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Abstracts

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ABS 1

EVALUATION OF THE RELATIONSHIP BETWEEN PATENT DUCTUS ARTERIOSUS AND THE PLATELET MASS INDEX IN PRETERM INFANTS

M. Kara[1], İ. Caner[2], K.Ş. Tekgündüz[1], İ. Polat[1], H. Keskin[1]

[1]Department of Pediatrics, Ataturk University Faculty of Medicine, Erzurum, Turkey

[2]Department of Pediatrics, Sakarya University Faculty of Medicine, Sakarya, Turkey

INTRODUCTION

Patent ductus arteriosus (PDA) is a significant cause of mortality and morbidity in preterm newborns. Some studies showed that hemodynamically significant PDA (hsPDA) is associated with low platelet count and predicted a high failure in the closure of DA after indomethacin treatment Opposite results are also reported in the literature. The inverse relationship between platelet size and platelet count in humans has prompted the development of platelet mass concept. Platelet mass has been proposed as a better predictor of production/regulation. Herein, we aimed to determine whether there is an association between platelet mass index (PMI) and PDA frequency in preterm newborns.

METHODS

Premature infants (≤ 32 gw) with PDA (n = 251) and a control group without PDA (n = 212) hospitalized in the neonatal intensive care unit (NICU) in 2010-2016 were evaluated. Patients with PDA were assessed for presence of hsPDA in the second days of life based on clinical follow up and echocardiographic findings. Infants with hsPDA were started on ibuprofen, and echocardiography was repeated after 72 h to assess closure of the ductus. Patients with hsPDA were next divided into two groups, those in which the ductus closed with medical treatment and those not responding to treatment and undergoing surgical ligation. PMI, platelet counts and indices including mean platelet volume (MPV) and platelet distribution width (PDW) of the infants in both groups were recorded.

RESULTS

Gestational age and birth weight were statistically lower in the group with PDA ($p < 0.0001$). Mean birth weights of cases with or without hsPDA differed significantly ($p = 0.035$) and were lower in the group with hsPDA. Platelet mass index, thrombocyte count, MPV and PDW had no effect on prevalence of PDA. There was no significant difference between the groups with and without hsPDA in terms of mean PMI, mean platelet count, MPV or PDW. PMI was higher significantly in the group, which the ductus did not close after ibuprofen therapy ($p = 0.028$) (**Tab. 1**).

CONCLUSIONS

PDA was not correlated with PMI, platelet counts, MPV and PDW. Interestingly PMI was higher in the group in which PDA did not close after ibuprofen therapy. It can be due to an inflammation that causes failure of medical closure treatment, since inflammation can increase platelet counts and PMI. We think that more randomized controlled studies are needed in this regard.

ABS 2

DIAGNOSIS OF DIGEORGE SYNDROME: THE CONTRIBUTION OF MOLECULAR GENETICS

Y. Halleb[1], H. Hadj-Abdallah[1], S. Nouri[2], A. Touati[1], M. Bellallah[2], J. Mathlouthi[2], N. Mahdhaoui[2], H. Sboui[2], A. Saad[1], D. H'mida[1]

Table 1 (ABS 1). Comparison of platelet mass index (PMI) and platelet counts according to groups.

Patient groups	PMI	p	Platelet count	p
Premature infants with PDA (n = 251)	1,684,806.77	0.127	210,051	0.081
Control group (n = 212)	1,749,046.70		222,716	
Mean of hsPDA group (n = 216)	1,698,047.69	0.212	211,657	0.274
Mean of without hsPDA group (n = 35)	1,603,091.43		200,142	
Medical closure group (n = 184)	1,645,892.93	0.028*	207,125	0.087
Failure of medical treatment group (n = 32)	1,997,937.50		237,718	

PMI: platelet mass index; PDA: Patent ductus arteriosus; hsPDA: hemodynamically significant PDA.

[1]Department of Cytogenetics, Molecular Genetics and Reproductive Biology, Farhat Hached Hospital, Sousse, Tunisia
[2]Department of Neonatology, Farhat Hachad Hospital, Sousse, Tunisia

INTRODUCTION
DiGeorge syndrome (DGS) is the most common microdeletion syndrome with an incidence of 1-4/6,000 births per year. Clinically the DGS is marked by a very heterogeneous clinical picture. Congenital heart disease is observed in 74% of cases. Cardiac involvement is more or less associated with thymic agenesis, hypocalcemia by parathyroid agenesis or hypoplasia, palatal malformations, malformative uropathy and facial dysmorphism. The genetic abnormality involved is a deletion 22q11.2, which extends in 90% of cases on 3 Mb and 1.5 Mb in 7 to 8% of the cases. Smaller deletions called nested deletions and point mutations of the TBX1 gene are also incriminated in DGS.
METHODS
The present work focuses on three suspected DGS patients addressed to the Molecular Genetics Unit of the Department of Cytogenetics, Molecular Genetics and Reproductive Biology of the Farhat HACHED University Hospital in Sousse during the years 2015 and 2016. Among the 3 newborns analyzed, 2 had heart disease associated with hypocalcemia in one patient and facial dysmorphism with cleft palate in the other. The third patient presented himself with facial dysmorphism and hypocalcaemia. All three patients underwent Multiplex Ligation-Dependent Probe Amplification (MLPA) analysis using the Holland P064 MRC set. It is a technique that allows the simultaneous detection of variation in the number of copies of several specific sequences of the genome. This new technique offers the possibility to diagnose 16 microdeletion syndromes with more than 40 probes including 7 probes specific to the DGS.
RESULTS
MLPA has shown in our 3 patients a deletion of the 7 probes specific to the DGS thus confirming the deletion 22q11.2 and therefore the DGS. In addition to being an alternative to the cytogenetic diagnosis of DGS, MLPA currently represents the reference technique in the diagnosis of all microdeletion syndromes including DGS. Indeed, the analysis by MLPA makes it possible to demonstrate the typical deletions of DGS, but also the nested small-sized deletions, which can be at the origin of a signal asymmetry in FISH, and therefore often underdiagnosed. Moreover, the MLPA has the advantage of being a simple and rapid technique to be carried out, of low cost, which requires only a small amount of DNA without prior cell culture. In the case where the DGS is discarded by the MLPA, this MLPA set allows to detect 15 other microdeletion syndromes, which can constitute differential diagnosis of the DGS such as the syndrome of Alagille. However, cytogenetic techniques retain ample space once the deletion is confirmed. Indeed, the DGS, sporadic in 80% of cases, can be inherited in 20% of the cases of one of the parents who could in this case be carrying a balanced cytogenetic anomaly not detected by the MLPA. Genetic counseling and especially the risk of recurrence can only be assessed after karyotype analysis of the parents.
CONCLUSIONS
Our study emphasizes the importance of molecular analysis by MLPA in confirming the diagnosis of DGS. Due to its reliability, speed and availability, the MLPA is the gold standard diagnostic for any clinical suspicion of the DGS. Indeed, this molecular analysis must be indicated in the presence of any suspicion of DGS as well as other microdeletion syndromes.

ABS 3

ASSOCIATION BETWEEN SIZE OF PATENT DUCTUS ARTERIOSUS AND CO-MORBIDITIES

S. Bellis[1], Y. Singh[2]

[1]Clinical School of Medicine, University of Cambridge, UK
[2]Neonatology and Paediatric Cardiology, Cambridge University Hospitals, UK

INTRODUCTION
Patent ductus arteriosus is associated with increased mortality and significant co-morbidities including increased incidence of intraventricular haemorrhage (IVH), acute pulmonary haemorrhage, bronchopulmonary dysplasia (BPD) and necrotising enterocolitis (NEC). However, there is no consensus on the management of PDA in preterm infants. The aims and objectives from our service evaluation project were: 1) To study the association between size of PDA and co-morbidities in our cohort; 2) To understand what proportion of PDAs need medical treatment or intervention.
METHODS
A retrospective observational study involved all infants diagnosed with a PDA in a single centre at the Rosie hospital Cambridge between 01/01/2012

to 31/12/2016. Duct dependent congenital heart conditions needing prostaglandin were excluded.

RESULTS

366 cases met the criteria of having a diagnosed PDA, or a post-operative PDA ligation. The median gestation was 26 weeks (range: 23-41 weeks). Of these, 221 of these were large, 74 were moderate, 67 were small and 4 could not be grouped. There was a strong association between the size of the PDA and co-morbidities such as IVH, BPD, NEC and acute pulmonary haemorrhage. Between 12-62% (range depending on the co-morbidity) of infants with large PDA had such co-morbidities as compared to 5-31% in small or moderate sized PDA. Of the 221 large PDAs, 123/221 (56%) needed medical or surgical treatment while only 13/141 (9%) of small or moderate sized PDAs needed medical or surgical treatment. All infants needing intervention for PDA were under 28 weeks of gestation.

CONCLUSIONS

Persistent PDA is more common in ELBW infants and is directly related to lower gestational age. In our cohort, an haemodynamically significant large PDA had a stronger association with co-morbidities than a small or moderate sized PDA. Around half of the large PDAs on echocardiography were treated with NSAIDs and all infants needing treatment were under 28 weeks of gestation.

ABS 4

EFFICACY OF MEDICAL TREATMENT IN CLOSING PATENT DUCTUS ARTERIOSUS IN ELBW INFANTS

S. Bellis[1], Y. Singh[2]

[1]Clinical School of Medicine, University of Cambridge, UK

[2]Neonatology and Paediatric Cardiology, Cambridge University Hospitals, UK

INTRODUCTION

Non-steroidal anti-inflammatory drugs (NSAIDs) remain the mainstay for the medical treatment of PDA. The published studies report different efficacy of NSAIDs in closure of PDA and they report different success rate at different gestational ages. The aims and objectives from our service evaluation project were: 1) To study the efficacy of NSAIDs treatment (ibuprofen and indomethacin) in closure of PDA; 2) To find out the success rate at different gestational ages with use of ibuprofen in ELBW infants.

METHODS

A retrospective observational study involved all the ELBW less than 28 weeks of gestation and diagnosed with a PDA in a single centre at the Rosie hospital Cambridge between 01/01/2012 to 31/12/2016. Duct dependent congenital heart conditions needing prostaglandin were excluded.

RESULTS

252 cases met the criteria of having a diagnosed PDA, or a post-operative PDA ligation. The median gestation was 25 weeks (range: 23-28 weeks). 83 infants were treated with ibuprofen and PDA was successfully closed in 50 cases (60% efficacy in closing PDA). Of the 23 infants treated with indomethacin, 15 (65%) had successful closure of PDA. There was no statistical significant difference in successful closure rate at different gestations after use of ibuprofen. The success rate ranged between 50-75%. About a quarter of infants (21 of the 83 infants) needed two courses of ibuprofen whilst 12 infants had PDA ligation.

CONCLUSIONS

Persistent PDA is more common in ELBW infants. In our cohort, around half of the large PDAs on echocardiography were treated with NSAIDs with an efficacy of 60-65% (as reported in the literature). There was no statistically significant difference in the closure of PDA after use of ibuprofen at different gestational ages.

ABS 5

ACETAMINOPHEN FOR CLOSING PDA. SHOULD IT BE A FIRST LINE THERAPEUTIC OPTION?

I. Tofé, M.D. Ruiz, M.P. Jaraba, M.V. Rodriguez, R.L. Rueda, M.D. Ordoñez, M.J. Parraga

Reina Sofia University Hospital, Cordoba, Spain

INTRODUCTION

Patent ductus arteriosus (PDA) is associated with co-morbidities among preterm leading to increased shunting of blood into the pulmonary circulation and potentially compromising circulation to systemic organs, sometimes leading to pulmonary haemorrhage and death. A large number of reports on the management of PDA have been published but still there is no consensus on which PDA should be treated and how best to treat. Paracetamol acts mainly by inhibiting peroxidase enzyme activity. Lesser cost and wider margin of safety have

Table 1 (ABS 5). Clinical characteristics of the study population.

	GA (w)	Gender	Birth weight (g)	Antenatal steroids	SO_4Mg prenatal	Age treatment/ days of treatment	Primary reason use paracetamol	Main outcome	Adverse events	Surgical ligation
1	28	M	716	1	+	**7/4**	thrombocytopenia, bleeding	no closed	no	+
2	29	M	1,000	1	-	**4/6**	bleeding	closed	no	-
3	25	F	560	1	+	**4/6; 7/6**	fail ibuprofen, IVH	no closed (2 courses)	no	+
4	29	F	1,120	1	+	**2/3**	IVH	closed	no	-
5	27	F	930	partial	unknown	**2/3; 16/3**	IVH	closed (2 courses)	no	-
6	31	M	1,860	0	-	**3/2**	thrombocytopenia, coagulopathy	closed	AST↑ ALT↑	-
7	32	F	1,495	1	-	**5/3**	thrombocytopenia, pulmonary hemorrhage	closed	AST↑	-
8	28	F	1,060	1	+	**35/6**	thrombocytopenia, IVH	closed	no	-
9	26	F	731	1	+	**3/3**	thrombocytopenia,	closed	no	-

become a potential first line therapeutic option for ductal closure.

METHODS

To describe our experience with endovenous paracetamol at a dose of 15 mg/kg/day for closing PDA in a case series of 9 preterm babies who either had contraindications with indomethacin or ibuprofen for closing PDA. To know the safety and efficacy.

RESULTS

29 preterm babies were diagnosed of significant PDA with reverse diastolic flow in a 2 year period in neonatal intensive care unit from December 2014 to January 2017. 3 had a spontaneous closure (10.3%), 11 received ibuprofen (with closure in 9; 2 required surgery for PDA ligation). 7 died (4 under ibuprofen treatment, 2 received no treatment and 1 underwent PDA ligation). 9 received endovenous paracetamol, 2 of them required PDA ligation. **Tab. 1** describes main clinical finding among infants who received paracetamol.

