Effect of hemodynamically significant patent ductus arteriosus on systemic blood flow, perfusion index and amplitude integrated electro-encephalogram in neonates

Thesis

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Mariam John Amin Ibrahim

Contents

List of Abbreviations

2D	:	Two-dimensional
A wave	:	Late active phase
AC	:	Arterial component
aEEG	:	Amplitude-integrated electroencephalographm
Ao	:	Aorta
AoCSA	:	Aortic root cross sectional area
ARF	:	Acute renal failure
BS-	:	Burst density <100 bursts/h
BS+	:	Burst density >100 bursts/h
BSA	:	Burst-suppression
C	:	Continuous
CBC	:	Complete blood count
cEEG	:	Conventional EEG
CFM	:	Cerebral function monitor
CHD	:	Congenital heart disease
CNS	:	Central nervous system
CI	:	Confidence interval
COX	:	Cyclo-oxygenase enzyme
CPAP	:	Continuous positive airway pressure.
CRP	:	C-reactive protein
CSF	:	Cerebrospinal fluid
CWD	:	Continuous wave Doppler
DAo	:	Descending aorta
DBP	:	Diastolic blood pressure
Dc	:	Discontinuous
DC	:	The non-pulsatile component
E wave	:	Early passive phase
ECMO	:	Extracorporeal membrane oxygenator
EDTA	:	Ethylenediaminetetraacetic acid
EEG	:	Electroencephalogram
ELBW	:	Extremely low birth weight
FiO2	:	Fractional concentration of inspired oxygen.
FnECHO	:	Functional echocardiography

List of Abbreviations (Cont.)

FT	:	Inactive flat
HFV	:	High frequency ventilation.
HsPDA	:	Hemodynamically significant PDA
Hz	:	Hertz
IBI	:	Interburst interval
IQR	:	Interquartile range
IR	:	Infrared
IV	:	Intra-venous
LA	:	Left atrium
LED	:	Light emitting diode
LPA	:	Left pulmonary artery
Lv	:	Low voltage
LV	:	Left ventricle
LVEDD	:	Left ventricular end-diastolic diameter;
LVESD	:	Left ventricular end-systolic diameter.
LVO	:	Left ventricular output
MAP	:	Mean airway pressure.
MBP	:	Mean blood pressure
MCA	:	Middle cerebral artery
mcV	:	Micro-volt
MPA	:	Main pulmonary artery
Mv	:	Mitral valve
NEC	:	Necrotizing enterocolitis
NICU	:	Neonatal intensive care unit
NIPPV	:	Non invasive positive pressure ventilation .
NSE	:	Neuron specific enolase
OD	:	Optical density
OR	:	Odds ratio.
PAI	:	Pulse Amplitude Index
PDA	:	Patent ductus arteriosus
PEEP	:	Positive end-expiratory pressure.
PGE2	:	Prostaglandin E2
PGI2	:	Prostacyclin
PI	:	Perfusion index

List of Abbreviations (Cont.)

PIP	:	Peak Inspiratory pressure.
PPG	:	Photoplethysmography
PPI	:	Peripheral perfusion index
PWD	:	Pulsed wave Doppler
RA	:	Right atrium
RDS	:	Respiratory distress syndrome
RPA	:	Right pulmonary artery
RV	:	Right ventricle
RVO	:	Right ventricular output
RVSP	:	Right ventricular systolic pressure
SaO2	:	Oxygen saturation
SBP	:	Systolic blood pressure
SET	:	Signal Extraction Technology
SIMV	:	Synchronized intermittent mandatory ventilation.
SV	:	Stroke volume
SVC	:	Superior vena cava
SWC	:	Sleep wake cycling
Ti	:	Inspiratory time.
Tv	:	Tricuspid valve
TV	:	Tidal volume.
VTI	:	Velocity time integral

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Introduction

Patent ductus arteriosus (PDA) is a major morbidity in preterm infants, especially in extremely premature infants less than 28 weeks. The clinical signs and symptoms of PDA in preterm infants are non specific and insensitive for making an early diagnosis of significant ductal shunting. Functional echocardiography is emerging as a new valuable bedside tool for early diagnosis of hemodynamically significant ductus, even though there are no universally accepted criteria for grading the hemodynamic significance ***(Sasi and Deorari, 2011).***

