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PARALLEL SESSION 28 - CIRCULATION 3

ID 303. REPRODUCIBILITY OF THE EL-KHUFFASH PDA SEVERITY SCORE AND PDA DIAMETER MEASUREMENTS IN EXTREMELY PRETERM INFANTS

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Introduction

Almost all randomised controlled trials use a Patent Ductus Arteriosus (PDA) diameter ≥ 1.5 mm as the primary criterion to ascribe haemodynamic significance to the PDA despite strong evidence that PDA diameter in isolation is a very poor predictor of adverse outcome in preterm infants. Our group have developed a PDA Severity Score (PDA_{sc}). We hypothesised that the calculation of the PDA_{sc} possesses superior intra- and inter-rater reproducibility when compared with the measurement of PDA diameter alone.

Methods

This cross sectional study assessed echocardiograms performed on infants < 30 weeks gestation at 36 to 72 hours of age between July 2020 and December 2022 to calculate the PDA_{sc}. Intra-observer reproducibility of the PDA_{sc} were assessed by blinded repeated measurements performed by one investigator (AS) 4 weeks apart. One set of those measurements was compared with blinded measurements by another investigator (RM) to assess inter-rater reliability.

Results

Echocardiograms from one 150 infants were examined. Their mean \pm SD gestation and birthweights were 26.5 ± 1.7 weeks and 903 ± 249 grams respectively. The PDA_{sc} has superior intra- and inter-reproducibility values when compared with PDA diameter measurements alone, with near perfect agreement values as demonstrated by a low bias and LOA, ICC values > 0.98 and COV values $< 1.5\%$ (Table 1). PDA diameter and LVO measurements demonstrated the poorest reproducibility values. The PDA_{sc} demonstrated near perfect agreement both within raters (Cohen's Kappa 0.97, $p < 0.01$) and between raters (Cohen's Kappa 0.94, $p < 0.01$) with regards to the threshold for treatment (a cut off ≥ 5.0). The PDA diameter threshold only demonstrated moderate agreement within raters (Kappa 0.57, $p < 0.01$) and between raters (Kappa 0.54, $p < 0.01$). In this cohort, 31% of infants with a low risk PDA_{sc} (< 5.0) also had a PDA diameter greater than 1.5mm.

Conclusion

In this study, we demonstrated excellent intra- and inter-rater reproducibility of the EL-Khuffash PDA Severity Score. Conversely, measurement of the PDA diameter illustrated much poorer intra- and inter-rater agreement. Future RCTs for PDA treatment should strongly consider abandoning the use of PDA diameter in isolation as a criterion for recruitment into clinical trials.

Table 1: Reproducibility analysis of the echocardiography parameters.

	Intra-Rater Reproducibility			Inter-Rater Reproducibility		
	Bias (95% LOA)	ICC (95% CI)	COV (%)	Bias (95% LOA)	ICC (95% CI)	COV (%)
PDA Score	0.1 (-0.9 - 1.0)	0.99 (0.98 - 0.99)	1.4%	0.0 (-1.1 - 1.2)	0.98 (0.97 - 0.98)	0.8%
PDA Diameter	0.1 (-0.7 - 0.9)	0.85 (0.80 - 0.89)	3.0%	0.1 (-0.9 - 1.2)	0.76 (0.67 - 0.83)	5.4%
PDA Max Velocity	0.0 (-0.4 - 0.5)	0.94 (0.92 - 0.96)	2.1%	0.0 (-0.5 - 0.5)	0.93 (0.91 - 0.95)	1.0%
LVO	3 (-46 - 52)	0.92 (0.89 - 0.94)	1.5%	-17 (-102 - 68)	0.76 (0.64 - 0.84)	8.4%
LV a'	-0.1 (-1.0 - 0.9)	0.94 (0.92 - 0.96)	1.6%	-0.2 (-1.5 - 1.1)	0.90 (0.86 - 0.93)	4.0%

LOA: Limits of agreement; ICC: Intraclass correlation coefficient; COV: Coefficient of variation; PDA: Patent Ductus arteriosus; LVO: Left ventricular output.



Table 1: Reproducibility analysis of the echocardiography parameters

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None declared



ID 446. Effects of a patent ductus arteriosus on intestinal mucus barrier in preterm newborns

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Background.

In contrast with term infants, preterm newborns have less mesenteric blood flow reserve. Their diminished reserve may increase their risk for developing intestinal ischemia when alterations in intestinal blood flow occur. Patent ductus arteriosus (PDA) has a profound impact on mesenteric perfusion. Objective is evaluation the effects of PDA on intestinal mucosal defense ability in preterm infants.