CONCLUSIONS

Paracetamol may be effective in the treatment of late PDA and could be an alternative to PDA ligation in patients with a contraindication for ibuprofen. No deaths were described under paracetamol treatment and there were two cases of hypertransaminasemia with spontaneous resolution.

ABS 6

PATENT DUCTUS ARTERIOSUS WITH HEMODYNAMIC REPERCUSSION IN VERY LOW WEIGHT PRETERM INFANTS TREATED WITH ORAL IBUPROFEN PRESENTS A HIGH RATE OF BRONCHOPULMONARY DYSPLASIA

M.M. Lourenço, E. Sacramento, F. Carmona, C. Calixto, F. Martin-Celini, G.H. Seribelli, W.A. Gonçalves-Ferri

Department of Pediatrics, Ribeirão Preto School of Medicine, University of São Paulo, Brazil

INTRODUCTION

Patent ductus arteriosus (PDA) is a common condition in preterm infants, especially in those with very low birth weight. The diagnosis of a hemodynamically significant PDA (HSDA) is challenging and a robust definition is lacking. Echocardiographic documentation of an important left-to-right transductal shunt, with measurable hemodynamically effects, is the basis for identification of a HSDA. The risks and benefits of therapies designed to close the PDA are controversial, and the decision whether or when to treat a PDA remains challenging. Oral ibuprofen seems to be as effective as intravenous ibuprofen. The aim of this study is to evaluate the outcomes of oral ibuprofen treatment in HSDA.

METHODS

This study was a retrospective observational cohort of two groups of very low birth weight (VLBW) infants admitted between 2014 and 2016. 73 patients with PDA that received medical treatment with oral ibuprofen were included. An echocardiographic evaluation (according to the American Society

of Echocardiography recommendations, 1980) was performed within the first 7 days of life and determined the presence and hemodynamic significance of the PDA. The cohort 1 included 35 infants with PDA without echocardiographic signs of hemodynamic repercussion; the cohort 2 included 38 infants with HSDA. We compared the two groups with regard to the mainly outcomes: mortality, time to full enteral feeds, intraventricular hemorrhage, chronic lung disease (CLD), pulmonary hemorrhage and necrotizing enterocolitis.

RESULTS

30% of the 456 VLBW infants admitted were identified having PDA. 79 infants (56%) received oral ibuprofen; 73 of them fulfilled criteria for the study. Cohort 1 included 48% of the infants and cohort 2 included 52%. There was no statistical difference in the mean gestational age, birth weight and SNAPPE-II score between the two groups. 69% of the babies with HSDA developed chronic lung disease, a significantly higher proportion compared to the other group; OR 5.045 (1.5-16.4 CI 95%). There was a statistically significant difference in duration of oxygen therapy; cohort 1 39% vs. cohort 2 58% (p = 0.026). In cohort 2 there was a positive association in days in hospital and in days in mechanical ventilation; HR (CI 95%) = 0.542 (0.306-0.960), p = 0.036 and HR = 0.407 (0.229-0.724), p = 0.002, respectively. The rest of the short-term outcomes remained similar between the two groups (**Tab. 1**).

CONCLUSIONS

We concluded that, regardless of treatment with oral ibuprofen, exposure to a hemodynamically significant PDA is associated with a higher rate of CLD and a higher duration of oxygen therapy. Future randomized controlled trials are warranted.

ABS 7

EFFECTIVENESS OF INDOMETHACIN, IBUPROFEN AND PARACETAMOL FOR PATENT DUCTUS ARTERIOSUS (PDA) IN PRETERM INFANTS: A NETWORK META-ANALYSIS

S. Mitra[1,2], I.D. Florez[1,3], M.E. Tamayo[3], Y. Zhang[1], B. Sadeghirad[1], A.M. Zea[1,3], L. Mbuagbaw[1], T. Vanniyasingam[1], L. Thabane[1]

[1]Department of Health Research Methods, Evidence, and Impact, McMaster University, Hamilton, Canada

[2]Department of Pediatrics, Dalhousie University, Halifax, Canada

[3]Department of Pediatrics, University of Antioquia, Medellin, Colombia

INTRODUCTION

Different pharmacotherapeutic interventions have shown effectiveness in the management of patent ductus arteriosus (PDA) in preterm infants. However, it is unclear which ones confer advantage over the rest. Objective: To determine the relative effectiveness of all the available interventions for closure of a hemodynamically significant (hs) PDA using Bayesian network meta-analysis.

METHODS

We conducted a systematic review of all randomized controlled trials (RCTs) evaluating intravenous (IV) or oral (PO): indomethacin, ibuprofen and paracetamol compared among them or to placebo

Table 1 (ABS 6). Outcomes of PDA with and without hemodynamic repercussion and oral ibuprofen treatment.

	Mean (n = 73)	Without repercussion (n = 35)	With repercussion PDA (n = 38)	HR/OR (CI 95%)	p-values
Duration in days of oxygen therapy (range)	54 (1-211)	39 (1-211)	58.5 (1-211)	**HR = 0.458** (0.271-0.773)	**p = 0.003**
Days in hospital (range)	106 (42-211)	91 (45-211)	120 (42-211)	**HR = 0.542** (0.306-0.960)	**p = 0.036**
Days in mechanical ventilation (range)	37 (0-201)	15 (0-201)	47 (0-201)	**HR = 0.407** (0.229-0.724)	**p = 0.002**
Days in parenteral nutrition (range)	15 (5-140)	14 (5-111)	16 (5-140)	HR = 0.697 (0.429-1.132)	p = 0.144
Necrotizing enterocolitis (%)	10 (13.7%)	6 (17.1%)	4 (10.5%)	OR = 0.644 (0.160-2.585)	p = 0.534
Chronic lung disease (%)	35 (53.8%)	12 (37.5%)	23 (69.7%)	**OR = 5.045** (1.551-16.412)	**p = 0.007**
Pulmonary hemorrhage (%)	13 (17.8%)	5 (14.3%)	8 (21.1%)	OR = 1.135 (0.270-4.772)	p = 0.863
Severe intraventricular hemorrhage (%)	9 (12.3%)	4 (11.4%)	5 (13.2%)	OR = 1.135 (0.270-4.772)	p = 0.863
Leukomalacia (%)	5 (6.8%)	3 (8.6%)	2 (5.3%)	OR = 0.469 (0.066-3.339)	p = 0.449
Retinopathy of prematurity(%)	13 (18.8%)	7 (21.9%)	6 (15.8%)	OR = 0.790 (0.183-3.416)	p = 0.752
Mortality (%)	9 (12.3%)	3 (8.6%)	6 (15.8%)	OR = 2.127 (0.476-9.505)	p = 0.323
Surgical ligation (%)	20 (27.4%)	6 (17.1%)	14 (36.8%)	-	p = 0.071

HR: Hazard-Ratio; OR: Odds Ratio.

for hs-PDA in preterm infants. Studies evaluating prophylactic pharmacotherapy were excluded. The primary outcome was primary closure of an hs-PDA. Secondary outcomes were need for a second course or surgical closure. We searched Medline, Embase, CENTRAL and grey literature. Two reviewers independently screened studies, extracted information, and assessed the risk of bias. A Bayesian network meta-analysis was performed to combine the pooled direct and indirect estimates for each outcome. The Surface under the Cumulative Ranking (SUCRA) probabilities of being the best to worst interventions was computed. The analysis was performed using the OpenBUGs software (v 3.2.3). The review was registered on PROSPERO international registry of systematic reviews (CRD42015015797).

RESULTS

In total 421 studies were retrieved, and 65 studies (4,397 infants) with 16 different comparisons were included. Indomethacin, ibuprofen and paracetamol were better than placebo to achieve PDA closure. In the ranking the best 3 interventions for achieving closure were PO-high-dose ibuprofen (Prob = 0.93), PO-paracetamol (Prob = 0.76), and IV-high-dose ibuprofen (Prob = 0.75) (**Fig. 1**). Placebo (Prob = 0.008) and IV-regular dose ibuprofen (Prob = 0.29) were ranked the worst interventions for PDA closure compared with the rest. PO-high-dose ibuprofen was also the best intervention for reducing the requirement of second course (Prob = 0.85) or surgical closure (Prob = 0.99).

CONCLUSIONS

Among preterm infants with hs-PDA, oral high dose ibuprofen seems to be the best intervention for achieving PDA closure followed by oral paracetamol and IV high-dose Ibuprofen. The first of its kind Bayesian network meta-analysis may help guide neonatologists and practice guideline developers choose the best pharmacotherapeutic option based on available evidence.

ABS 8

PRENATAL DIAGNOSIS OF THE SYSTEMIC BLOOD FLOW RESTRICTION DEFECTS IMPROVES HEMODYNAMIC STABILITY OF THE NEONATES WITH CONGENITAL CARDIAC DEFECT AT THE ADMITTANCE IN NEONATAL INTENSIVE CARE UNIT

M. Cucerea[1,2], M. Simon[1,2], M. Ungureanu[2], R. Marian[1], E. Moldovan[3], M. Rusneac[2], C. Gliga[2], L. Suciu[1]

[1]University of Medicine and Pharmacy Tîrgu Mureş, Tîrgu Mureş, Romania

[2]County Emergency Hospital Tîrgu Mureş, Regional Neonatal Intensive Care Department, Tîrgu Mureş, Romania

[3]Emergency Institute of Cardiovascular Diseases and Transplant Tîrgu Mureş, Tîrgu Mureş, Romania

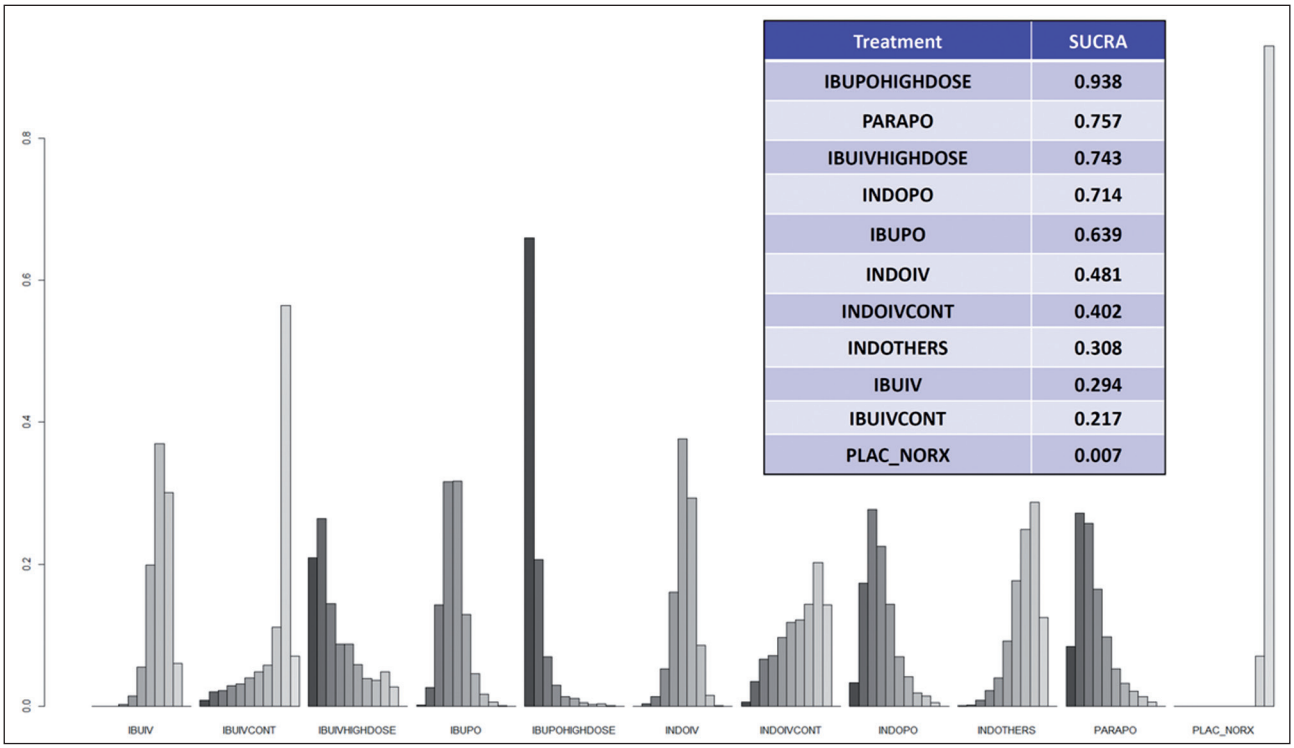

Figure 1 (ABS 7). Ranking the best 3 interventions for achieving patent ductus arteriosus (PDA) in preterm infants.

INTRODUCTION

Aortic stenosis, coarctation of the aorta, interrupted aortic arch and left hypoplastic syndrome are congenital heart diseases with restriction of the systemic blood flow where the systemic circulation is dependent on the patency of ductus arteriosus. The postnatal constriction of the ductus may cause systemic hypoperfusion, severe congestive heart failure and death. Objective: To investigate whether antenatal diagnosis of systemic blood flow restriction defects influence the hemodynamic stability during the preoperative intensive care hospitalization compared with those infants with only postnatal diagnosis.

METHODS

Retrospective review of all cases (n = 39) of coarctation of the aorta, interrupted aortic arch and left hypoplastic syndrome between January 2014 to December 2016 for all neonates who had been born in or transferred to the Neonatal Intensive Care Unit of the tertiary level academic Hospital Tirgu Mureş, for inclusion in our study. Variables of illness severity scores (SNAP-II and CRIB-II) were recorded, the presence/absence of femoral pulses, pre/postductal mean blood pressure and oxygen saturations, respiratory distress, urinary output, pO_2/FiO_2 ratio, necessity of respiratory support and prostaglandin (PGE1) treatment for maintenance of ductal patency. A univariate and multivariate analysis was conducted an all variables.