Natural ductal closure is inversely related to gestational age and birth weight. The incidence of PDA ranges from 15% to 37% in newborn babies less than 1750 grams; this is very high compared to incidence of 2/1000 in term newborns. However, this does not mean that all PDA in preterm infants are hemodynamically significant warranting treatment ***(Jegathesen et al., 2008).***

The presence of PDA has significant effects on myocardial functions as well as systemic and pulmonary blood flow. Preterm newborns adapt, by increasing the left ventricular contractility, and thereby maintaining the effective systemic blood flow even when the left to right shunts equals 50% of the left ventricular output. This is mainly accomplished by an increase in stroke volume (SV) rather than heart rate. This increase in stroke volume is primarily due to reduction in after load and simultaneous increase in left ventricular preload ***(Shimada et al., 1994).***

Despite the increased left ventricular output, there is a significant redistribution of blood flow to major organ systems, with the presence of *ductal steal* seen in PDA due to left to right shunt, the maximum of which occurs at the beginning of the cardiac systole when the pressure gradient is maximum ***(Clyman, 2006).***

This steal phenomenon may lead to systemic hypoperfusion, despite increased cardiac output. Hence hemodynamically significant PDA (HsPDA) has a negative effect on cerebral circulation and oxygenation, which may lead to injury to the immature brain ***(Lemmers et al., 2008).***

With the emergence of functional echocardiography, the identification of PDA with hemodynamic significance is made well before the clinical manifestations set in. This emerging practice of identifying significant ductus early in life, often within first 24 hours, by in house echocardiography and instituting treatment is called early targeted treatment ***(Osborn et al., 2003)***.

The hemodynamically significant PDA is determined echocardiographically with Trans-ductal diameter ≥ 1.4 mm, Left pulmonary artery diastolic flow peak velocity ≥ 0.2 cm/secand left atrium/ aortic root ratio ≥ 1.4. ***(El Hajjar et al., 2005).***

First line treatment is optimizing oxygen delivery by treating anemia and achieving adequate arterial oxygen tension, as well as employing fluid restriction and diuretics ***(Yates, 2012).***

The pharmacological basis for medical therapy is the use of non selective cyclo-oxygenase (COX) inhibitors, which inhibits prostaglandin synthesis and causes ductal constriction. The two most widely studied and used non selective COX inhibitors are indomethacin and ibuprofen ***(Narayanan and Clyman, 2003).***

Many studies have compared the use of oral ibuprofen versus intra-venous (IV) indomethacin and IV ibuprofen and have confirmed the high closure rates and favorable safety profile of oral ibuprofen. This is why we use oral ibuprofen in our hospital in addition to its availability and cheapness ***(Yang et al., 2013; Erdeve et al., 2012).***

Despite three decades of intense research enrolling thousands of preterm infants, evidence for the long term benefits of pharmacological closure of PDA is inconclusive and debatable. There is an emerging school of thought advocating conservative approach, with medical therapy reserved for compelling indications like refractory hypotension or congestive heart failure attributed to large ductal shunt ***(Bose and Laughon, 2007).***

The decision to treat PDA depends on 3 factors - the spontaneous closure rate, adverse effect of ductal patency, and risk benefit of treatment ***(Benitz, 2010).***

The hemodynamic condition of newborn infants is often assessed by clinical variables such as heart rate, blood pressure and capillary refill. However, these markers are all poorly correlated to central blood flow, which seems to be a more accurate variable for determining the hemodynamic condition of newborn infants ***(Sehgal and McNamara, 2008)***.

Central blood flow can be measured in the great vessels entering or leaving the heart and the most commonly measured flows in newborn infants are right ventricular output (RVO), left ventricular output (LVO) and superior vena cava (SVC) flow. Studies in preterm infants have shown that abnormal central blood flow is associated with poor neuro developmental outcome ***(Hunt et al., 2004).***

Perfusion index (PI) is a noninvasive method of measuring peripheral perfusion and represents an objective assessment of the strength of the pulse. Perfusion Index may be a promising adjunct to the assessment of circulatory status in the newborn. The foot PI measured by pulse oximetry seems to be mre feasible for monitoring peripheral perfusion in the neonatal intensive care unit ***(Zaramella et al., 2005; De felice et al., 2002).***

The relation between perfusion index and systemic blood flow has yet to be studied, especially in neonates with HsPDA. We will try to achieve this in our present study.

Although several neuro-imaging and neurophysiologic methods have been developed, cerebral function monitoring has not been included in the routine neonatal intensive care unit (NICU) yet. Electroencephalography (EEG) is considered the standard method for intermittent evaluation of functional brain