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DESIGNAÇÃO DA ÁREA DO PROJECTO

Neonatologia

TÍTULO DISSERTAÇÃO/MONOGRAFIA (riscar o que não interessa)

Delivery room management of infants with less than 27 weeks of gestational age

ORIENTADOR

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Delivery room management of infants with less than 27 weeks of gestational age

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ABSTRACT

BACKGROUND: The medical management of a preterm birth is a challenge and there is not a definite consensus on how to deal with this situation. The aim of this study was to evaluate the effect of delivery room (DR) management on clinical condition (temperature, peripheral oxygen saturation, blood glucose level, hemoglobin level, mean blood pressure and pH) on the NICU (Neonatal Intensive Care Unit) admission of preterm infants born before 27^{+0} weeks of gestational age (GA).

METHODS: This study was performed among all preterm infants with a GA between 23^{+0} and 26^{+6} weeks admitted to the level III NICU of *Centro Hospitalar Universitário de São João* between 1st January 2005 and 31th December 2018. Maternal demographics, gestation information, infants' characteristics, DR and NICU data were evaluated.

RESULTS: A total of 65 preterm neonates were included in this study. The admission pH was associated to the administration of epinephrine in DR [B= -0.786; p = 0.003; 95%CI (-1.282;-0.290)]; blood glucose level to body weight on birth [B= 0.253; p = 0.006; 95%CI (0.078-0.428)] and epinephrine in DR [B= 72.719; p = 0.02; 95%CI (12.530-132.908)]; body temperature to epinephrine administrated in DR [B= -1.703; p = 0.001; 95%CI (-2.692;-0.714)]; and hemoglobin level to early CPAP in DR [B= 6.008; p = 0.013; 95%CI (1.356-10.660)].

CONCLUSIONS: DR procedures can have negative or positive effects on early outcomes of preterm newborns. It is crucial to research more about its impact to optimize the NICU management of this particular and challenging neonatal group.

Key words: preterm birth, extremely low gestational age, delivery room management, neonatal intensive care unit, neonatal mortality, neonatal resuscitation, limit of viability

Introduction

The World Health Organization states that a preterm birth occurs before 37 completed weeks of gestation or less than 259 days from the first date of a woman's last menstrual period (LMP) [1]. Prematurity accounts for 5 to 18% of worldwide births and is one of the leading causes of death in children under five years old [1]. In fact, it is one of the main causes of neonatal mortality [2,3] and is related with many neurodevelopmental disturbances, severe impairment and chronic diseases later in life [4,5]. Among preterm infants, the risk of development of abnormalities and mortality are uncertain in the extremely low gestational age newborns (ELGANs), born with less than 28 weeks [2].

The management of a preterm birth is delicate and complex, since it implicates medical, social and ethical issues and challenges [6]. As for this, there is no definite consensus in developed countries on how to approach these cases, even though there are many evidence-based recommendations and published guidelines [7].

Delivery room (DR) procedures in the first minutes of life may have a significant impact on the short and long-term outcomes of preterm infants. This period is referred to as the "Golden Hour", a term which is also applied in emergency medicine [8]. The management of preterm infants in this critical hour aims a better neonatal outcome especially in ELGANs. It should be held by specialized professionals and is structured by many components such as antenatal counselling and team briefing, resuscitation, temperature maintenance, support of the cardiorespiratory system, early nutritional care, hypoglycaemia and infection prevention, initiation of breast feeding, monitoring and communication with family [9].

The aim of this study was to evaluate the effect of DR management on clinical condition (pH, hemoglobin level, blood glucose level, peripheral oxygen saturation, mean blood pressure and body temperature) on NICU (Neonatal Intensive Care Unit) admission of preterm infants born before 27^{+0} weeks of gestational age (GA).

Materials and methods

This retrospective observational study was performed among all preterm infants with a GA between 23^{+0} and 26^{+6} weeks admitted to level III NICU of *Centro Hospitalar Universitário de São João*, over 14 years (1st January 2005 until 31th December 2018), with an average of 450 admissions per year [10].