Methods.

Preterm neonates (gestational age 29–33 weeks) who were admitted to the NICU of the Pediatric Institute by name K. Faradjeva were included in this prospective observational study and were divided into two groups: the first group consisted of 20 infants with PDA and the second group consisted of 51 infants without PDA. Intestinal trefoil factor (ITF) and Mucin 2 (MUC 2) were chosen as a marker of mucosal restitution and repair. Serum ITF and MUC 2 were quantified by ELISA on 1–3 day of life (DOL). Results were compared by Mann–Whitney test.

Results.

Compared with 2–nd group, the neonates with PDA had lower levels of ITF and MUC–2 (ITF – 15.0±3.3 ng/ml, MUC 2 – 12.59±1.79 ng/ml – in the first group and 35.8±4.9 ng/ml, 14.92±1.239 ng/ml respectively – in the second group). These differences were significant only relation to ITF (p<0.05)



Conclusion.

The low level of ITF in preterm infants with PDA may reduce compensatory protective mechanisms of mucus layer and predispose them to intestinal pathology.

None declared



ID 792. THE ROLE OF CEREBRAL, RENAL, AND ABDOMINAL NIRS TO DETECT SIGNIFICANT PATENT DUCTUS ARTERIOSUS IN VERY PRETERM INFANTS : A PILOT STUDY

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Background: Hemodynamically significant patent ductus arteriosus (hsPDA) is characterized with systemic hypoperfusion and pulmonary overcirculation. Systemic hypoperfusion with subsequent decrease of tissue oxygenation can be detected using near-infrared spectroscopy (NIRS) applied at cerebral, renal, and abdominal area. The aim of this study is to evaluate the use of regional saturation (cerebral/CrSO₂, renal/RrSO₂, and abdominal/SrSO₂) to detect hsPDA in very preterm infants.

Methods: Forty-one very preterm infants (birth weight <1500 gr and gestational age <32 weeks) were monitored continuously with cerebral, renal, and abdominal NIRS immediately after birth until ductus arteriosus was closed. All infants were prospectively evaluated using echocardiography to detect hsPDA within 24-hour after birth daily during NIRS application. Echocardiography criteria to diagnose hsPDA were the following : 1). ductal diameter \geq 1.5 mm, 2). La:Ao ratio \geq 1.5, 3). LPA diastolic velocity > 0.2 m/s and 4). Absent or retrograde diastolic flow at superior mesenteric artery (SMA), anterior cerebral artery (ACA), or renal artery. Mean value of regional NIRS during its application were compared between hsPDA and no-hsPDA group.

Results: Of 41 infants, there were 11 infants with hsPDA and 30 with no hsPDA. A lower mean (\pm SD) of CrSO₂ was detected in hsPDA group (65 ± 8.1) than in no hsPDA group (75 ± 6.3) ($p < 0.001$). The median (IQR) of RrSO₂ was lower in hsPDA group (60.4 (54;76) than in no hsPDA group 83.5 (77;82) ($p < 0.001$). Abdominal regional saturation were also lower in hsPDA group with median of 30 (22;38) vs 37.5 (30;54) in no hsPDA group ($p = 0.032$).

Conclusion: Lower cerebral, renal, and abdominal regional saturations were associated with the presence of hsPDA in preterm infants.

Variable	No-hsPDA (n=30)	hsPDA (n=11)	p
Gestational Age(weeks), median (IQR)	29.5 (26;30)	29 (28;30)	0.76
Birth Weight (gram), median (IQR)	1010 (772;1291)	1100 (750;1170)	0.54
Male (%)	14 (73.7)	5 (26.3)	0.95
Apgar 1 – min, median (IQR)	4 (3;6)	5(4;6)	0.26
Apgar 5-min, median (IQR)	6 (5;7)	7 (5;7)	0.63
Age of Diagnosis PDA (hours), median (IQR)		48 (24;72)	
Full Cover antenatal steroid (%)	8 (80)	2 (20)	0.77
Caesarean section (%)	23 (71.9)	9 (28.1)	0.54
IUGR (%)	9 (69.2)	4 (30.8)	0.49
UTI (%)	11 (78.6)	3 (21.4)	0.43
Surfactant (%)	26 (76.5)	8 (23.5)	0.27
Mechanical Ventilation (%)	23 (79.3)	6 (20.7)	0.16

Baseline Characteristics

Baseline Characteristics

None declared

ID 587. The Effect of Antenatal Magnesium Sulphate Exposure on Patent Ductus Arteriosus in Premature Infants

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Background: Magnesium sulphate (MgSO₄) has been shown to be effective for neuroprotection of the fetus. Extracellular magnesium causes ductus arteriosus closure to be delayed. There is conflicting evidence from studies regarding the relationship between antenatal MgSO₄ administration and patent ductus arteriosus (PDA). This study aims to evaluate the association between antenatal MgSO₄ exposure and PDA.

