ID: 515
TITLE: SHOCK IN THE FIRST 72 HOURS OF LIFE IN VERY LOW BIRTH WEIGHT INFANTS: DOPAMINE OR DOBUTAMINE?
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CONTENT:

During the transition to extraterine life, preterm infants have a higher risk of developing circulatory failure and shock. Different pharmacological agents are used for the management of hemodynamic instability in this transition period. The main drugs used as first choice in the hemodynamic approach in this period are dopamine and dobutamine, but evidence about which inotrope should be used is lacking. The objective is to evaluate the association between dopamine or dobutamine use and unfavorable outcomes in very low birth weight infants with shock in the first 72 hours.

Cohort study. Preterm infants <1500g born between 2010 and 2018 were included, excluding deaths in the delivery room, malformations, and concomitant use of dopamine and dobutamine. Patients were divided into 2 groups: Group 1: use of dopamine. Group 2: use of dobutamine. The choice of the first drug in the shock (defined as the presence of hypotension-arterial pressure less than gestational age) was determined by the medical staff. Outcomes: pulmonary hemorrhage, death until 7 days, intraperiventricular hemorrhage and leukomalacia were evaluated. In order to estimate the gross and adjusted relative risks, simple and multiple log-binomial regression models were considered. The covariates were sepsis, SNAPPEII, delivery hemorrhage and gestational age. The software used was SAS 9.4 and R3.5.1

For the study 1268 neonate with birth weight <1500g were selected and 316 (24.9%) required vasoactive drug. Of these, 22 (6.9%) presented malformations and 155 (49%) used associated dopamine and dobutamine and were excluded from the analysis, completing the study 139 patients. Of these, 50 (35.9%) used dopamine and 89 (64.0%) used dobutamine. The means of gestational age and birth weight of patients who used dopamine and dobutamine were 868.10g (SD 299.78) and 26.88 weeks (SD 2.82) vs 858.99g (SD 279.24) and 27.50 weeks (SD 2.88). The dopamine use was associated with death until seven days of life (adjusted RR(CI95%)= 1.53 [1.04: 2.77]). However, the use of dobutamine was associated with occurrence of pulmonary hemorrhage (adjusted RR(CI95%)= 2.21, [- 1.13: 4.31]). No association was found between the use of dobutamine or dopamine with perinventricular hemorrhage or leukomalacia.

The use of the dopamine as the first choice in shock in the first 72 hours in very low birth weight infant is associated with death until 7 days of life. However, the use of dobutamine is associated with pulmonary hemorrhage. Therefore, according to our data, dobutamine is the drug indicated for the premature patient in the first 72 hours; however the use was associated with unfavorable outcomes, so the use should to be done with criteria.

IMAGES:
[https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=a04d1260940f5fdf9b14753833648cd3-MjAxOS0wNSM1Y2UyNyJy2Yzd0NDVI](https://www.eiseverywhere.com/eselectv3/v3/events/351149/submission/files/download?fileID=a04d1260940f5fdf9b14753833648cd3-MjAxOS0wNSM1Y2UyNyJy2Yzd0NDVI)

Table 1: Association between dopamine or dobutamine use and unfavorable outcomes.
COI: NONE DECLARED
ID: 751

**TITLE:** PRETERM INFANTS’ CARDIOVASCULAR RESPONSE TO CARDIO-RESPIRATORY EVENTS DURING TRANSITIONAL PERIOD.

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**CONTENT:**

Intermittent episodes of hypoxemia and/or bradycardia, also defined as cardio-respiratory events (CRE), are frequent in preterm infants and may result in transient hypoxia and hypoperfusion of target organs; concomitant changes in cardiac output (CO), cardiac contractility (CC) or systemic vascular resistances (SVR) may contribute to affect end-organ perfusion during CRE. In this study we aimed to explore cardiovascular hemodynamic changes determined by different CRE types in preterm infants during the first 72 hours (h) after birth, a period characterized by a significant hemodynamic instability with high risk of clinical complications.

During the first 72h, non-invasively ventilated newborns (gestational age <32 weeks, birth weight <1500 g) underwent a continuous, non-invasive pulse oximetry and electrical velocimetry monitoring for the assessment of the following parameters: arterial oxygen saturation (SpO2), heart rate (HR), stroke volume (SV), CO, CC, SVR. The monitoring data were simultaneously recorded via ICM+ software (Cambridge Enterprise Ltd, UK). CRE ≥10 sec were defined as isolated desaturation (ID, SpO2<85%), isolated bradycardia (IB, HR<100 bpm or <70% baseline) and combined desaturation/bradycardia (DB). Percentage changes (%Δ) of the recorded parameters between pre-event baseline and event nadir were analysed and compared among ID, IB and DB by Kruskal-Wallis test. Significance level was set at p<0.05.

A total of 767 events from 22 neonates (mean gestational age 30±2 weeks) were analysed. Of these, ID were 457 (59.6%), IB 121 (15.8%) and DB 189 (24.6%). SV and CO were indexed for the infants’ weight, whereas SVR were adjusted for their body surface area. Changes in cardiovascular parameters during different CRE event types are shown in Figure 1. As expected, %ΔHR decreased significantly during DB and IB compared to ID, but there was no difference between DB and IB. Compared with ID, DB and IB showed significantly increased %ΔSV and %ΔSVR, whereas a greater negative variation was observed for %ΔCO. %ΔCC reached significantly lower values during DB compared with ID and IB.