RESULTS

Both SNAP-II and CRIB-II score were lower in the antenatal diagnosed group compared to postnatal diagnosed group ($p < 0.05$). The need of respiratory support was lower for those neonates included in antenatal diagnosed group (OR 0. 19, 95% CI 0.04 to 0.85), and increased doses of PGE1 for maintaining ductal patency were used in neonates with postnatal diagnosed disease: mean initial dose of PGE1 0.047 µg/kg/minute (SD 0.02), mean minimal dose of PGE1 0.03 µg/kg/minute (SD 0.02) and mean maximum dose of PGE1 0.077 µg/kg/minute (SD 0.03) compared to 0.026 µg/kg/minute (SD 0.01), 0.014 µg/kg/minute (SD 0.01) and 0.034 µg/kg/minute (SD 0.02).

CONCLUSIONS

Antenatal diagnosis of the systemic blood flow restriction defects is associated with lower severity illness scores at admittance into Neonatal Intensive Care Unit and with improved quality of care during preoperative hospitalization.

ABS 9

ASSOCIATION BETWEEN ASYMPTOMATIC PATENT DUCTUS ARTERIOSUS BEYOND THE EARLY POSTNATAL PERIOD AND 3-YEAR NEUROLOGICAL OUTCOME

K. Inomata, S. Taniguchi, T. Inoue, A. Kawase, Y. Kondo

Department of Neonatology, Perinatal Center, Kumamoto City Hospital, Kumamoto, Japan

INTRODUCTION

A hemodynamically significant patent ductus arteriosus (hsPDA) causes various complications such as left ventricular insufficiency, pulmonary hemorrhage, bronchopulmonary dysplasia (BPD), renal failure, necrotizing enterocolitis (NEC), periventricular leukomalacia (PVL), and intraventricular hemorrhage (IVH). Some infants are noted to have a non-hemodynamically significant PDA, asymptomatic PDA (asPDA) beyond the first week of life. In extremely premature infant, it is not clear whether asPDA beyond the first week of life influences their neurological and respiratory outcomes in later life. The objective of this study was to determine the relationship between asPDA beyond the first week of life and short- and long-term respiratory and neurological outcomes.

METHODS

We performed a retrospective study between January 2008 and May 2013 involving infants born at < 28 weeks' gestation who were admitted to the neonatal intensive care unit (NICU) of Kumamoto City Hospital, a tertiary perinatal center in Japan. Infants were classified into 3 groups, the asPDA group, the hsPDA group and the closed DA group, between day 7 and 13. Presence of a left-to-right shunt of the DA demonstrated on echocardiography and more than two symptoms was defined as hsPDA, while asPDA was defined as non-hemodynamically significant PDA, with no or one symptom. Primary outcome was death or neurodevelopmental impairment (NDI) at 3 years of age. Secondary outcomes were a short-term respiratory outcome (death or severe BPD) and long-term respiratory outcome (home oxygen therapy, home mechanical ventilation or tracheostomy at 3 years of age).

RESULTS

Twenty-four infants were included in the asPDA group, eight in the hsPDA group and 104 in the closed DA closed group. Gestational age and birth

Table 1 (ABS 9). Short- and long-term outcomes in the 3 different groups.

	asPDA	hsPDA	closed DA
Short-term outcome			
Death or severe BPD	14/24 (58)[a]	4/8 (50)	37/104 (36)[a]
Long-term outcome			
Death or NDI	6/22 (27)	5/7 (71)	25/97 (26)
NDI	5/22 (23)	2/7 (29)	18/97 (19)
Any respiratory suupport at 3 years of age	0/21 (0)	0/4 (0)	4/90 (4)

Data are presented as n (%).
[a]asPDA vs. closed DA, $p < 0.05$.
asPDA: asymptomatic PDA; hsPDA: hemodynamically significant patent ductus arteriosus; BPD: bronchopulmonary dysplasia; NDI: neurodevelopmental impairment.

weight did not significantly differ between the two groups (24.9 ± 1.7 vs. 24.4 ± 1.3 vs. 25.5 ± 1.5 weeks and 711 ± 195 vs. 693 ± 101 vs. 758 ± 178 g), respectively. Frequency of death or NDI was 6/22 infants (27%) in the asPDA group, 5/7 infants (71%) in the hsPDA group and 25/97 infants (26%) in the closed DA group. No significant difference was observed in each group. Frequency of death or severe BPD in asPDA group was significantly higher than that in the closed DA group (14/24, 58% vs. 37/104, 36%, respectively; $p = 0.04$). There was no significant difference between the groups in terms of the requirement for any respiratory support at 3 years of age. Results are presented in **Tab. 1**.

CONCLUSIONS

Although asPDA beyond the first week of life affected the deterioration of short-term respiratory outcome, it did not influence 3-year respiratory and neurological outcomes.

ABS 10

THE USE OF SPECKLE TRACKING ECHOCARDIOGRAPHY TO ASSESS MYOCARDIAL PERFORMANCE IN MONOCHORIONIC DIAMNIOTIC TWINS WITH AND WITHOUT TWIN TO TWIN TRANSFUSION SYNDROME

C.R. Breatnach[1], A.T. James[1], F. Malone[2], N. McCallion[1,3], O. Franklin[4], A. EL-Khuffash[1,3]

[1]Department of Neonatology, The Rotunda Hospital, Dublin, Ireland

[2]Department of Obstetrics and Gynecology, Royal College of Surgeons in Ireland, Dublin, Ireland

[3]Department of Pediatrics, Royal College of Surgeons in Ireland, Dublin, Ireland

[4]Department of Pediatric Cardiology, Our Lady's Children's Hospital, Crumlin, Dublin, Ireland

INTRODUCTION

Data on myocardial performance in monochorionic diamniotic (MCDA) twins during the early neonatal period is lacking. These infants are at risk of developing twin to twin transfusion syndrome (TTTS) and exhibit myocardial dysfunction during fetal life. Selective laser photocoagulation of communicating vessels (SLPCV) may arrest this condition. We hypothesise that infants exposed to TTTS would exhibit lower values for strain and strain rate measured using speckle tracking echocardiography (STE) during the early neonatal period. We aimed to assess myocardial performance using STE in donors and recipients of MCDA twins with TTTS and compare them with a cohort of uncomplicated MCDA twins and those with selective intrauterine growth restriction (IUGR).

METHODS

We performed a prospective observational study of 4 twin groups: Uncomplicated MCDA twins, MCDA twins with selective IUGR, MCDA twins with TTTS in receipt of SLPCV (TTTS & LASER) and MCDA twins with TTTS who did not receive SLPCV (TTTS no LASER). Serial echocardiography was performed on day one, day two and between days 5-7 of life. Assessment of myocardial performance included the use of STE to measure left (LV) and right (RV) longitudinal strain and systolic strain rate. The twin pairs were then divided by weight into a smaller (or donor) and bigger (or recipient) set and a comparison of functional parameters was made between the groups.

RESULTS

Forty-seven twin pairs were enrolled in the study: 21 sets of uncomplicated MCDA twins; 14 had selective IUGR; 6 TTTS no LASER, and 6 were TTTS & LASER. The gestational age and birth

weights were lower in the selective IUGR pairs (31.6 weeks) and the TTTS no LASER pairs (29.3 weeks) when compared with Uncomplicated (35.9 weeks) and TTTS & LASER (34.0 weeks) pairs (p = 0.03). Recipient TTTS no LASER infants had lower LV and RV strain, which persisted throughout the first week (**Fig. 1**). Function measurements in the Donor twins of all 4 groups were comparable, and in the TTTS no LASER group, significantly higher than the recipient counterparts (**Fig. 1**).

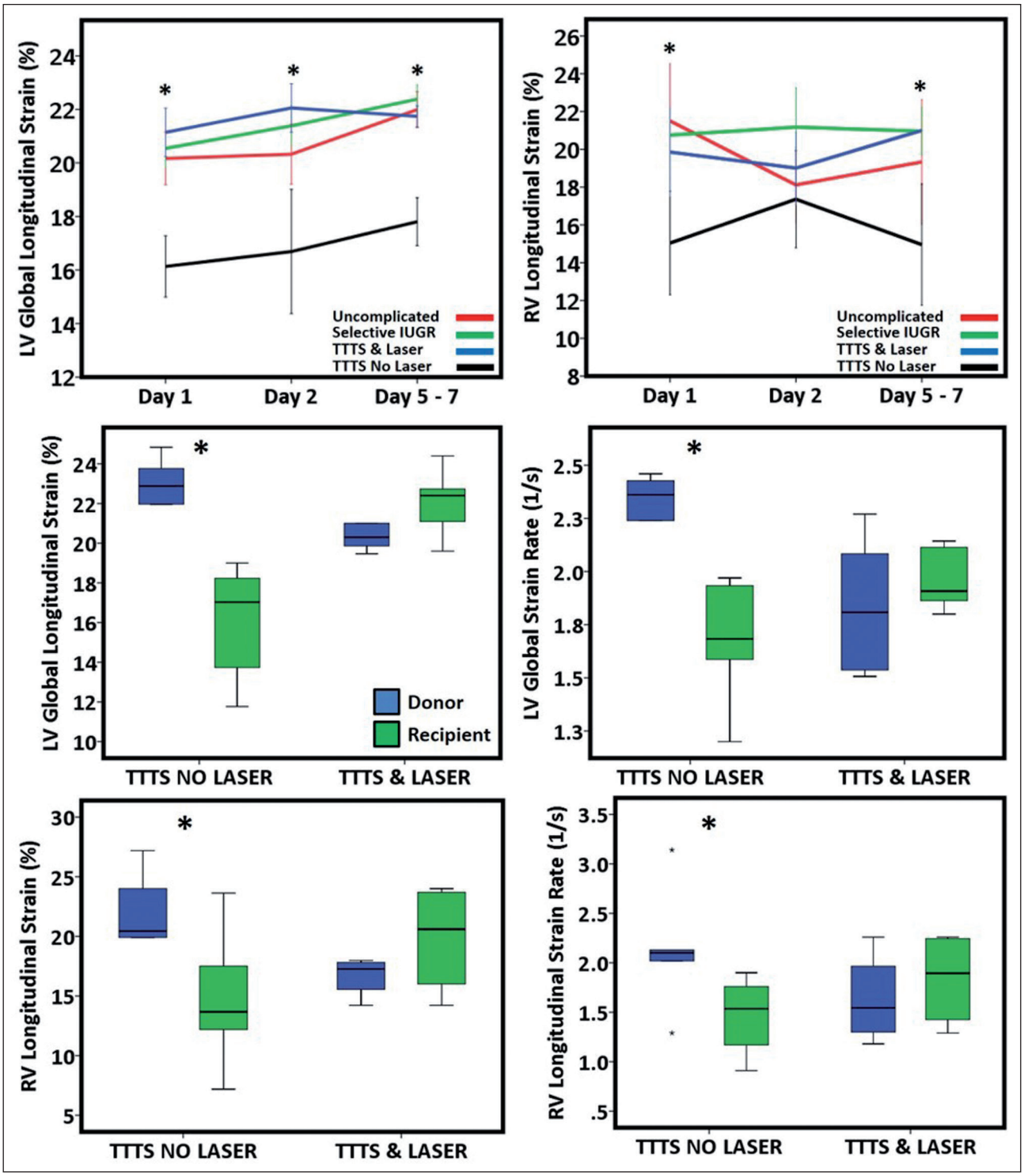

Figure 1 (ABS 10). Change in LV and RV function in the Larger/Recipient twin of the four groups over the first week of age (top panel) & LV and RV strain and systolic strain rate in the two TTTS groups (lower two panels). Infants in TTTS no LASER Group had lower LV and RV function throughout the study period. The recipient twins of the TTTS no LASER Group have lower LV and RV function when compared with the donor twins. There are no differences in function between the recipient/donor twin pair of the TTTS & LASER Group.

CONCLUSIONS

This is the first study to highlight the poor myocardial performance in MCDA recipient twins exposed to TTTS who do not undergo SLPCV. This may have important implications for the antenatal management of those infants and highlights the need for close monitoring of their haemodynamic status during the early neonatal period. Further study is warranted to explore this condition further.

ABS 11

INCIDENTAL FINDINGS ON ROUTINE TARGETED NEONATAL ECHOCARDIOGRAPHY PERFORMED IN PRETERM INFANTS LESS THAN 29 WEEKS GESTATION

A. Smith[1], C.R. Breatnach[1], A.T. James[1], O. Franklin[2], A. El-Khuffash[1,3]

[1]Department of Neonatology, The Rotunda Hospital, Dublin, Ireland

[2]Department of Cardiology, Our Lady's Children's Hospital, Crumlin, Dublin, Ireland

[3]School of Medicine (Department of Paediatrics), Royal College of Surgeons in Ireland, Dublin, Ireland

INTRODUCTION

Targeted neonatal echocardiography (TnECHO) is performed for a wide variety of indications including the assessment of suspected congenital heart disease (CHD), appraisal of myocardial function and evaluation of patent ductus arteriosus (PDA). With the growing use of TnECHO, the discovery of incidental findings is increasing and includes umbilical venous catheter (UVC) complications (malpositioned umbilical catheters, liver haematomas), CHD, pericardial effusions and persistent pulmonary hypertension (PH). The aim of this study was to quantify the rate of incidental findings identified on elective research echocardiograms performed on infants less than 29 weeks gestation.

METHODS

This was a retrospective study of echocardiograms performed within the first 24 hours of age on infants less than 29 weeks gestation over a three-year period for research purposes. Infants who had echocardiograms performed for clinical purposes were excluded. Incidental findings identified on echocardiogram and pertinent clinical data were recorded.

RESULTS

Echocardiograms performed at a median [IQR] 10 [7-13] hours on 145 infants with a gestation and birthweight of 26.9 [25.7-28.0] weeks and 940 [750-1,130] grams respectively were reviewed. Forty three (30%) infants had a total of 54 (37%) unexpected findings. The vast majority comprised of malpositioned UVCs where the tip was identified in the left atrium. The rate of CHD was 10%, the commonest being an atrial septal defect. One infant had an incidental finding of total anomalous pulmonary venous drainage, and another with transposition of the great arteries. The remainder of the findings included liver haematomas, pericardial effusions and unexpected PH (**Tab. 1**). The presence of unexpected findings on TnECHO was independently associated with chronic lung disease or death when controlling for gestation (Adjusted OR 3.6 [95% CI 1.4-9.6]).

