Real-world impact of routine screening and early targeted PDA treatment approach on intraventricular hemorrhage in extremely low gestational age neonates: A single-center pre-post cohort study

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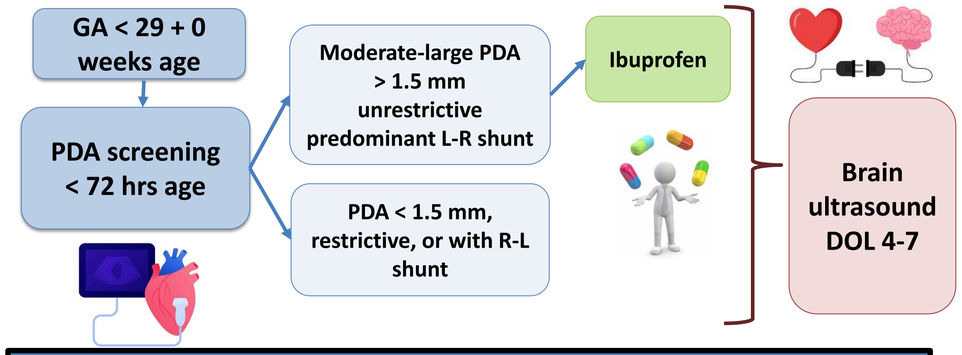
Aim

To reduce the incidence of intraventricular hemorrhage in extremely low gestational age neonates [ELGANs, <29 weeks gestational age] by implementing early Patent Ductus Arteriosus (PDA) screening using Targeted Neonatal Echocardiography (TNE) and targeted pharmacological treatment.

Importance

Intraventricular Hemorrhage (IVH) is a leading cause of brain injury and future neurodevelopmental deficit. Despite controversy surrounding PDA management, emerging research suggests that early PDA screening and pharmacological treatment may influence IVH outcomes.

Framework



Change plan

We implemented practice change from "**symptomatic treatment**" of PDA, to "**routine screening and targeted treatment**", meaning that all the infants born before the 29 weeks of gestation had PDA screening within the first 72 hours of age. We compared IVH rate and other neonatal outcomes for 2 epochs: 18 months pre- and post-implementation.

Results

Table 1- TNE implementation metrics

	Pre-Epoch (N=282)	Post-Epoch (N= 256)	p value
TNE performed for PDA	133 (47.2)	239 (93.4)	**<0.01**
Age at first TNE for PDA	4 (3, 6)	2 (2, 3)	**<0.01**
Received treatment for PDA	99 (35.1)	107 (41.8)	0.11
Age at first treatment for PDA	6 (4, 10)	3 (2, 5)	**<0.01**

Table 2- Demographics and baseline characteristics

Perinatal Characteristics	Pre-Epoch (N=282)	Post-Epoch (N= 256)	p value
Gestational age, weeks	26.4 (1.9)	26.3 (1.8)	0.74
Birthweight, grams	875 (256)	871 (240)	0.85
Female sex	126 (45)	121 (47)	0.55
Small for gestational age	28 (9.9)	19 (7.4)	0.30
Maternal age, years	32.7 (5.4)	32.3 (5.5)	0.36
Multiple pregnancy	67 (23.8)	66 (25.8)	0.59
Rupture of membranes > 18 hrs	108 (38.3)	92/252 (36.5)	0.67
Antenatal Steroids complete course	198 (70.2)	173/255 (67.8)	0.55
Antenatal Steroids partial course	68 (24.1)	65/255 (25.5)	0.71
No antenatal steroids	16 (5.7)	16/ 255 (6.3)	0.58
Intrapartum MgSO4	258 (91.5)	200/254 (78.7)	<0.01
Outborn	21 (7.4)	16 (6.2)	0.58
C-section	156 (55.3)	136 (53.1)	0.61
Delayed cord clamping performed	165 (58.5)	134/250 (53.6)	0.25
Apgar score 10 min	8 (6, 8.5)	8 (5.5, 9)	0.80
Umbilical cord pH	7.24 (0.12)	7.24 (0.11)	0.84
Chest compression or epinephrine during resuscitation	5 (1.8)	12 (4.7)	0.05
Early onset sepsis	9 (3.2)	10 (3.9)	0.65