After the approval of the institutional Ethics Committee, clinical records were reviewed and the data was collected. We excluded pregnancies with complications such as major congenital or chromosomal anomalies, a TORCH infection (Toxoplasmosis; Others - such as syphilis, parvovirus B19 or varicella-zoster; Rubella; Cytomegalovirus; and Herpes) and fetal hydropsis. The outborn infants and those transferred to other healthcare units in the first 24h of life were excluded too.

We did a demographic and perinatal characterization of the mother: age; GA (recorded as complete weeks) – assessment was based on menstrual age (in women with regular menstrual cycles), ultrasound examination (when a discrepancy of two or more weeks existed between the age derived by menstrual dating and the one derived sonographically, or in the absence of a menstrual date) [11] or the New Ballard Score (in the absence of obstetrical indexes) [12]; previous pregnancies; singleton or multiple gestation; assisted reproductive technology; smoking habits; usual medication, alcohol or drug consumption; complete cycles of antenatal corticosteroid (ACS) therapy; administration of magnesium sulfate; disorders associated with pregnancy such as: gestational diabetes, renal failure, hypertensive disease (defined as maternal blood pressure >140 mmHg systolic and >90 mmHg diastolic), preeclampsia (defined as hypertension accompanied with proteinuria), low platelets (HELLP syndrome), feto-fetal transfusion syndrome; clinical chorioamniotitis; placental abruption; placenta previa; fetal growth restriction (defined as estimated fetal

weight < 10^{th} centile for gestational age in Fenton's growth charts [13]); and abnormal umbilical flow.

Due to protocol changes in our centre, the ACS administrated to women before February 2014 was betamethasone followed by the use of dexamethasone since March 2014. A course consisted on two doses of 12mg of intramuscular betamethasone with 24-hour interval or four doses of 6mg intramuscular dexamethasone every 12 hours.

Data from peripartum period and labour were also studied. This information included preterm premature rupture of membranes (defined as membrane ruptured <18 hours before delivery), infant's gender and birth weight, type of delivery, abnormal amniotic fluid, fetal presentation and Apgar score at 1^{st} and 5^{th} minutes <5 or <7, respectively.

DR procedures such as oxygen administration, neonatal resuscitation (endotracheal intubation, chest compressions, epinephrine), ventilation equipments (invasive mechanic ventilation, early CPAP - continuous positive airway pressure), surfactant administration and umbilical cord pH level (arterial and venous) were included as well.

Neonates' hemoglobin level (g/dL), platelets (10^3/uL), blood glucose level (mg/dL), peripheral oxygen saturation (SpO2%), respiratory (cycles per minute) and heart (beats per minute) rates, systolic, diastolic and mean blood pressure (mmHg), temperature (degrees Celsius, ºC) and pH level were evaluated on the newborn admission to the NICU. Neonatal death was also considered.

Regarding clinical condition when NICU admission, we considered: anemia if hemoglobin (Hb) level < 12 g/dL [14]; hypoglycaemia if blood glucose level < 40 mg/dL; hypoxia if SpO2 < 94%; hypotension when mean blood pressure (BP) < GA [15]; hypothermia if temperature < 36.5ºC [15]; and acidosis if blood pH < 7.25.

The sample was divided in two major groups for the analysis: 24 or 25 weeks of GA and 26 weeks of GA. The preterms born at 23 weeks of GA were only 5 so we decided not to include them in the analysis and show their data separately.

Statistical analysis

Statistical analysis was performed using SPSS, version 25. Categorical variables were analyzed by absolute and relative frequencies and continuous variables were analyzed according to their distribution by mean (± standard deviation) for symmetric distribution or median (minimum–maximum) for asymmetric distribution. Categorical variables were evaluated by Chi-squared or Fisher's Exact Test and continuous variables by Independent T Test or Mann–Whitney U Test.