Table 1 (ABS 11). Rate and type of unexpected findings.

Complication	Frequency
Overall unexpected pathology	54 (37%)
Number of infants with pathology	43 (30%)
Total number of infants with a UVC inserted	87 (60%)
Malpositioned UVC identified on TnECHO	24/87 (28%)
Tip in left atrium	18/24 (75%)
Tip in the right atrium	2/24 (8%)
Tip in the liver	4/24 (17%)
Liver haematomas	4/87 (17%)
CHD	15 (10%)
Atrial septal defect (number, proportion, median size in mm)	7/15 (47%), 5.2 [4.5-5.2]
Ventricular septal defect (number, proportion, median size in mm)	4/15 (27%), 2.3 [1.7-3.1]
Pericardial effusion	3 (2%)
Unexpected PH	5 (3%)

Unless stated, the denominator for the values is 145.
UVC: umbilical venous catheter; TnECHO: targeted neonatal echocardiography; CHD: congenital heart disease; PH: pulmonary hypertension.

CONCLUSIONS

There is a high rate of unexpected findings discovered on screening echocardiograms in preterm infants less than 29 weeks gestation. Malpositioned UVCs when deep are more likely to be found in the left rather than the right atrium contrary to common knowledge. This is likely due to the persistent fetal channels directing inferior vena cava flow across the foramen ovale. Routine TnECHO screening of preterm infants may be warranted to identify the high likelihood of unexpected findings.

ABS 12

A CLINICAL SCORING SYSTEM AS A DIAGNOSTIC TOOL FOR HEMODYNAMICALLY SIGNIFICANT PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS

N. Okur, H.G. Kanmaz, M. Buyuktiryaki, G.K. Simsek, F.E. Canpolat, N. Uras, S.S. Oğuz

Neonatology Division, Zekai Tahir Burak Maternity Teaching Hospital, Ankara, Turkey

INTRODUCTION

Currently echocardiography is the best and reliable tool to diagnose hemodynamically significant patent ductus arteriosus (hsPDA). However in most neonatal intensive care units (NICU) echocardiography is not readily available in most of the times especially in night and weekend shifts and diagnosis of PDA depends on the clinical findings and symptoms. We aimed to invent a clinical scoring system and assess its sensitivity and specificity to diagnose hsPDA.

METHODS

A clinical scoring system which contains eight different parameters (murmur, hyperactive precordium, pulse pressure, tachycardia, hypotension, FiO_2 requirement, pH, respiratory support) with three different severity index (mild/none [0], moderate [1] and severe [3]) was designed. All preterm infants whose gestational age ≤ 32 weeks were examined by blind pediatric cardiologists for hsPDA in the first three days of life. Following criteria was used to define hsPDA, diastolic turbulence flow in pulmonary artery (left to right or bidirectional shunt), left atrium/aortic root diameter ratio > 1.5, ductal size > 1.5 mm. Clinical scoring was performed by two investigators right before echocardiographic examination and the worst value was recorded within twelve hours prior to evaluation. Demographic characteristics were obtained from the medical files.

RESULTS

One hundred and sixty four preterm infants were evaluated. Median gestational age was 28.5 ± 2 (24-32) weeks and birthweight was 1,078 ± 269 grams. Median score was 4 (0-16). Total score was significantly correlated with hsPDA ($r = 0.61$, $p < 0.01$). Each parameter individually correlated with hsPDA, murmur was the most significant one ($r = 0.74$, $p < 0.01$). The AUC was 0.87 for total score and diagnosed hsPDA with 81% specificity and 85% sensitivity. Cut-off level was 4.5 for total score.

CONCLUSIONS

Clinical scoring system described in this study significantly correlated with echocardiographic findings and could be simply and successfully use to diagnose hsPDA, especially when echocardiographic examination could not to be performed.

ABS 13

THE SUDDEN CHANGE IN CARDIAC FUNCTION AFTER PATENT DUCTUS ARTERIOSUS LIGATION MEASURED BY ELECTRICAL CARDIOMETRY IN AN EXTREME LOW BIRTH WEIGHT INFANT

Y.H. Chien[1,2], K.Y. Chao[1,3,4], Y.L. Chen[1,5], L.Y. Tsai[1,6], C.E. Chiang[7], S.C. Mu[1,8]

[1]Department of Pediatrics, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan

[2]Department of Pediatrics, National Taiwan University Hospital, Taipei, Taiwan

[3]Graduate Institute of Clinical Medical Sciences, College of Medicine, Chang Gung University Taoyuan, Taiwan

[4]Department of Respiratory Therapy, Fu Jen Catholic University, Taipei, Taiwan

[5]School of Medicine, Taipei Medical University, Taipei, Taiwan

[6]College of Public Health, Institute of Occupational Medicine and Industrial Hygiene, National Taiwan University, Taipei, Taiwan

[7]Department of Respiratory Therapy, Shin Kong Wu Ho-Su Memorial Hospital, Taipei, Taiwan

[8]School of Medicine, Fu Jen Catholic University, Taipei, Taiwan

INTRODUCTION

Surgical ligation of patent ductus arteriosus (PDA) often developed a period of cardiopulmonary deterioration, usually occurring 6-14 hours after ligation. The causes of the post-ligation deterioration were unknown. There were few studies of the effects of PDA ligation on cardiac function. Electrical Cardiometry (EC) was a noninvasive continuous monitoring of hemodynamic parameters. The parameters of flow time corrected (FTC), cardiac index (CI), index of contractility (ICON), and systemic vascular resistance index (SVRI) represented preload, contractility and afterload, respectively. We expected to realize the change of cardiac function during PDA ligation by continuous measure of EC.

CASE REPORT

We presented an extreme low birth weight (ELBW) infant delivered via emergent caesarean section at 29 weeks gestation due to fetal distress. Apgar score was 7 at 1-minute and 8 at 5-minutes and birth weight was 990 g. Because of grade III respiratory distress syndrome, endotracheal intubation was performed and Surfactant was given. The ventilator setting and respiratory condition were improving gradually. Empirical antibiotics and trophic feeding began after birth. At the 4th day of life, continuous heart murmur was heard and widened pulse pressure was also noted. Chest X-ray revealed enlargement of cardiac size and increasing lung congestion. Cardiac ultrasonography showed large PDA with size of 5 mm and continuous left to right shunt. Enlargement of left atrium was noted and left atrium and aortic root ratio was 2.15. The diastolic flow of descending aorta and superior mesenteric artery measured by pulse wave was reverse and absent, respectively. Therefore, hemodynamic-significant PDA was diagnosed. Fluid restriction was then performed and surgical ligation of PDA was indicated.

RESULTS

Surgical PDA ligation was then performed at the 5th day of life. We used EC to continuously measure parameters of cardiac function, including FTC, CI, ICON and SVRI during the whole operation. The cardiac function had dramatic and sudden change at the time of PDA ligation. We observed that the parameters of FTC, CI and ICON decreased, oppositely, SVRI increased (**Fig. 1**). There was

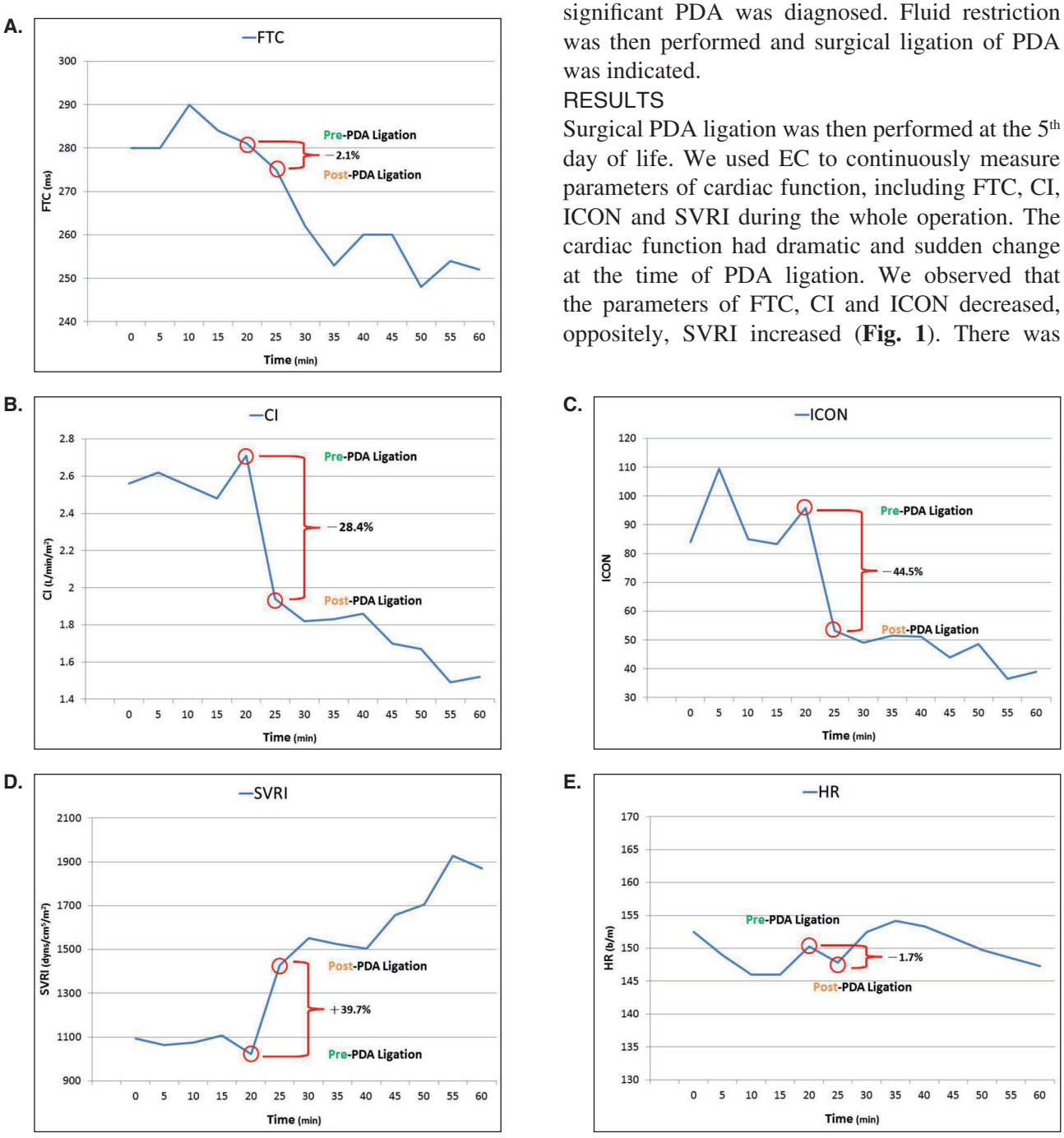

Figure 1 (ABS 13). The sudden change of cardiac function during PDA ligation. **A.** Flow time corrected (FTC) decreased gradually. **B.** Cardiac index (CI) decreased 28.4%. **C.** Index of contractility (ICON) decreased 44.5%. **D.** Systemic resistance index (SVRI) increased 39.7%. **E.** Heart rate (HR) no obvious change.

no obvious change in heart rate. PDA ligation was done smoothly and no post-ligation hypotension was noted. The ELBW then grew up gradually in neonatal intensive care unit.

CONCLUSIONS

According to continuous measure by EC, we realized the sudden change of cardiac function after PDA ligation. The FTC (preload) and CI/ICON (contractility) decreased suddenly, oppositely, the SVRI (afterload) increased suddenly. The dramatic change of PDA ligation represented a return to normal non-shunt condition; however, it might also explain the post-ligation cardiopulmonary deterioration, especially in low GA and large PDA ELBWs.

ABS 14

HEMODYNAMIC CHANGES RELATED TO DUCTUS CLOSURE IN PRETERMS

A. Rodríguez Sánchez de la Blanca, N. González Pacheco, C. Ramos Navarro, M. Arriada Redondo, N. Navarro Patiño, E. Sanz López, M. Sánchez Luna

Neonatology Division, Gregorio Marañón Hospital, Madrid, Spain

INTRODUCTION

Closure of a patent ductus arteriosus (PDA) in preterm infants generates hemodynamic changes which are related with low cardiac output situations. The aim of this study is to analyze, by a cardiac output monitor based on electrical velocimetry, those changes in preterm babies.

METHODS

Prospective observational study which includes preterm newborn infants of a gestational age less than 28 weeks, with a heart ultrasound diagnosis of a significant PDA, which requires intravenous ibuprofen or surgical closure. All patients were monitored with the system at the time of treatment indication and during the next 72 hours. Measurements obtained one hour before starting the therapy were defined as the patient's baseline values. We analyzed the differences, respect to the basal measurement, observed at different periods of time (1, 8, 24, 48 and 72 hours) for each group. The results are shown as median and interquartile range. The pre/post ductal closure treatment parameters were compared by a non parametric test: Wilcoxon.

RESULTS

During a 12 months period, 18 patients were included. The median gestational age in the ibuprofen group (12/18) was 26^{+5} weeks (25^{+5}-27^{+3}) and a median weight of 875 g (670-1,010). The cardiac output (CI) value was 0.29 l/kg/min (0.24-0.34). Among the patients with confirmed ductus closure (50%), a significant CI decrease was shown (0.24 vs 0.29 l/kg/min; p = 0.03) after 72 hours (3 ibuprofen doses). A statistically significant decrease in systolic volume (SVI) was found: 1.62 ml/kg vs 1.88 ml/kg; p = 0.03 with a decrease in contractility (ICON): 85 vs 140; p = 0.02. The gestational age in the surgical group (6/18) was 25^{+2} weeks (24-26^{+3}) with a weight of 745 g (660-820) g. All patients in this group showed a decrease in the immediate postoperative CI (1 hour after surgery) 0.24 vs 0.30 l/kg/min, p 0.05 and a significant decrease in contractility (ICON: 77 vs 147, p 0.03). In addition, a tendency to decrease in SVI (1.54 vs 1.83 ml/kg, p = 0.06), as well as an increase in systemic vascular resistance (10,615 vs 8,797 dyns/cm^2, p 0.08), were detected. This deterioration was transient without significant differences in the remaining periods of time evaluated.