Table 4: Adjusted odds ratios (AOR) of primary and secondary clinical outcomes for post- vs. pre-PDA screening after adjusting for covariates using propensity score method

	Raw odds ratio (95% CI)	MLR analysis aOR (95% CI)	PSM analysis aOR (95%CI)
IVH grade ≥ 2	0.64 (0.40, 1.03)	0.6 (0.37, 1)	0.62 (0.37, 1.04)
All grades IVH	**0.40 (0.28, 0.57)**	**0.33 (0.23, 0.49)**	**0.31 (0.21, 0.46)**
IVH grade 3 /4	0.59 (0.34, 1.04)	0.56 (0.31, 1)	**0.51 (0.28, 0.94)**
Mortality	0.96(0.55, 1.65)	0.84 (0.45,1.56)	0.75 (0.39, 1.43)
BPD †	0.98 (0.68, 1.4)	0.9 (0.59, 1.37)	0.81 (0.53,1.26)
BPD moderate or severe †	1.16 (0.8, 1.69)	1.21 (0.79, 1.87)	1.01 (0.64, 1.59)
Composite outcome mortality or BPD	0.97 (0.69, 1.37)	0.87 (0.57, 1.31)	0.79 (0.52, 1.21)

Propensity score method matched cohort (n=243 in each group) accounting for gestational age, small for gestational age, no antenatal corticosteroids, outborn status, delayed cord clamping and resuscitation at birth with chest compression/epinephrine. † = for survivors only.

Table 3- Comparison of primary and secondary outcomes and TNE implementation

	Pre-Epoch (N=282)	Post-Epoch (N= 256)	p value
Primary outcome			
*IVH grade ≥ 2	54/280 (19.3)	34/255 (13.3)	0.06
Distribution of ultrasound diagnosis of various brain injuries			
*All grades IVH [n %)]	180/280 (64.3)	107/255 (42.0)	**<0.01**
IVH grade 1	126/280 (45)	73/255 (28.6)	**<0.01**
IVH grade 2	17/280 (6.1)	13/255 (5.1)	0.63
IVH grade 3	13/280 (4.6)	2/255 (0.8)	**0.01**
IVH grade 4	24/280 (8.6)	19/255 (7.5)	0.63
†PHVD [n %)]	7/251 (2.8)	10/229 (4.4)	0.35
€†Cystic PVL [n %)]	3/251 (1.2)	5/229 (2.2)	0.39
Other prematurity -related outcomes in all patients			
Any pulmonary hemorrhage [n %)]	15 (5.3)	21 (8.2)	0.18
Spontaneous Intestinal Perforation [n %)]	9 (3.2)	6 (2.34)	0.56
Necrotising Enterocolitis [n %)]	49 (17.4)	37 (14.45)	0.37
Late onset sepsis [n %)]	54 (19.2)	60 (23.43)	0.22
Mortality [n %)]	31 (11.0)	27 (10.6)	0.87
Composite outcome mortality or BPD	160 (56.7)	143 (55.8)	0.84
†Days of invasive ventilation PDA (median, IQR)	1 (0, 7)	1 (0, 6)	0.99
†Any BPD [n %)]	129/251 (51.39)	116/229 (50.88)	0.87
†BPD moderate or severe [n %)]	85/251 (33.86)	85/229 (37.28)	0.46
†Retinopathy of Prematurity > stage 3 [n %)]	21/228 (9.21)	24/204 (11.76)	0.39
PDA-related Outcomes			
Number of medical courses for PDA (median, IQR)	1 (1, 2)	1 (1, 2)	0.23
PDA device closure or surgical ligation [n %)]	10 (3.55)	9 (3.52)	0.98

*2 patients in the Pre-implementation and 1 in post implementation died prior to diagnosis of IVH on brain ultrasound. † In infants who survived to discharge

Lessons Learned

Our project demonstrates the real-life impact of early targeted pharmacological PDA closure on improving IVH rate, without causing an increase in overall rate of PDA treatment.

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