Cardiovascular responses to CRE differ significantly in relation to the event type, with possible clinical implications in terms of end-organ perfusion. In particular, the occurrence of bradycardia results in a transient CO decrease and SVR increase that, in the presence of concomitant hypoxia, may further reduce O2 delivery to end organs. Moreover, concomitant hypoxia may also play a role in the reduction of CC observed during DB.

**IMAGES:**

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Figure 1. Percentage changes from baseline of arterial oxygen saturation (%ΔSpO2), heart rate (%ΔHR), stroke volume (%ΔSV), cardiac output (%ΔCO), heart contractility (%ΔHC) and systemic vascular resistances (%ΔSVR) among different types of cardio-respiratory events (isolated desaturation, isolated bradycardia and combined desaturation and bradycardia) and results of pairwise comparison.
COI: None declared
ID: 523
TITLE: HEMODYNAMIC STUDY OF NEONATAL PIGS WITH SEPTIC SHOCK TREATED WITH METHYLENE BLUE: NEOPIG STUDY.
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CONTENT:

Introduction: Hemodynamic shock is an independent predictor of early mortality in neonates. The medications currently available for the shock are very aggressive and were associated with sequela.

Methylene blue (MB) promotes cGMP inhibition and have been advocated for the treatment of refractory shock. There are case reports about MB use in cardiac surgery or thoracic trauma in children, however the use of MB in neonatal patients is still controversial. There are not studies with neonatal animal models and MB in septic shock. The objective was to assess the methylene blue effects in neonatal animals with septic shock.

The neonate pigs (3 – 8 days of life) were separated in 4 groups (n group = 5 animals):
• Control: Animals sedated and ventilated (6 hours).
• Sepsis: Animals sedated, ventilated (6 h) and infusion of LPS Escherichia coli 0.06 mg/kg.
• Methylene Blue (sham): Animals sedated, ventilated (6 h) and administration of MB.
• Sepsis/ Methylene Blue: Animals sedated, ventilated (6 h) and infusion of LPS Escherichia coli and administration of MB.

Every animal received invasive monitoring for 6 hours. Echocardiogram was performed at the start of the experiment, after diagnosis of shock (decrease 20% in mean arterial pressure) and immediately after the installation of MB. Administration of MB: bolus of 2mg/kg (15 min), after 1 hour in continuous infusion at the dose of 0.5-2 mg/kg/h.

20 neonatal pigs were evaluated. The treated group had lower nitrate and Cyclic guanosine monophosphate (cGMP) values than the sepsis group, however, these values did not return to normal level (animal control level).

There was an increase in Invasive Arterial Pressure (20%), however, these levels were not maintained in the subsequent hours and did not return to normal level (animal control level).

The bicarbonate values and base excess improved and reached the normal levels (animal control level). (figure 1).

There was an increase in pulmonary artery pressure although no statistical difference in relation to PO2. There was no change in ventricular function and vena cava distensibility (Echocardiography evaluation).

Methylene blue elevates mean arterial pressure, but does not have the effect of reversing hemodynamic shock in neonatal septic animals. However, there was improvement of metabolic biomarkers (bicarbonate and Base excess), probably indicating a possible improvement in tissue perfusion. Studies should be performed to analyze the role of MB as adjuvant therapy in the treatment of septic shock.

I M A GE S:
https://www.eiseverywhere.com/eiselectv3/v3/events/351149/submission/files/download?fileID=efc9f6f24cb37497cdd4c01e5a206d71-MjAxOS0wNSM1Y2UyNyY2YzgwZDhi

Figure 1. Mean values of blood bicarbonate (HCO3-) and base excess (BE) of the control (PC), sepsis (PS), methylene blue (PA) and methylene blue + sepsis/treatment group (PSA).
COI: None declared
ID: 585

**TITLE:** THE HYPOTENSION IN PRETERM (HIP) INFANT TRIAL

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**CONTENT:**

The definition and management of low blood pressure (BP) in immature infants is controversial. A mean BP less than gestational age (GA) is the most common indication for intervention and volume followed by dopamine is the most commonly used treatment (standard approach). We wished to determine whether observational approach compared to this standard approach affects survival without significant brain injury at 36 weeks corrected GA in infants born before 28 weeks’ GA.

This randomised trial was conducted at 10 sites across Europe and Canada. Infants born before 28 weeks’ gestation were eligible for inclusion if they had mean BP less than their GA that persisted ≥15 minutes in the first 72 hours of life, an indwelling arterial line and a cerebral ultrasound free of significant (≥ grade III) intraventricular haemorrhage (IVH). Participants were randomly assigned to standard approach group – saline bolus followed by a dopamine infusion – or to observational approach group – saline bolus followed by a placebo (saline) infusion. Caregivers and outcome assessors were masked to group assignment. The primary outcome was survival to 36 weeks corrected GA without severe brain injury. The study was stopped early due to enrolment difficulties.

58 infants were enrolled between Feb 2015 and Sept 2017. There were no differences in GA, birth weight, Apgar scores, male sex, multiplicity, mean BP and mean lactate at enrolment between the groups (Table). There was no difference in the rate of the primary outcome between the standard approach group and the observational approach group [18/29 (62%) vs 20/29 (69%), p=0.58]. There were no differences in the rates of the individual components of the primary outcome, any degree of IVH or NEC /SIP between the two groups (Table). Among infants born before 26 weeks, additional treatments for low BP were used less often in the standard approach group [2/19 (10%) vs 12/19 (48%), p=0.002].

Conducting trials of haemodynamic support in extremely preterm infants is challenging. Though this study lacked power, we did not detect differences in clinical outcomes between standard or observational approaches to treatment. These results will inform future studies in this area; in the interim, either treatment approach appears reasonable.
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COI: None declared