CONCLUSIONS

The surgical closure of the PDA in preterm infants causes a transient deterioration of cardiac function with a documented decrease in the left ventricular output. The hemodynamic changes detected after pharmacological PDA closure are similar to those, although it seems those patients present a better clinical tolerance to changes in the cardiac output.

ABS 15

NOVEL METHODS TO CHARACTERIZE RIGHT VENTRICULAR – PULMONARY ARTERIAL COUPLING IN EXTREME PRETERM INFANTS WITH LATE ONSET PULMONARY HYPERTENSION

P. Levy[1,2], M. Patel[1], S. Choudhry[1], M. Holland[3], T. Sekarski[1], A. Hamvas[4], G. Singh[1]

[1]*Pediatrics, Washington University School of Medicine, Saint Louis, MO, USA*

[2]*Pediatrics, Goryeb Children's Hospital, Morristown, NJ, USA*

[3]*Radiology, Indiana University, Indianapolis, IN, USA*

[4]*Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA*

INTRODUCTION

Pulmonary hypertension (PH) can exert significant load to the right ventricle (RV) that can affect RV-pulmonary arterial coupling. RV function

is a key determinant of prognostic outcome, but conventional measures of RV function are poor markers for risk stratification. RV-PA can be assessed with the RV length-force relationship (tricuspid annular plane systolic excursion [TAPSE] vs. pulmonary artery systolic pressure [PASP]). Pulmonary artery acceleration time (PAAT) is a validated non-invasive surrogate of PASP. We hypothesize that the relationship TAPSE vs. PAAT provides a non-invasive index of the RV-PA coupling in the extreme preterm infants. We sought to evaluate RV work from the length-force relationship as markers of RV functional status in preterm infants with PH.

METHODS

In a prospective study of 117 preterm infants (< 29 weeks at birth) enrolled through the Prematurity and Respiratory Outcomes Program (PROP, U01 HL101794) we measured tricuspid annular plane systolic excursion (TAPSE) for length shortening, RV strain, and fractional area of change (FAC) for quantitative assessment of RV systolic function; and PA acceleration time (PAAT) and PAAT/RV ejection time (RVET) to evaluate PA compliance and resistance. TAPSE x PAAT was calculated to develop length-force relationship as indices of RV work. Conventional measures of RV functional status included RV hypertrophy (RVH) and/or dilatation and septal motion (hypokinetic or paradoxical). PH was identified in infants with a combination of TR jet estimated RVSP > than 40 mmHg, RVSP/sBP > than 0.5, cardiac shunt with right-to-left flow at 36 weeks premenstrual age (PMA). Echocardiographic, maternal and infant factors were compared between preterm infants with and without PH.

RESULTS

PH was identified at 36 weeks PMA in 15% (n = 17) of preterm infants. Quantitative measures of RV function, RV work, and pulmonary vascular resistance and compliance were all significantly reduced in patients with PH compared to those without PH ($p < 0.05$ for all, **Tab. 1**). Conventional measures of RV function were present in less then 20% of all patients. We accounted for the contribution of gestational age, gender, and the presence of CLD in the analysis.

CONCLUSIONS

Quantitative echocardiographic measures of RV function (strain, TAPSE, FAC), RV work, and pulmonary hemodynamics (PAAT) are sensitive methods to detect RV dysfunction in preterm infants with PH. TAPSE x PAAT ratio, as the index of the length-force relationship may be developed to assess RV reserve under stress in extreme preterm infants.

Table 1 (ABS 15). Infant and maternal characteristics between preterm, infants and without PH at 36 week post-menstrual age.

	No PH (n = 100)	Yes PH[a] (n = 17)	p-values
Infant data			
Gestational age (GA, weeks)	26.6 ± 1.4	26.2 ± 1.4	0.2
Birth weight (grams)	905.6 ± 216	914.8 ± 124	0.86
Small for gestational age	3 (3%)	0	0.48
Gender (female)	57 (57%)	7 (41%)	0.25
Antenatal steroids (yes)	85 (85%)	13 (76%)	0.32
Surfactant	100 (100%)	17 (100%)	NA
CLD[b]	59 (59%)	13 (76%)	0.14
Maternal data			
Chorioamnionitis	11 (11%)	0	0.16
Preeclampsia	26 (26%)	1 (6%)	0.2
Gestational HTN	23 (23%)	3 (18%)	0.64
Gestational DM	5 (5%)	0	0.35
Smoking	25 (25%)	3 (18%)	0.53
Echocardiographic measures			
RV global systolic function			
RV FAC (%)	33.1 ± 5.5	29.7 ± 6.4	0.02
TAPSE (cm)	1.03 ± 0.2	0.86 ± 0.2	0.003
RV FWLS (%)	-21.6 ± 3.7	-19.7 ± 2.7	0.04
Pulmonary hemodynamics			
PAAT (msec)	54.5 ± 17.6	43.8 ± 6.3	0.02
PAAT:RVET	0.28 ± 0.09	0.22 ± 0.05	0.01
RV work			
TAPSE x PAAT (cm/msec)	57 ± 28	36 ± 14	< 0.001
TAPSE x (PAAT:RVET) (cm)	0.29 ± 0.13	0.18 ± 0.08	< 0.001

Values are expressed as mean ± SD or number with percentile.
PH: pulmonary hypertension; CLD: chronic lung disease; RV: right ventricle; LV: left ventricle; FAC: fractional areas of changes; TAPSE: tricuspid annular plane systolic excursion; FWLS: free wall longitudinal strain; PAAT: pulmonary artery acceleration time; RVET: RV ejection time.
[a]PH, pulmonary hypertension: PH was defined as any infant with any conventional echocardiographic signs identified by an estimated RVSP > than 40 mmHg, a ratio of RVSP to sBP > than 0.5, any cardiac shunt with right-to-left flow, unusual degree of RV hypertrophy or dilatation, or any degree of ventricular septal wall flattening.
[b]CLD, chronic lung disease, defined as the need for any respiratory support at 36 weeks PMA, using a modified NIH definition. CLD was diagnosed in 59% (n = 69) of the patients, of which 14 (20%) had PH. The remaining three patients with PH did not have CLD.

ABS 16

EMERGING QUANTITATIVE ECHOCARDIOGRAPHIC MARKERS OF PULMONARY VASCULAR DISEASE AND RIGHT VENTRICULAR DYSFUNCTION IN EXTREME PRETERM INFANTS WITH LATE PULMONARY HYPERTENSION

P. Levy[1,2], C. Brennan[1], M. Patel[1], S. Choudhry[1], A.A. Sanchez[3], A. EL-Khuffash[4], C. Breatnach[4], O. Franklin[5], A. Hamvas[6], G. Singh[1]

[1]Pediatrics, Washington University School of Medicine, St. Louis, MO, USA

[2]Pediatrics, Goryeb Children's Hospital, Morristown, NJ, USA

[3]Pediatrics, University of Minnesota, Minneapolis, MN, USA

[4]Neonatology, The Rotunda Hospital, Dublin, Ireland

[5]Cardiology, Our Lady's Children's Hospital Crumlin, Dublin, Ireland

[6]Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA

INTRODUCTION

Cardiac dysfunction is a key determinant of morbidities in late onset (~36 weeks PMA) pulmonary hypertension (PH) in preterm infants. Although several quantitative echocardiography parameters to measure right (RV) and left ventricular (LV) function have been developed, their relative clinical utility in PH in preterm infants is not known. We hypothesize that quantitative measures of RV function and pulmonary hemodynamics provide more sensitive markers of PH and RV dysfunction than the conventional qualitative measures. The aims of this study were to characterize cardiac function and pulmonary hemodynamics in preterm infants with late onset PH using emerging quantitative echocardiography and identify parameters to distinguish disease from health.

METHODS

A prospective echocardiographic study was conducted in 117 preterm infants (< 29 weeks at birth) enrolled through the Premature and Respiratory Outcomes Program (PROP, NCT01435187). Conventional and quantitative echocardiographic measures of cardiac function and pulmonary hemodynamics were measured at 36 weeks PMA. Measurements included conventional functional indices, LV and RV strain, and RV specific measurements for tricuspid annular plane systolic excursion (TAPSE) and percent fractional area change (FAC). Pulmonary artery acceleration time and tricuspid regurgitation jet velocity derived RV systolic pressures were measured to evaluate

Table 1 (ABS 16). A. Infant data and echocardiographic measures between infants with and without PH. **B.** Conventional vs. quantitative echocardiographic classification of late pulmonary hypertension in extreme preterm infants.

	No PH (n = 100)	Yes PH[a] (n = 17)	p-values
Infant data			
Gestational age (GA, weeks)	26.6 ± 1.4	26.2 ± 1.4	0.2
Birth weight (grams)	905.6 ± 216	914.8 ± 124	0.86
Small for gestational age	3 (3%)	0	0.48
Gender (female)	57 (57%)	7 (41%)	0.25
Antenatal steroids (yes)	85 (85%)	13 (76%)	0.32
Surfactant	100 (100%)	17 (100%)	NA
CLD[b]	59 (59%)	13 (76%)	0.14
Echocardiographic measures			
RV global systolic function			
RV FAC (%)	33.1 ± 5.5	29.7 ± 6.4	0.02
RV GLS (%)	-20.1 ± 5.4	-17.1 ± 1.8	0.03
RV global systolic function			
TAPSE (cm)	1.03 ± 0.2	0.86 ± 0.2	0.003
RV FWLS (%)	-21.6 ± 3.7	-19.7 ± 2.7	0.04
Pulmonary hemodynamics			
PAAT (ms)	54.5 ± 17.6	43.8 ± 6.3	0.02
PAAT:RVET	0.28 ± 0.09	0.22 ± 0.05	0.01
LV global systolic function			
LV GLS (%)	-20.4 ± 2.7	-21.1 ± 2.3	0.37

Lung disease status at 36 weeks PMA	**PVD**	**No PVD**
Conventional method		
CLD	n = 13 (19%)	n = 56
NO CLD	n = 4 (8%)	n = 44
Quantitative method		
CLD	n = 36 (63%)	n = 33
NO CLD	n = 9 (19%)	n = 39

Values are expressed as mean ± SD or number with percentile.
PH: pulmonary hypertension; CLD: chronic lung disease; RV: right ventricle; FAC: fractional areas of changes; GLS: global longitudinal strain; TAPSE: tricuspid annular plane systolic excursion; FWLS: free wall longitudinal strain; PAAT: pulmonary artery acceleration time; RVET: RV ejection time; LV: left ventricle; PVD: pulmonary vascular disease.
[a]PH, pulmonary hypertension: PH was defined as any infant with any conventional echocardiographic signs identified by an estimated RVSP > than 40 mm Hg, a ratio of RVSP to sBP > than 0.5, any cardiac shunt with right-to-left flow, unusual degree of RV hypertrophy or dilatation, or any degree of ventricular septal wall flattening.
[b]CLD, chronic lung disease, defined by the need for any respiratory support at 36 weeks PMA, using a modified NIH workshop definition [1].
Note: We accounted for the contribution of gestational age, gender, and the presence of CLD in the analysis.

pulmonary hemodynamics. All measures were compared between infants with and without PH. PH was identified in infants by two methods: 1) standard conventional echocardiographic approach with two or more signs of PH using the tricuspid regurgitation jet to give qualitative estimates, such as an estimated RVSP > than 40 mmHg, a ratio of RVSP to sBP > than 0.5, any cardiac shunt with right-to-left flow, unusual degree of RV hypertrophy or dilatation, or any degree of ventricular septal wall flattening; and 2) emerging validated quantitative PH approach with cut-offs of pulmonary artery acceleration time < 43, RV Strain < -17, RV FAC < 31. We accounted for the presence of chronic lung disease (CLD) and gestational age at birth in the analysis.

RESULTS

CLD was diagnosed in 59% (n = 69) of the patients. Using the conventional approach, PH was identified at 36 weeks PMA in 15% (n = 17) of preterm infants. Quantitative measures of RV function (systolic strain, TAPSE, FAC) and pulmonary hemodynamics (PAAT) were all significantly reduced in patients with PH by conventional echocardiography compared to those without PH (**Tab. 1A**). Of the 17 patients with PH by conventional methods, 4 infants (8%) did not have CLD. Using the quantitative approach PH was identified in 37% (n = 43), of which 9 infants (19%) did not have CLD (**Tab. 1B**). LV function, as measured by strain, was persevered between groups (**Tab. 1B**).

CONCLUSIONS

RV dysfunction and abnormal pulmonary hemodynamics are characteristic of PH in preterm infants. Emerging quantitative echocardiographic measures of RV function (strain, TAPSE, RV FAC) and pulmonary hemodynamics (PAAT) are more sensitive methods to detect cardiopulmonary dysfunction in preterm infants with late PH than traditional conventional methods.

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ABS 17

TREATMENT FOR PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS – LESS IS MORE?

T. Hundscheid, W. de Boode

Paediatric Department, Division of Neonatology, Radboudumc Amalia Children's Hospital, Nijmegen, the Netherlands

INTRODUCTION

In preterm infants a patent ductus arteriosus (PDA) is common. It is associated with mortality and major morbidity such as bronchopulmonary dysplasia (BPD), necrotizing enterocolitis (NEC) and intraventricular haemorrhage (IVH). Causality between the haemodynamic changes related to a PDA and these adverse outcomes has never been proven. Randomised controlled trials (RCTs) show that although treatment with a cyclooxygenase inhibitor (COXi) does lead to a higher ductal closure rate compared to placebo, it does not show beneficial effects on outcome. Together with concerns about side effects of treatment, this has lead to a conservative treatment in many clinics. Our aim is to review the literature on mortality and morbidity (BPD, NEC and IVH) for a conservative approach of the PDA in preterm infants.