The impact of DR management on NICU admission was evaluated using linear regressions.

A p value <0.05 was considered as statistically significant.

Results

During the study period, 65 preterm neonates with GA between 23^{+0} and 26^{+6} weeks admitted to the NICU of *Centro Hospitalar Universitário de São João* were eligible from a total of 197 and included in this study. Maternal data is described in Table 1 whereas newborn data is summarized in Table 2.

Comparing neonates with 24-25 weeks of GA (n=33) to 26 weeks of GA (n=27), the univariate analysis in Table 1 showed statistically significant differences in gemelarity [19 (57.6%) vs 6 (22.2%); p = 0.006)], gestational diabetes [4 (12.1%) vs 10 (37.0%); p = 0.033], preeclampsia [1 (3.0%) vs 6 (22.2%); p = 0.039] and abnormal umbilical flow [0 vs 5 (18.5%); p = 0.015]. In Table 2, we also found through the univariate analysis that there

were statistically significant differences between the two groups regarding body weight at birth [695.6 (±126.8) vs 840.7 (±179.5); p = 0.001], eutocic delivery [24 (72.7%) vs 7 (25.9%); p < 0.001], endotracheal intubation in DR [30 (90.9%) vs 17 (63.0%); p = 0.026], invasive MV in DR [31 (93.9%) vs 18 (66.7%); p = 0.009], early CPAP in DR [2 (6.1%) vs 10 (37.0%); p = 0.004], surfactant in DR [15 (45.5%) vs 5 (18.5%); p = 0.028] and death [24 (72.7%) vs 8 (29.6%); p = 0.001].

Multivariate regression analysis of our sample was performed to control potential confounding variables and is shown in Table 3. The admission pH was associated to the administration of epinephrine in DR [B= -0.786; p = 0.003; 95%CI (-1.282;-0.290)]; body temperature was also related to epinephrine administrated in DR [B= -1.703; p = 0.001; 95%CI (-2.692;-0.714)]; the blood glucose level to body weight on birth [B= 0.253; p = 0.006; 95%CI (0.078-0.428)] and epinephrine in DR [B= 72.719; p = 0.02; 95%CI (12.530-132.908)]; and hemoglobin level to early CPAP in DR [B= 6.008; p = 0.013; 95%CI (1.356-10.660)].

About the 5 preterms with 23 weeks of GA: 3 (60%) cases were in multiple gestations; 4 (80%) mothers had antenatal corticotherapy but no complete cycles; 1 mother (20%) had preeclampsia; 1 (20%) had HELLP syndrome; and 3 (60%) had clinical chorioamniotitis. 100% of the preterms were intubated, submitted to invasive MV and had oxygen supplementation. 1 (20%) has had surfactant administration.

Discussion

A preterm infant is fragile and immature and needs special care, time and attention. Prenatal risk factors, gestational age, likelihood of survival, potential complications and parental wishes should be factors taken into consideration when planning the management in DR [16, 17].

A study performed in our centre states that ELGANs delivered between 23 and 25 weeks of GA have high morbidity at discharge since there is an increased risk of respiratory distress syndrome, patent ductus arteriosus, early or late sepsis, intraventricular hemorrhage, retinopathy of prematurity and necrotizing enterocolitis. This poor prognosis makes it difficult to decide whether or not to intervene [18]. Soares C. *et al* concluded that from 2010 to 2012 there were more newborns in our NICU that had their therapy limitated, DNR (do not resuscitate) decision or were submitted to palliative care when compared to investigations from years before [19].

We must heed the concept of viability when defining management strategies. Newborns delivered between $23^{0/7}$ and $24^{6/7}$ weeks of GA are considered to be in the "gray zone" of viability by Portuguese Society of Neonatology [20]. Even though this definition is changing over time due to progresses that have been made in treatments and biomedical technology, it is globally agreed that bellow 22 weeks of GA the likelihood of death is high and infants born with 26 weeks or more of GA have high likelihood of survival [21]. Initiating and withdrawing intensive care is a question that has been discussed over time but more longitudinal studies including large numbers of preterm neonates are warranted to help neonatologists in the clinical decision-making process. Each NICU should also share their results and statistics in order to reach a consensus and establish policies [22, 23].