Methods: Preterm infants born between 240/7 and 316/7 weeks were included. Infants who died during the first 72 hours of life and had significant congenital abnormalities were excluded. Echocardiographic and clinical evaluations were used to define PDA and hemodynamically significant PDA (hsPDA). The treatments were planned in accordance with the unit's standard protocols.

Results: The study included 300 preterm infants, 32.6% (n=98) of whom were exposed to antenatal MgSO₄. The gestational age (GA) and the birth weight (BW) of infants were lower (p=0.012, and p<0.001, respectively) and the exposure to antenatal steroids was higher in the MgSO₄ group (p=0.039). While hsPDA rates were pretending to be higher in the infants who exposed antenatal MgSO₄ (OR:2.034, 95% CI: 1.161–3.564, p=0.012), with adjustment for antenatal steroid administration, GA, and BW; hsPDA incidences were found to be similar (OR:1.6, 95% CI: 0.849–3.118, p=0.146). The rates of PDA ligation and open PDA at discharge were similar between groups. A cumulative MgSO₄ dose of greater than 20 g was associated with an increased risk of hsPDA (crude OR:2.476, 95% CI: 0.893–6.864, p=0.076; adjusted OR:3.829, 95% CI: 1.068–13.728, p=0.039). However, the cumulative dose had no impact on the ligation rates or open PDA at discharge. The rates of prematurity-related morbidities and mortality were similar.

Conclusion: This study showed that antenatal MgSO₄ exposure increased the incidence of hsPDA but had no effect on the rates of PDA ligation or open PDA at discharge. Based on the results, antenatal MgSO₄ administration with an established neuroprotective effect should not be regarded with concern.

	Exposed to MgSO ₄ (n=98) n (%)	Not exposed to MgSO ₄ (n=202) n (%)	Crude OR (95%CI)	P	Adjusted OR* (95%CI)	P
Any PDA (at first ECHO)	49 (50)	96 (47.5)	1.104 (0.681-1.789)	0.687	0.778 (0.443-1.369)	0.384
Moderate to large PDA (at first ECHO)	39 (39.8)	69 (34.2)	1.274 (0.774-2.097)	0.340	0.863 (0.480-1.550)	0.621
Medical treatment (hsPDA)	30 (30.6)	36 (17.8)	2.034 (1.161-3.564)	0.012	1.600 (0.849-3.018)	0.146
PDA ligation ^a	6/49 (12.2)	14/96 (14.6)	0.714 (0.250-2.040)	0.699	0.370 (0.115-1.197)	0.097
PDA on discharge ^b	13 (15.1)	17 (9.7)	1.666 (0.769-3.610)	0.193	1.206 (0.517-2.812)	0.664
Subgroup analysis for GA < 28 weeks						
Any PDA (at first ECHO)	31 (81.6)	42 (75)	1.476 (0.533-1.476)	0.452	1.229 (0.418-3.613)	0.708
Moderate to large PDA (at first ECHO)	28 (73.7)	35 (62.5)	1.680 (0.682-4.141)	0.258	1.368 (0.524-3.572)	0.522
Medical treatment (hsPDA)	23 (60.5)	20 (35.7)	2.760 (1.180-6.455)	0.018	2.763 (1.148-6.653)	0.023
PDA ligation ^a	6/28 (21.4)	12/35 (34.3)	0.523 (0.167-1.636)	0.262	0.457 (0.139-1.502)	0.197
PDA on discharge ^b	7/26 (26.9)	11/37 (29.7)	0.871 (0.285-2.661)	0.808	0.642 (0.197-2.097)	0.463

*Adjustments for Antenatal steroids exposure, gestational age and birth weight, in the subgroup analysis for antenatal steroid exposure and birth weight

^aOnly the patients who have moderate-large PDA(at first ECHO) were included.

^bPatients who died before discharge or required PDA ligation were excluded.

Only one patient whose gestational age <28 w, required transcatheter PDA closure procedure after discharge in antenatal MgSO₄ group. No patient whose gestational age <28 w, required transcatheter PDA closure procedure after discharge in the other group.

ECHO: echocardiography

Comparison of PDA between groups

Comparison of PDA between groups

None declared.