METHODS

We performed a literature search in PubMed with the terms PDA, premature and conservative treatment, limited to the past ten years. Studies with more than 25% treatment rate in the conservative group will be excluded. We analysed the references of reviews and included articles, to gain additional studies. If possible, we will perform a meta-analysis of the available RCTs. If not, we will compare outcome with the most recent Vermont Oxford Network (VON) database from 2009 (n = 43,566) as published by Horbar (2012). If outcome is not given as number or percentage but only compared to another cohort within the study we will present the available ratios.

RESULTS

Our search revealed 36 hits, of which eight could be included, together with two additional studies from the references. As no RCTs were found a meta-analysis could not be performed. We could analyse nine, mainly retrospective, cohort studies with a total of 23,217 patients, of which 10,898 (46.9%) where treated conservatively. These groups had a mean gestational age of 24.5 to 28.3 weeks. Their mortality and morbidity are presented in **Tab. 1**, together with the comparing VON database. The other study (n = 5,562) compared the composite of mortality and morbidity between different treatment options in a Japanese and Canadian cohort. The adjusted odds ratios (95%-confidence interval) for both indomethacin and ligation versus conservative treatment were 0.95 (0.65-1.38) and 1.80 (1.22-

Table 1 (ABS 17). Outcome in patients treated conservatively for their patent ductus arteriosus (PDA) compared to the Vermont Oxford Network (VON) database (2009).

	Total (n)	CTG (n)	Mortality (%)	BPD (%)	NEC (%)	IVH (%)
Cohort studies						
Vanhaesebrouck et al. (2007)	30	30	13.3	6.7	0	3.3
Mirea et al. (2012)	3,556	577	12.5	27.1	6.0	21.6
Saddeck et al. (2015)	494	187	51.3	25.7	7.5	19.8
Rolland et al. (2015)	103	91	17	35	3	21
Sung et al. (2016)	178	97	9.3	38.0	12.4	12.4
Lokku et al. (2016)	5,824	1,486	10.8	23.1	6.9	16.9
Letshwiti et al. (2017)	371	72	2.9	17.6	5.9	8.8
Slaughter et al. (2017)	12,018	8,130	13.1	30.9	NA	NA
Mohammed et al. (2017)	643	228	10.5	5.0	8.8	6.6
VON Database (2009)						
Horbar et al. (2012)	43,566	NA	12.7	26.3	5.3	6.1

CTG: conservative treatment group; BPD: bronchopulmonary dysplasia; NEC: necrotizing enterocolitis; IVH: intraventricular haemorrhage; NA: not available; VON: Vermont Oxford Network.

2.66), respectively. For indomethacin only this was 1.00 (0.72-1.38) and 0.93 (0.71-1.22), respectively.

CONCLUSIONS

These cohort studies on conservative management in PDA show a large variation in outcome, which are grossly comparable to the VON database. At the moment, available evidence for the management of a PDA in prematurity reveals a state of clinical equipoise. To gain evidence, we are currently conducting a multicentre RCT comparing conservative management with early COXi treatment (BeNeDuctus trial; Clinicaltrials.gov NCT02884219).

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DECLARATION OF INTEREST

The BeNeDuctus trial is funded by The Netherlands Organization for Health Research and Development (ZonMw) (grant 843002622).

ABS 18

PULSE OXIMETRY SCREENING IN THE ASYMPTOMATIC NEWBORNS

S. Chaudhry[1], Y. Singh[2]

[1]*Paediatric specialty registrar, Addenbrooke's Hospital, Cambridge, UK*

[2]*Neonatology and Paediatric Cardiology, Cambridge University Hospitals, UK*

INTRODUCTION

The current screening tools (fetal anomaly screening and routine neonatal examination) fail to detect up to 39-50% of critical congenital heart defects (CHDs). However, the addition of pulse oximetry screening (POS) as an adjunct may detect up to 92% critical CHDs. Retrospective audit with the following two outcomes: 1) to assess the uptake of the pulse oximetry screening on the postnatal ward; 2) to review the efficacy of the pulse oximetry screening in detecting CHDs and other non-cardiac conditions such as sepsis.

METHODS

A retrospective observational study involved all eligible infants for POS and born between September 2015 to April 2016. Infants already admitted to NICU and already symptomatic infants were excluded.

RESULTS

A total of 3,646 eligible infants for POS were identified from the patient records and uptake was 98% (3,574 of 3,646 babies). In around two-third infants screening was performed within 4-8 hours as recommended by the local guideline. 64 infants (1.7%) were noted to have abnormal POS results (POS positive results). 3 babies were diagnosed with CHD. The defects were as follows: 1) small ASD, 2) critical pulmonary stenosis with right heart, 3) AVSD with mild TR. 2 babies had minor findings like PFO on echocardiography and 1 was antenatal diagnosis of AVSD. Echo was performed in 9 out of 64 (14%). The remaining 33 of 64 (51%) babies had significant non-cardiac pathologies such as sepsis (11), suspected sepsis (5), RDS (5), feeding issues (8) and jaundice (4). 25 of the 64 (39%) babies had no significant cardiac or non-cardiac pathologies (false positive).

CONCLUSIONS

When pulse oximetry screening is performed early it has slightly higher false positive rate as compared to the reported studies. However, it helps in detecting other non-cardiac conditions in otherwise well infants. In our cohort, it did not put any extra burden on echocardiography services.

ABS 19

CHANGES IN THE MANAGEMENT OF PATENT DUCTUS ARTERIOSUS OVER 10 YEARS IN A TERTIARY NEONATAL CENTRE

D. Panjwani, S. Mittal

Neonatal Unit, University Hospital Leicester, Leicester, UK

INTRODUCTION

There continues to be significant variation in the management of neonates with patent ductus arteriosus (PDA). Over the past decade, few changes have been made to management of PDA. One important event was the elimination of use of Indomethacin, which is a non-steroidal anti-inflammatory drug (NSAID). Looking at the recent years, there has also been an increase in survival of extremely preterm neonates (< 26 weeks gestation). These babies are likely to present with PDA and therefore a management strategy may be beneficial.

METHODS

This study aims to look at the changes in management and outcome of babies less than 30 weeks gestation with an echocardiographic diagnosis of PDA. This study was done in 2 parts. The initial part was conducted in 2011 and looked at management of babies with PDA over a four-year period, between July 2007-June 2011 (Cohort 1). The second study was conducted looking at babies with PDA between January 2015 to December 2016 (Cohort 2). For both parts of the study, babies under 30 weeks gestation were identified using the electronic Badger patient record system. Data was collected retrospectively using the same proforma and analysed using Microsoft® Excel®.

RESULTS

A total of 262 babies were identified. The summary of results is shown in **Tab. 1**. In Cohort 1, conducted between July 2007 and June 2011, a total of 154 babies were identified as having PDA. 32% of babies were born extremely preterm (before 26 weeks gestational age) and 19% of babies had a birth weight less than 850 grams. In Cohort 2, conducted between January 2015 and December 2016, 108 babies were identified as having PDA. 37% of babies were extremely preterm born.

Table 1 (ABS 19). Changes in management and outcome of babies less than 30 weeks gestation with an echocardiographic diagnosis of patent ductus arteriosus (PDA) between July 2007-June 2011 (Cohort 1) and between January 2015 to December 2016 (Cohort 2).

	2007-2011 (Cohort 1)	2015-2016 (Cohort 2)
Number	154	108
NSAID	84 (55%)*	40 (37%)
Ligation	29 (19%)	11 (10%)
NEC (surgical treatment)	14 (9%)	10 (9%)
ROP (laser treatment)	10 (6%)	18 (17%)
Home O_2	29 (19%) (n = 126)	29 (27%) (n = 90)
Died	28 (18%)	18 (17%)

NSAID: non-steroidal anti-inflammatory drug

CONCLUSIONS

Treatment of preterm PDA remains a continuing conundrum for Neonatologists. Over the past decade, there appears to be movement towards a more conservative approach in UHL.

An increase in survival of extreme preterm neonates may contribute to an increased incidence of PDA. In view of this, more evidence is required to provide consensus. We hope the ongoing Baby Oscar study will be able to provide robust evidence in prophylactic treatment of PDA.

ABS 20

COARCTATION OF THE AORTA – THE CONGENITAL HEART DEFECT WITH A MILLION FACES

M. Simon[1], R. Sánta[2], L.M. Suciu[1], Z.S. Gáll[1], R. Marian[1], M. Rusneac[2], C. Gliga[2], M.C. Cucerea[1]

[1]Neonatology Department, University of Medicine and Pharmacy Tirgu-Mures, Tirgu-Mures, Romania

[2]Neonatology Department, Mures County Emergency Hospital Tirgu-Mures, Tirgu-Mures, Romania

INTRODUCTION

Coarctation of the aorta that is present in the newborn is one of the congenital heart defects with ductal dependent systemic circulation that, if not diagnosed antenatally, can remain silent at the beginning and mimic clinical manifestations of other neonatal pathology, like sepsis, or pulmonary

pathology, persistent pulmonary hypertension or even persistent ductus arteriosus, when the ductal patently begins to constrict. The authors present the unrelated cases of four newborns, first admitted to the neonatal intensive care unit for other suspected pathology that eventually showed to be ductal dependent coarctation of the aorta.

CASE REPORTS

The authors present the cases of four newborns, without prenatal suspicion of congenital heart disease, with various clinical presentation, with first suspected diagnose other than coarctation of the aorta, but were diagnosed by echocardiographic examination in less than 24 hours after first clinical signs, and stabilized before surgical intervention.

Case 1

B., 34-week male twin, birth weight 2,000 g, premature rupture of membranes, born by cesarean section, with good postnatal adaptation is sent from a level 2 maternity on day 4 of life with the suspicion of sepsis. At admittance he presented poor capillary refill, sweating, cold extremities, lethargy absent femoral pulses, severe acidosis. Echocardiography showed critical coarctation of the aorta with closed ductus arteriosus. Cultures were negative. After reopening the ductus with PGE1 infusion, clinical appearance of the newborn improved, acidosis was corrected, peripheral circulation reestablished. He underwent correction at the postnatal age of 3 weeks.

Case 2

B., 40-week female newborn, birth weight 4,200 g, born by natural birth, after an uncomplicated pregnancy, without adaptation problems at birth. After 36 hours developed tachypnea, desaturations, and a heart murmur of grade II/6. Pulmonary Rx showed hypervascularity of the lungs. Cultures were negative. Echocardiography revealed coarctation of the aorta, constricted ductus arteriosus and left to right shunt led to pulmonary hypertension. Reopening of the ductus lowered pulmonary blood pressure, improved general status. The coarctation was corrected at 4 weeks of life.

Case 3

S., 28-week male premature infant, birth weight 950 g, with mild respiratory distress syndrome, surfactant replacement through LISA method in the first 30 minutes of life, was stable on CPAP in the first 2 weeks of life. On day 16 a heart murmur was detected, staff interpreted as persistent ductus arteriosus, due to absence of acidosis, normal diuresis, normal values of blood pressure. Echocardiography detected critical coarctation of the aorta, with slightly constricted ductus arteriosus, and PGE1 infusion was introduced. The correction of the coarctation was performed at the age of 12 weeks at 1,850 g due to irresponsiveness of the ductus to PGE1 and early signs of congestive heart failure.

Case 4

V., 40-week male infant, born vaginally after physiological unmonitored pregnancy. Postnatal adaptation was good. He presented fever, metabolic acidosis, and hypotension on day 3 of life, and was sent for admittance to our unit with the suspicion of perinatal infection. Blood culture was positive for *E. coli*. Due to the presence of a heart murmur echocardiography was performed, which described coarctation of the aorta and aortic arch hypoplasia. PGE1 infusion was started along with antibiotics. He was operated at the age of 26 days.

CONCLUSIONS

Neonatal period is characterized by overlapping of uncharacteristic signs. In the presence of a heart murmur with poor peripheral circulation, or respiratory distress, or inexplicable metabolic acidosis, an echocardiogram should be performed in order to rule out or diagnose heart defects especially coarctation of the aorta, that are ductus dependent. In these cases initiation of PGE1 infusion can be lifesaving and permits the medical team to plan surgical repair.

ABS 21

RARE CONGENITAL MITRAL VALVE MALFORMATION

R. Stroescu, A. Popoiu, M. Gafencu, O. Marginean, G. Doros

"Louis Turcanu" Emergency Hospital for Children, University of Medicine and Pharmacy "Victor Babes", Timisoara, Romania

INTRODUCTION

Double orifice mitral valve (DOMV) is an uncommon anomaly that was first described by Greenfield in 1876. Since that time, more than 200 cases have been reported. Aim of the study is to present this rare mitral congenital malformation-DOMV, characterized by a unique fibrous annulus with 2 orifices that open into the left ventricle. The subvalvular structures may present various degree of anomalies, specially the tensor apparatus. The mitral inflow may be normal, stenotic or insufficient.

CASE REPORTS

We present 2 cases of double mitral orifice, both males. In both patients an ECG, echocardiography and thoracic X-ray was done. In the first case, the disease started at 3 weeks after birth with pulmonary edema, hepatomegaly and hepatic cytolysis. The echocardiography showed a double mitral orifice with a larger orifice anterior and a smaller posterior, with grade III mitral insufficiency that was reduced after diuretic treatment. The second is a 3 years old boy, admitted in the hospital for irritative persistent cough since 6 weeks. A simultaneous systolic murmur was the reason for an echocardiography and a double mitral orifice with 2nd degree mitral insufficiency with pulmonary stasis was detected. After diuretic treatment the evolution was good. They both need further monitoring to assess possible augmentation of the mitral regurgitation or even stenosis.