However, it is known that in many cases golden hour interventions have a notorious role as they can avoid neonatal mortality in preterms and minimize complications such as bronchopulmonary dysplasia, severe neurologic injury, retinopathy of prematurity, necrotizing enterocolitis and hospital-acquired infections [8]. The main goal of DR management in the first hour of life is a better neonatal outcome and these medical procedures based on the best available evidence are very important especially in ELGANs[9].

Our main search question was to determine how the early management of preterms born before 27^{+0} weeks of GA interferes with clinical parameters on NICU admission. DR interventions have a huge impact on the transition of the newborn to the extra uterine life and we must be concerned that this impact can be positive or negative [24]. Studying the association between DR procedures and pH, hemoglobin and blood glucose level, peripheral oxygen saturation, mean blood pressure and body temperature on admission to NICU will possibly contribute to the optimization of therapeutic options for these preterms.

In our sample, the administration of epinephrine in DR decreased the admission pH in 0.786 units. The infusion of epinephrine can be required in neonatal reanimation. Cardiopulmonary arrest leads to poor tissue perfusion which compromises cellular delivery of nutrients and oxygen. This can cause elevation of blood lactate levels which reflect insufficient transport of oxygen to the tissues and a decrease of pH values, potentially complicating metabolic acidosis [25]. This is a possible explanation for the association found between the administration of catecholamines and its effect on pH values in NICU admission. There are not many studies exploring the relation between these two variables in the preterm newborn so it would be pertinent to enhance research in this field.

Nevertheless, a recent study from 2020 reports that lower pH values during neonatal transition causing progressive acidosis and hypoxemia are themselves causes of bradycardia or asystole [26]. The measure of pH values on umbilical cord is recommended for infants in high risk situations or Apgar scores < 7. Bethany A. *et al.* agree that there is also a risk of acidosis in normal range Apgar levels so there is potential utility in measuring cord blood pH values universally [27]. In our centre, obtaining and recording the umbilical cord pH values on delivery was not a usual practice especially before 2010. Even though that information was collected in our study, there was evident missing data on this variable. As consequence, we cannot be assured that the acidosis on NICU admission was caused by the same mechanisms

that caused umbilical cord acidosis which promoted cardiac arrest or if it was a consequence of cardiac failure and poor tissue perfusion. As mentioned before, more investigation must be done.

We also found that epinephrine administration in DR decreased the body temperature on NICU admission in 1.703ºC. These results are not consistent with a study performed among preterms which states that the incidence of hypothermia in NICU admission was lower in preterms that required DR interventions [28]. However, the inclusion criteria of their sample, temperature cut-off value and population differences may contribute to these contradictory results so we should not discard our findings. In our perspective, the higher incidence of admission hypothermia when epinephrine is administrated in DR is explained by body surface exposition. Even though WHO recommendations [28] to maintain body temperature are respected during stabilization and transfer to NICU, epinephrine administration is the last step on neonatal resuscitation algorithm [25] and we do believe that infants who need amines have their body surface more time exposed through stabilization than the others who don't need it. In fact, warmer DR and the use of neonatal thermic wraps contribute to maintain infants' body temperature on values that are compatible with homeostasis [28]. But the more intervention needed, the longer skin is uncovered to streamline interventions and this contributes to heat loss. The premature infants have immature thermoregulatory mechanisms and their skin is thinner compared to term infants which leads to higher heat loss through evaporation [29].

