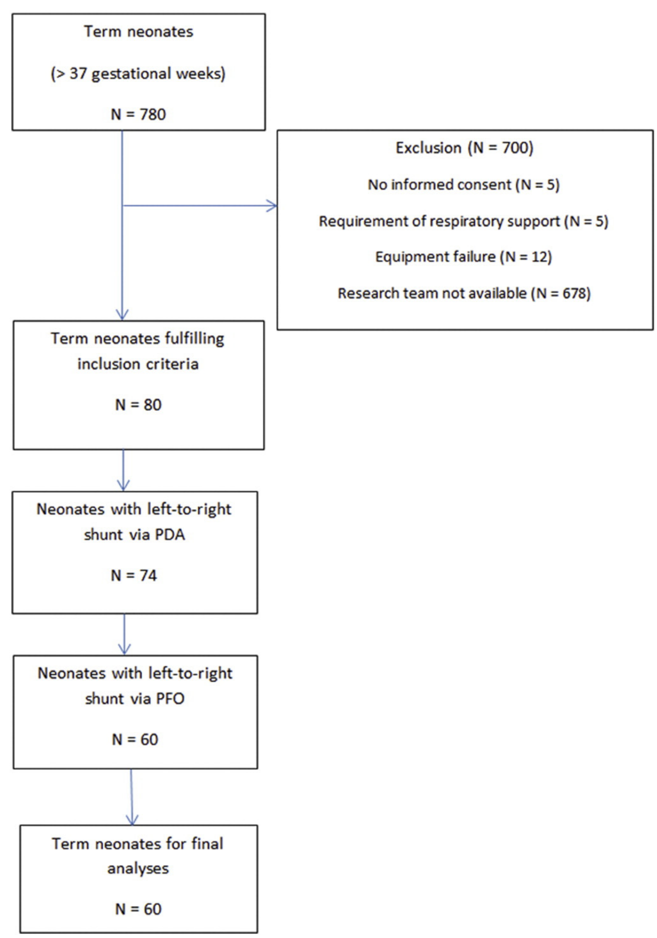

Fig. 1. Flow diagram showing the number of included neonates and rationales for exclusion.