CONCLUSIONS

The literature describes by now around 200 cases. We considered important to present this rare malformation, which can be easily missed in neonates.

ABS 22

COINCIDENTAL LEFT ATRIAL THROMBUS

I. Mungan Akin, P. Canizci, S. Sevuk Ozumut, S. Arslanoglu

Neonatology Division, Department of Pediatrics, Istanbul Medeniyet University Göztepe Education and Research Hospital, Istanbul, Turkey

INTRODUCTION

Neonatal atrial thrombus is a very rare condition and has been reported only a handful of times in the literature thus far. Mortality is high, irrespective of treatment. Atrial thrombus is typically associated with either catheter placement, specific structural abnormalities such as congenital heart disease, or hypercoagulability states.

CASE REPORT

A baby boy, born at term as the first living child from the 3rd gestation of consanguineous parents was admitted to our emergency room with jaundice. On postnatal 84th hour of life, he had a total bilirubin value of 23.5 mg/dl with prominent hypoglycemia (4 mg/dl) and increased lactate (10.6 mmol/l) level and hepatomegaly. After blood and urine samples were obtained for possible metabolic and endocrinopathies, enteral feeding was ceased, phototherapy and dextrose infusion was started. In order to achieve adequate blood glucose levels, glucose perfusion rate was increased up to 8 mg/kg/min, and decrease in lactate levels were observed. Biochemical analysis revealed hyperuricemia (11.8 mg/dl) and hypertriglyceridemia (944 mg/dl). Gluconeogenesis defects and glycogen storage diseases were thought for differential diagnosis and abdominal ultrasonography and echocardiography was performed on the 7th day of life. On echocardiography there was a mobile 8 x 9 mm mass attached with a thin stalk to the wall of left atrium. He was consulted with Pediatric Cardio-vascular surgery unit and operated under emergency conditions. The mass was resected and pathology revealed that it was a thrombus with 1.6 x 0.4 x 1 cm in size. Low molecular weight heparin (LMWH) was started and patient was evaluated for predisposing conditions for thrombosis (catheterization, congenital heart diseases, dehydration, polycythemia or thrombophilia), which were all found to be normal. Patient was diagnosed as glycogen storage disease type 1 and his diet was regulated and discharged with LMWH. The thrombophilia panel was also checked from parents and repeated when the baby was 6 months old, but all of the results were normal with no genetic (MTHFR and prothrombin genes) predisposition.

CONCLUSIONS

In literature, neonatal intracardiac thrombus cases are most commonly (90%) related with catheter insertion or congenital cardiac abnormalities, arrhythmia or coagulation defects. Neonatal atrial thrombus cases especially on the left side, is far more rare and due to the potential of aortic thrombus, their course is much more fatal. As there were no risk factors and no clinical finding in our patient, it was just coincidentally recognized and resected and avoided a life-threatening condition. We think this case is unique; as the patient's first admission to ER was only neonatal jaundice, but it ended up with a diagnosis of glycogen storage disease and left atrial thrombus.

ABS 23

IBUPROFEN AND INDOMETHACIN DIFFERENTIALLY REGULATE VEGF AND ITS RECEPTORS IN DUCTUS ARTERIOSUS ENDOTHELIAL CELLS

H. Sallmon[1], S. Akanbi[1], S.C. Weber[2], A. Gratopp[3], C. Rheinländer[1], P. Koehne[1]

[1]*Department of Neonatology, Charité University Medical Center, Berlin, Germany*
[2]*Department of Congenital Heart Disease/Pediatric Cardiology, Deutsches Herzzentrum, Berlin, Germany*
[3]*Division of Pediatric Emergency and Intensive Care Medicine, Charité University Medical Center, Berlin, Germany*

INTRODUCTION
Cyclooxygenase inhibitors are widely applied to facilitate ductal closure in preterm infants. The mechanisms that lead to patent ductus arteriosus closure are incompletely understood. Vascular endothelial growth factor plays pivotal roles during ductal closure and remodeling. The aim of this investigation was to investigate the effects of ibuprofen and indomethacin on the expression of vascular endothelial growth factor and its receptors in a rat ductus arteriosus endothelial cell culture model.
METHODS
Protein expression of vascular endothelial growth factor, vascular endothelial growth factor receptor -1 and -2 was confirmed in rat ductus arteriosus and aorta by immunohistochemistry. Fetal rat endothelial cells were isolated from ductus arteriosus and aorta using immunomagnetic cell sorting and treated with ibuprofen or indomethacin. mRNA-expression levels were assessed by quantitative polymerase chain reaction analysis.
RESULTS
In ductal endothelial cells, ibuprofen significantly induced vascular endothelial growth factor and its receptor 2 (but not receptor 1), while indomethacin did not alter the expression levels of the vascular endothelial growth factor system. In contrast, ibuprofen significantly induced vascular endothelial growth factor and its receptors 1 and 2 in aortic endothelial cells, whereas indomethacin only induced vascular endothelial growth factor receptor 2.
CONCLUSIONS
Our results indicate differential effects of ibuprofen and indomethacin on the expression levels of the vascular endothelial growth factor system in ductus arteriosus endothelial cells. In addition, vessel-specific differences between ductal and aortic endothelial cells were found. Further *in vivo* studies are needed to elucidate the biological significance of these findings.

ABS 24

PERICARDIAL EFFUSION: SEVERE COMPLICATION OF CENTRAL VENOUS CATHETERIZATION IN THE NEWBORN (REPORT OF 12 SURVIVORS)

S. Nouri Merchaoui, J. Methlouthi, H. Ayache, M. Bellalah, I. Kacem, H. Barbouche, A. Ghith, N. Mahdhaoui, H. Seboui

Neonatology Department, Farhat Hached Hospital, Sousse, Tunisia

INTRODUCTION
The use of central catheters in the neonatal period is essential for the management of sick or premature infants. It is nevertheless associated with a number of risks. Myocardial perforation resulting in pericardial effusion is a rare but severe complication with high mortality. We report twelve observations of newborns surviving such a complication.
CASE REPORTS
There were 11 preterm infants of gestational age below 32 weeks and a newborn infant at term. Birth weights ranged from 690 g to 2,150 g. The KTVC was of the internal jugular venous catheter (KTVC) type in two cases, of a umbilical vein catheter in 5 cases and of an epicutaneo cava catheter in 5 cases. The time between the insertion of the KT and the finding of the PE was 2 to 10 days. Abrupt installation of symptoms was noticed in all cases. Symptoms were respiratory distress in 3 newborns and a state of shock in 9 newborns of which 4 had gone to extreme bradycardia at less than 50 beats per minute. The position of the catheter was at the level of the right atrium in all cases. The diagnosis of PE was confirmed by cardiac ultrasound in 6 cases and by thoracic ultrasound in 2 cases. Diagnosis was suspected on clinical data in 4 newborn infants who had severe bradycardia. Treatment consisted of surgical drainage in 4 cases and a pericardial puncture without ultrasound in 8 cases of tamponade. Evolution was rapidly favorable in all cases. Only one newborn died at a distance from this incident because of sepsis.
CONCLUSIONS
Pericardial effusions are rare but potentially severe complications of central catheters in newborns. They are generally associated with the intracardiac position of the catheters. Diagnosis should be suspected in the presence of any unexplained respiratory or cardiac symptoms with an increase in the cardiothoracic index in a newborn with a central catheter. The prognosis of this complication is largely conditioned by the precocity of the diagnosis and the effectiveness of the treatment.

ABS 25

GENETIC ABNORMALITIES AND CONGENITAL HEART DISEASE

S. Nouri Merchaoui[1], J. Methlouthi[1], H. Ayech[1], M. Bellaleh[1], I. Kacem[1], H. Barbouche[1], A. Ghith[1], S. Mougou[2], D. Hmida[2], N. Mahdhaoui[1], H. Seboui[1]

[1]Neonatology Department Farhat Hached Hospital Sousse, Sousse, Tunisia
[2]Cytogenetics and Molecular Biology Department Farhat Hached Hospital Sousse, Sousse, Tunisia

INTRODUCTION

Congenital cardiopathies (CC) complicate almost 1% of births. Although most often isolated, a genetic abnormality is found in nearly 15% of the CC according to the literature.

The objective of this work is to specify the genetic abnormalities involved in CC.

METHODS

This is a retrospective study carried out in the maternity and neonatal center of Sousse for an 8-year period. During this study, the various etiologies, including genetic abnormalities found in the genesis of CC.

RESULTS

During the study period 181 cases of CC were diagnosed. Heart disease was isolated in 128 newborns (70.71%). Chromosomal abnormalities were present in 34 newborns (18.8% of cases) and genetic syndromes in 5 newborns (2.76%). Chromosomal aberrations were dominated by trisomy 21 (14 newborns, 41.2%). There were 6 cases of atrioventricular canal (AVC), 3 cases of interventricular communication (IVC), 2 cases of interauricular communication (IAC), 2 cases of pulmonary stenosis (PS) and 1 case of unique ventricle (UV). A 22q11 deletion was found in 13 newborns (38.2%). These were 3 cases of UV, 3 cases of AVC, 2 cases of Fallot tetralogy, 1 case of triatrial heart, 1 case of common truncus arteriosus, 1 case of pulmonary atresia, 1 case of tricuspid anomaly and one case of agenesis of the pulmonary valve. The other anomalies were trisomy 18 in 3 newborns, trisomy 13 in 2 newborns, translocation (14,21) in a newborn and a mosaic abnormality in a newborn. The CC was integrated into a genetic syndrome in 5 cases. It was a Holt-Oram syndrome in one case, an Ellis Van Creveld syndrome in one case, a Pierre Robin sequence in one case, a Bardet-Biedel syndrome in one case and a VACTERL association in one case. The cardiopathy was dominated by the AVC found in 3 neonates.

CONCLUSIONS

Cytogenetic analysis for an abnormality of chromosome number or structure is indicated for most congenital heart disease diagnosed in antenatal or postnatal, with the exception of simple transplantation of large vessels (TGV) Never associated with an abnormality of number of chromosomes. In the newborn, dysmorphology will guide the genetic investigation. The detailed description of the cardiac phenotype to the geneticist is essential. Indeed, there are, more often, cardiopathies specific to certain syndromes. Identifying a genetic cause for CC will allow for early detection in subsequent pregnancies and genetic counseling for families.

ABS 26

USE OF PROSTIN IN A TERTIARY NEONATAL UNIT

R. Prasad, H. Wood, O. Nolan, S. V. Rasiah

Neonatal Intensive Care Unit, Birmingham Women's and Children's NHS Foundation Trust, Birmingham, UK

INTRODUCTION

Prostaglandin is predominantly used when a duct-dependent cardiac lesion is suspected or identified. Many babies are diagnosed with a duct dependent cardiac abnormality in the antenatal period by foetal echocardiography. Postnatal duct-dependent cardiac abnormalities are diagnosed based on clinical signs or failed pulse-oximetry screening which prompt postnatal echocardiography. Prostaglandin is also used in the management of severe persistent pulmonary hypertension of the newborn (PPHN) in conditions like congenital diaphragmatic hernia (CDH). The aim of our study was to audit the use of prostaglandin in a tertiary neonatal unit.

METHODS

Neonates treated with prostaglandin between 01/04/2009 and 31/03/2017, were identified from the Badger.net electronic patient database using the search terms "prostin", "prostaglandin", "dinoprostone", "alprostadil". Each individual patient record was reviewed to collect data on indication, diagnosis and outcome using a standardised proforma.

RESULTS

253 babies were treated with prostaglandin. Their gestation ranged between 26-42 weeks and their birth weight ranged between 720-4,500 g. Indications for prostaglandin included: 190 antenatal cardiac abnormalities, 19 congenital diaphragmatic hernia,

29 postnatal clinical signs, 15 failed pulse-oximetry. Of the babies who failed pulse-oximetry screening, 10 (66%) had cardiac abnormalities and 5 (34%) had PPHN. The cardiac abnormalities identified following a failed pulse-oximetry screening included 3 Transposition of the great arteries, 4 right ventricular outflow tract obstruction and 3 left ventricular outflow obstruction. Their outcomes were as follows: 83% of babies were transferred to the specialist centre; 7% of babies were discharged home; 10% of babies died on the neonatal unit.

CONCLUSIONS

The predominant indication for prostaglandin infusion was for antenatally diagnosed duct-dependent cardiac abnormalities. As the centre for managing antenatally detected CDH, we use prostaglandin infusion for the management of severe PPHN in these babies. We found that pulse-oximetry screening was helpful in the postnatal detection of duct-dependent cardiac abnormalities in asymptomatic babies with a "normal" foetal anomaly scan.

ABS 27

THE USABILITY OF ICON FOR NEONATOLOGY

W.P. de Boode, B.M. Wulterkens, B.A.M. Nieuweweme

Radboud UMC Nijmegen, University of Twente, Nijmegen, the Netherlands

INTRODUCTION

The cardiac output (CO) is an important parameter for hemodynamic monitoring in neonates. The ICON® is a device that measures the CO continuously and non-invasively. In this pilot study the usability of ICON is investigated in different conditions such as term versus preterm neonates, spontaneous ventilation compared with mechanical ventilation, the influence of a patent ductus arteriosus (PDA), the influence of a lower core temperature, displacement of one of the electrodes and critically ill neonates suffering from excessive edema.

METHODS

In total, fifteen patients are measured. Measurement failed in seven measurements because of several limitations. Average CO and stroke volume (SV) per hour give an overview of the measurement. The CO, heart rate (HR), SV and SQI are compared with the moving average (± SD) to examine the variability of the signal. During some measurements length and weight settings were changed. Finally Bland-Altman analysis is used for analyzing the agreement between HR detected by the olden standard ECG and detected by ICON.

RESULTS

Results show a decrease in CO after displacement of one of the electrodes, an increase in CO after closing PDA, ambiguous outcomes during measurement of a patient receiving HFO and no signal detection during measurement of a patient experiencing excessive edema. Bland-Altman analysis shows a wide range in LOA, which indicates that the methods do not detect HR equivalent. Also did a 10 percent discrepancy in the length or weight settings give an alteration up to 13 percent of the SV.