Within our cohort, the increase of 1g in body weight was associated with an increase of 0.253 mg/dL of blood glucose level measured on NICU admission. The physiologic explanation for the higher body weight on birth and an increase in glucose level is intuitive. In utero, gluconeogenesis is minimized whereas glycogen synthesis is stimulated. After birth, there is a switch in insulin/glucagon ratio and other factors that trigger

gluconeogenesis. This process is highly dependent on precursors such as fatty acids, glycerol, amino acids and lactate. An increase in body weight can be explained by more fat sources which will allow glucose production and therefore a raise in blood glucose level [30]. We must be aware that the glucose metabolism is uncertain and unstable in extremely preterm infants [31]. The first two hours of birth are known to be a metabolic period of adaptation [30]. Our conclusion is applied to our sample, which does not discard that lower body weight can be related to higher glucose level as stated in other studies [32]. Each case is individual and many external and internal factors are involved in neonatal glucose pathway. On one hand, factors such as continuous hepatic glucose release, insulin resistance and abnormal proinsulin processing by pancreatic β cells can predispose to hyperglycaemia [31]. On the other hand, limited fat and glycogen stores, immature gluconeogenesis pathways and higher metabolic state due to relatively larger brain dimensions may contribute to hypoglycaemia [33]. The normal glucose level is not well established in neonatology, despite the extensive literature, but we must be informed about the range that is globally accepted since both extremes can have deleterious neurodevelopmental effects [30, 32, 33].

Epinephrine administration also seems to be associated with blood glucose level, leading to an increase of 72.719 mg/dL. This is consistent with literature. The neonatal release of endogenous catecholamines is stimulated by physiological stress of transition to life outside the uterus [33]. Since they share similar receptors, exogenous epinephrine will have the same effects: maintains blood pressure, blocks insulin release and action, promotes liver glycogenolysis, stimulates gluconeogenesis and consequently blood glucose level increases [32,33].

Our results also support a relation between early CPAP in DR and hemoglobin level in NICU. Early CPAP seems to be associated with an increase in hemoglobin level of 6.088 g/dL. 20% of our sample was submitted to this respiratory support device. The 2019 Update

of European Consensus Guidelines on the Management of Distress Respiratory Syndrome states that spontaneously breathing neonates should be early stabilized in DR with CPAP instead of being intubated to reduce bronchopulmonary dysplasia [34]. A 2019 study in our center agrees that CPAP failure is associated with increased risk of mortality and morbidities mainly in infants with < 29 weeks of GA (unpublished data). What we do know is that anemic preterms require more time on early CPAP to successful weaning [35]. This is likely explained by the decreased oxygen delivery and increased cardiac load and breathing work. But how does early CPAP in DR increases hemoglobin concentration? We can think that preterms that require early CPAP are in better clinical state than those who are intubated so their clinical parameters are more likely to be normal ranged and this includes hemoglobin levels. The inferior limit of hemoglobin is proportional to prematurity grade in anemia of prematurity [14]. This is definitely a question that has to be investigated since literature fails to explore this association.

We should recognize the inherent weaknesses of a retrospective study. This is a limitation of this investigation but it is difficult to perform prospective studies in ELGANs as the prevalence of cases in our NICU is low. Indeed, the number of patients was not large enough to have statistically significant results in all outcomes. Another limitation is that we only included data from a single institution.

The main strengths of this study were the detailed data included and the innovating research question. Literature extensively lacks in studying DR management and the effect in clinical condition of preterms in NICU so it would certainly be valuable to design more and larger clinical trials with this study question.

Conclusions

DR procedures can have benefic effects and improve the outcomes of extremely preterm neonates. However, they may unexpectedly interfere with clinical parameters and have undesirable repercussions. More investigation has to be done in this field in order to optimize the NICU management of this particular and challenging neonatal group.

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NOTES

The authors report no conflicts of interest.

TABLES

Table 1.— *Maternal data*

	Total [a] n = 60	**GA = 24-25w** n = 33	**GA = 26w** n = 27	**p value**
Maternal age < 35 (years), n(%)	26 (43.3)	4 (12.1)	22 (81.5)	0.294*
Previous gestations, n(%):	28 (46.7)	14 (41.4)	14 (51.9)	0.228*
Multiple gestation	25 (41.7)	19 (57.6)	6 (22.2)	**0.006***
FFTS	4 (6.7)	2 (6.1)	2 (7.4)	0.530**
ART, n(%)	14 (23.3)	10 (30.3)	4 (14.8)	0.223**
Maternal exposure, n(%):				
Tobacco	4 (6.7)	1 (3)	3 (11.1)	0.318**
Alcohol	2 (3.3)	1 (3)	1 (3.7)	0.999**
Drugs	1 (1.7)	0	1 (3.7)	0.450**
Medication	18 (30)	9 (27.3)	9 (33.3)	0.610*
Antenatal corticotherapy, n(%):	57 (95)	31 (93.9)	26 (96.3)	0.999**
Complete cycles	38 (63.3)	19 (57.6)	19 (7.4)	0.568**
Magnesium sulfate, n(%)	3 (5)	1 (3)	2 (7.4)	0.583**
Gestation diseases, n(%):				
Gestational diabetes	14 (23.3)	4 (12.1)	10 (37)	**0.033****
Renal failure	1 (1.7)	0	1 (3.7)	0.450**
Hypertensive disease	0	0	0	----
Preeclampsia	7 (11.7)	1 (3)	6 (22.2)	**0.039****
HELLP Syndrome	3 (5)	0	3 (11.1)	0.085**
Chorioamniotitis	33 (55)	15 (45.5)	18 (66.7)	0.100*
Placental abruption	14 (23.3)	6 (18.2)	8 (29.6)	0.297*
Placenta previa	0	0	0	----
FGR, n(%)	9 (15)	3 (9.1)	6 (22.2)	0.276*
Abnormal umbilical flow, n(%)	5 (8.3)	0	5 (18.5)	**0.015****
Membrane rupture > 18h, n(%)	6 (10)	3 (9.1)	3 (11.1)	0.989**

GA: gestational age; FFTS: feto-fetal transfusion syndrome; ART: assisted reproductive technology; HELLP syndrome: hemolysis, elevated liver enzyme levels and low platelet count; FGR: fetal growth restriction
* Chi square test; ** Fisher's exact test