CONCLUSIONS

It can be concluded that non-invasive CO measurement in the clinical setting with ICON® is not reliable and not recommended at this moment. When in the future the measurements show higher agreement with reality, then it should be taken into account that the weight and length of a neonate has a big influence in the measurement.

ABS 28

ASSESSMENT OF NEONATAL HEART RATE IMMEDIATELY AFTER BIRTH USING DIGITAL STETHOSCOPE, HAND HELD ULTRASOUND AND ELECTROCARDIOGRAPHY

B. Treston, J. Semberova, R. Kernan, E. Crothers, A. Branagan, N. O'Cathain, J. Miletin

Department of Neonatology, The Coombe Women and Infants University Hospital, Dublin, Ireland

INTRODUCTION

The extent and initiation of cardiopulmonary resuscitation of neonates in the delivery room is largely guided by neonatal heart rate (HR). This is usually assessed by stethoscope auscultation. New Neonatal Resuscitation Guidelines have recommended the use of Electrocardiography (ECG) for HR determination during resuscitation as this was found to be the most accurate and efficient method to detect and monitor HR. Our aim was to determine the time to achieve first HR after delivery by handheld ultrasound (HUS), digital stethoscope (DS) and ECG, and compare these to auscultation, and observe the differences in HR achieved.

METHODS

Women who were planned for elective caesarean sections were recruited prior to delivery. Two

physicians attended these deliveries, one assessed the HR by stethoscope auscultation and the second assessed the HR using either HUS (Mortara, Signos RT Personal Ultrasound), DS (Littmann® 3200, 3M, US) or ECG. The time to achieve first HR and the HR recorded was noted. Then, when both modalities were recorded, a simultaneous HR was recorded.

DISCUSSION

Sixty participants were recruited in total (twenty in each modality group). The mean birth weight (± SD) of the cohort was 3.46 kg (± 0.43) and mean gestational age was 38.8 (± 0.83) weeks of gestation. The median time from birth to first HR recording by ECG was 98 seconds (compared to 85 seconds by stethoscope; p = 0.002), the median time to achieve HR after placing the device was 13 seconds (compared to 13 seconds by stethoscope, p = 0.74). The median time from birth to achieve HR by HUS was 113.5 seconds (compared to 90 seconds by stethoscope; p = 0.02), the median time to achieve HR after placing the device was 28 seconds (compared to 15 seconds by stethoscope, p = 0.007). The median time from birth to achieve HR by DS was 120 seconds (compared to 130 seconds by stethoscope; p = 0.37), the median time to achieve HR after placing the device was 45 seconds (compared to 11 seconds by stethoscope, p = 0.015). There was no reading of HR in six patients in digital stethoscope group (due to technical reasons). The mean difference between stethoscope and ECG in the HR was -10 bpm, between stethoscope and handheld US was +5 bpm and between stethoscope and digital stethoscope was +32 bpm.

ABS 29

NEW IBUPROFEN DOSAGE REGIMEN FOR PATENT DUCTUS ARTERIOSUS FOLLOWING SIMULATIONS BASED ON PHARMACOKINETIC-PHARMACODYNAMIC EVIDENCE

R. Flint[1,2,3], R. ter Heine[2], E. Spaans[1], D. Burger[2], J. de Klerk[1], K. Allegaert[4,5], C. Knibbe[6,7], S. Simons[1]

[1]Department of Paediatrics, Division of Neonatology, Erasmus University Medical Center – Sophia Children's Hospital, Rotterdam, the Netherlands

[2]Department of Pharmacy and Radboud Institute of Health Sciences (RIHS), Radboudumc, Nijmegen, the Netherlands

[3]Department of Pharmacy, Erasmus MC, Rotterdam, the Netherlands

[4]Department of Paediatric Surgery, Erasmus University Medical Center – Sophia Children's Hospital, Rotterdam, the Netherland

[5]Department of Development and Regeneration KU Leuven, Leuven, Belgium

[6]Leiden Amsterdam Center for Drug Research (LACDR), Division of Pharmacology, LACDR, Leiden University, Leiden, the Netherlands

[7]Department of Clinical Pharmacy, St Antonius Hospital, Nieuwegein, the Netherlands

INTRODUCTION

Ibuprofen is the first choice pharmacological treatment for patent ductus arteriosus (PDA) in preterm infants with only 60% effectiveness following the licensed 10 mg/kg single dose on day 1, followed by 5 mg/kg on day 2 and 3 (10-5-5). Despite the endless number of studies on ibuprofen for PDA and the various suggested dose adjustments, an improved and accepted dosing regimen is still lacking. We intended to combine evidence on ibuprofen dosage regimens and their effect on PDA closure to propose an S-ibuprofen target concentration. Simulation of plasma concentration-time profiles would serve to compare different dosing regimens, and guide the way to an optimal ibuprofen dosage regimen.

METHODS

Simulations of plasma concentration-time profiles of R- and S-ibuprofen were performed with the single population PK model for S-ibuprofen in preterm infants for several dosing regimens in typical preterm infants with PDA (PNA 24 hours, BW 840 grams) using NONMEM. We proposed to aim for a predefined target level S-ibuprofen of 43 mg/L at 72 hours after start of therapy, to maintain the reversible competitive inhibitory effect of S-ibuprofen on COX-2. This target was abstracted from simulations of the most effective studied intravenous dosage regimen on closure of the ductus, 20-10-10 mg/kg single dose per day, whereas the through concentration of the conventional 10-5-5 regimen was determined to be 21 mg/L.

RESULTS

The simulations revealed that a preterm neonate with postnatal age of 24 hours may optimally receive an ibuprofen loading dose of 17 mg/kg, followed by a maintenance dose of 7.2 mg/kg/day in twice-daily until sufficient effect has been achieved or treatment needs to be terminated for other reasons. In comparison with 20-10-10, a 13% lower total 3-day dosage led to comparable trough concentrations, together with 28% lower peak concentrations, a 26% reduced peak concentration range. In order to reach the same target S-ibuprofen concentration of 43 mg/L with continuous infusion, a loading dose of 14 mg/kg was required, followed by a maintenance dose of 6.5 mg/kg/day. Plasma concentration-time profiles after restarting a

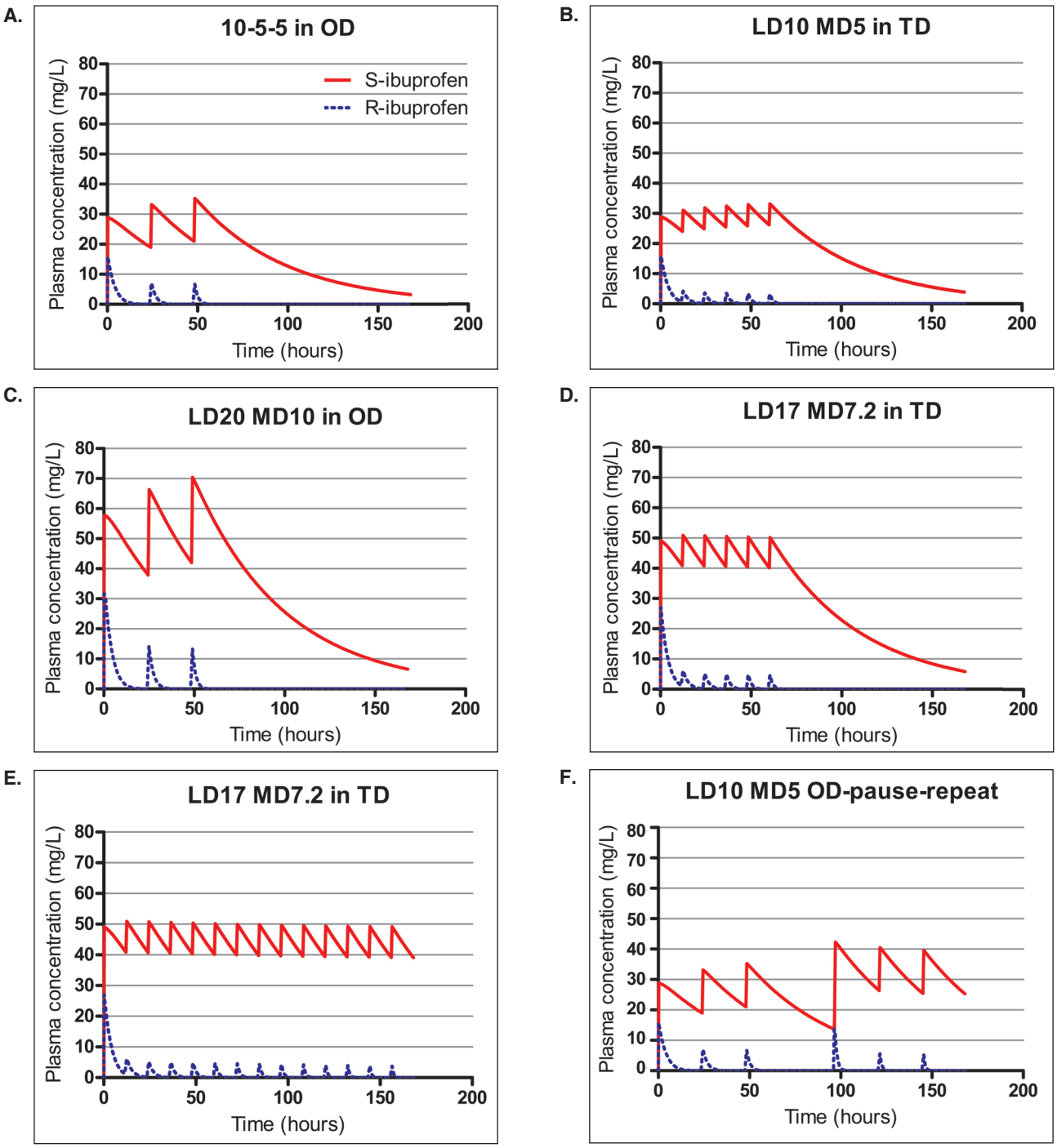

Figure 1 (ABS 29). Simulation on predicted plasma concentration-time profile of R- and S-ibuprofen.

Population predictions were performed for 1 typical neonate with a bodyweight of 840 grams and a postnatal age of 24 hours.

The following dosing regimens are shown in the graphs **A-G**.

A. 10 mg • kg^{-1} LD, followed by 5 mg • kg^{-1} • day^{-1} in once-daily on day 2 and 3. **B.** 10 mg • kg^{-1} LD, followed by 5 mg • kg^{-1} • day^{-1} in twice-daily on day 1-3. **C.** 20 mg • kg^{-1} LD, followed by 10 mg • kg^{-1} • day^{-1} in once-daily on day 2 and 3. **D.** 17 mg • kg^{-1} LD, followed by 7.2 mg • kg^{-1} • day^{-1} in twice-daily on day 1-3. **E.** 17 mg • kg^{-1} LD, followed by 7.2 mg • kg^{-1} • day^{-1} in twice-daily on day 1-7. **F.** 10 mg • kg^{-1} LD, followed by 5 mg • kg^{-1} • day^{-1} on day 2 and 3, and a second course 10-5-5 on day 5-7. **G.** 14 mg • kg^{-1} LD, followed by 6.5 mg • kg^{-1} • day^{-1} by continuous infusion on day 1-3.

LD: loading dose; MD: maintenance dose; OD: once-daily; TD: twice-daily.

second 3-day course of 10-5-5 on day 5, showed a substantial dip in S-ibuprofen plasma concentration on day 4 together with a high peak concentration on day 5 (**Fig. 1**).

CONCLUSIONS

Based on current knowledge that the licensed ibuprofen dosage regimen is insufficient for treating PDA, we suggest to use a loading dose of 17 mg/kg, followed by a maintenance dose of 7.2 mg/kg/day in twice-daily until sufficient effect has been achieved. Thereby, sufficient inhibition of COX-2 may be achieved, without exposing preterm infants to unnecessarily high S-ibuprofen peak concentrations that have not been proven safe. The proposed regimen requires prospective evaluation.

ABS 30

WHAT IS THAT PULSATING ON THE ANTERIOR ABDOMINAL WALL?

O. Nolan, R. Prasad, P. Miller, M. Singh, S.V. Rasiah

Birmingham Women's Hospital, Neonatal Department, Birmingham, UK

INTRODUCTION

Pentalogy of Cantrell is a rare syndrome comprising of defects in the heart, pericardium, diaphragm, abdominal wall and sternum affecting approximately 5.5 people per million. It is thought to arise from an abnormality in midline embryonic tissue development. This is a case of classical Pentalogy of Cantrell.

CASE REPORT

A male Caucasian baby with antenatal diagnosis of complex cardiac disease (TAPVD, DORV, VSD and PS) and no other antenatal abnormalities was born at term by elective caesarian section. Baby was born in good condition, did not require any resuscitation but was noted at delivery to have an abdominal wall defect at the level of the umbilicus but extending superior to this. The defect was strongly pulsatile below the xiphisternum on observation and palpation. The baby was taken to the neonatal unit and a post natal echo showed mesocardia, DORV, VSD, PS and query cor triatriatum. The pulmonary veins came to a confluence behind the left atrium but did flow from this to the left atrium. The baby remained clinically and haemodynamically stable. He was self-ventilating in air with saturations > 90%. No other defects were noted on examination. An abdominal USS showed an underlying pulsatile area in the epigastrium which was in continuity with the heart and was thought to represent the apex or an aneurismal segment. The baby was reviewed on the neonatal unit by a paediatric cardiologist and paediatric surgeon. His abdominal defect was dressed appropriately and transferred to the local tertiary paediatric cardiology and surgical center, where a diagnosis of Pentalogy of Cantrell was confirmed.

CONCLUSIONS

Although Pentalogy of Cantrell is rare, incomplete variants are less so and therefore it is important that babies born with superior abdominal defects will be investigated for cardiac defects.