Table 2.— *Newborn data*

	Total [a] n = 60	**GA = 24-25w** n = 33	**GA = 26w** n = 27	**p value**
Delivery Room				
Gender:				
Male, n(%)	31 (51.7)	20 (60.6)	11 (40.7)	0.126*
Female, n(%)	29 (48.3)	13 (39.4)	16 (59.3)	
Birth anthropometrics:				
Body weight (g), mean (±SD)	760.9 (168)	695.6 (126.8)	840.7 (179.5)	**0.001ϙ**
Type of delivery, n(%):				
Euctocic	31 (51.7)	24 (72.7)	7 (25,9)	**<0.001***
C-section	29 (48.3)	9 (27.3)	20 (74)	
Abnormal amniotic fluid, n(%)	7 (11.7)	6 (18.2)	1 (3.7)	0.116**
Fetal presentation, n(%):				
Cefalic	45 (75)	25 (75.8)	20 (75)	0.658*
Pelvic	15 (25)	8 (24.2)	7 (25.9)	
Apgar 1st min <5, n(%)	36 (60)	22 (66.7)	14 (51.9)	0.051**
Apgar 5th min <7, n(%)	27 (45)	14 (42.4)	13 (48.2)	0.6587*
Oxygen, n(%)	60 (100)	33 (100)	27 (100)	---
Endotracheal intubation, n(%)	47 (78.3)	30 (91)	17 (63)	**0.026***
Compressions	2 (3.3)	1 (3)	1 (3,7)	0.999**
Epinephrine	7 (11.7)	4 (12.1)	3 (11,1)	0.999**
Invasive mechanic ventilation, n(%)	49 (81.7)	31 (93.9)	18 (66.7)	**0.009****
Early CPAP, n(%)	12 (20)	2 (6.1)	10 (37)	**0.004****
Surfactant, n(%)	20 (33.3)	15 (45.5)	5 (18.5)	**0.028***
Umbilical cord pH, median (min-max):				
Arterial	7.3 (3.4-7.4)	7.3 (7.2-7.4)	7.3 (3.4-7.4)	0.459ϙ
Venous	7.3 (7-7.4)	7.3 (7.2-7.4)	7.3 (7-7.4)	0.662ϙ
NICU				
Admission pH, median (min-max)	7.3 (3.4-7.5)	7.3 (6.9-7.5)	7.3 (3.4-7.5)	0.376ϙ
Admission pH < 7.25, n(%)	22 (36.7)	14 (42.4)	8 (29.6)	0.446*
Hemoglobin (g/dL), mean (±SD)	15.02 (2.5)	14.54 (2)	15.59 (2.9)	0.112ϙ
Hemoglobin < 12 g/dL, n(%)	5 (8.3)	3 (9.1)	2 (7.4)	0.989**
Platelets (10^3/uL), mean (±SD)	186.29 (53.2)	192.36 (43.2)	178.13 (64.5)	0.336ϙ
Blood glucose level (mg/dL), mean (±SD)	86.80 (60.1)	92.62 (49.9)	79.25 (71.9)	0.461ϙ
Blood glucose level < 40mg/dL, n(%)	7 (11.7)	2 (6.1)	5 (18.5)	0.213**
SpO2, median (min-max)	95 (36.4-100)	93.5 (36.4-100)	96 (64-100)	0.417ϙ
SpO2 < 94%, n(%)	25 (41.7)	15 (45.5)	10 (37)	0.458*
Respiratory rate (cpm), mean (±SD)	45.9 (14.1)	45.7 (13.6)	46.2 (15)	0.886ϙ
Heart rate (bpm), mean (±SD)	154.1 (21.5)	156 (24.7)	151.8 (17)	0.461ϙ
Blood pressure (mmHg), mean (±SD):				
Sistolic	46.3 (12.7)	44.7 (11.1)	48.2 (14.3)	0.320ϙ
Diastolic	25.8 (12.5)	24.9 (8.9)	26.9 (15.3)	0.545ϙ
Mean	32.6 (11.5)	31.5 (8.7)	34 (14.4)	0.442ϙ
Mean BP < GA, n(%)	13 (21.7)	5 (15.2)	8 (29.6)	

Temperature (°C), mean (±SD)	36 (1.2)	36 (1.3)	36 (0.9)	
Temperature < 36.5ºC, n(%)	35 (58.3)	18 (54.6)	17 (63)	0.347*
Death, n (%)	32 (52.3)	24 (72.7)	8 (29.6)	**0.001***

GA: gestational age; NICU: Neonatal Intensive Care Unit; CPAP: continuous positive airway pressure; BP: blood pressure; SpO2: peripheral oxygen saturation

* Chi square test; ** Ficher's exact test; ♀ Independent t test

[a] 5 newborns with 23wk of GA were excluded from the analysis

Table 3.— Multivariate analysis by linear regression

NICU outcome	Independent variable*	B value	95% CI	p value
Blood glucose level	Epinephrine	72.719	12.530; 132.908	0.020
	Birth body weight	0.253	0.078; 0.428	0.006
Temperature	Epinephrine	-1.703	-2.692; -0.714	0.001
Hemoglobin level	Early CPAP	6.008	1.356; 10.660	0.013
pH level	Epinephrine	-0.786	-1.282; -0.290	0.003

* All associations were adjusted for gestational age, birth weight, complete cycles of corticotherapy, gestational diabetes, preeclampsia, chorioamniotitis, abnormal umbilical flow, type of delivery and delivery room interventions (compressions, epinephrine administration, surfactant, endotracheal intubation, early CPAP and invasive mechanic ventilation).

ANEXO I - Normas da Revista Minerva Pediatrica

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