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Joana Maria Soares Ferreira

The golden hour in infants <32 weeks of gestational age

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Ao meu pai,

À minha mãe,

Aos meus irmãos, Vera e Filipe.

The golden hour in infants <32 weeks of gestational age

Joana Ferreira, Henrique Soares, Filipa Flor-de-Lima, Mário Mateus, Hercília Guimarães

Abstract

The Golden Hour in perinatal and neonatal medicine refers to the period of time since the infant is born until he is stabilized, usually defined as the first hour after birth. This period of time has an important impact in the outcomes of the newborns, especially in those born prematurely. The aim of our study was to evaluate the impact of golden hour in the short-term outcomes of newborn infants with gestational age less than 32 weeks.

We performed a retrospective study of infants with less than 32 weeks of gestational age, born between December 2012 and December 2014, and admitted to our center, a level III neonatal intensive care unit (NICU). Those with major congenital anomalies, hydrops and chromosomal abnormalities, outborn sand those transferred to other centers were excluded. Data about demographics, prenatal and peripartum periods, procedures performed after birth, laboratory data in the first hour of life, evolution NICU and outcomes assessed at discharge were recorded.

Our study included 84 newborns. The multivariate analysis by logistic regression showed association between Apgar score at 5th minute <7 and development of sepsis (p=0.022), hyaline membrane disease (p=0.033), brochopulmonary dysplasia (p=0.012) and patent ductus arteriosus (p=0.006). Also ventilation with positive pressure and mechanical ventilation at birth were associated with hyaline membrane disease (p=0.014 and p=0.009, respectively) and vascular catheters with brochopulmonary dysplasia development (p=0.025). No other statistically significant associations were found between golden hour variables and short term outcomes.

The golden hour is a crucial period with impact in neonatal outcomes and these results confirm our hypothesis that the golden hour has an impact on newborn outcomes with less than 32 weeks old. We should be aware to this period and optimize all variables to minimize neonatal morbidity.

Keywords

Golden Hour, premature, newborn, outcomes, morbidity, neonatal.

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Introduction

The concept “golden hour” in perinatal and neonatal medicine refers to the period of time since the infant is born until he is stabilized, usually defined as the first hour after birth. During this period of adaptation to extrauterine life, changes may occur in the newborn leading to associated morbidity and mortality (1).

Neonatal outcomes depend on the gestational age at delivery. This means that, the lower the gestational age, the greater risk of morbidity and mortality (2).

Advances in premature infant care have increased survival in many premature newborn infants. However, mortality remains a real and serious outcome even in developed countries (3). The morbidity is also high in premature infants. The main complications associated with

prematurity are intraventricular hemorrhage, cystic periventricular leukomalacia, pneumothorax, bronchopulmonary dysplasia, complications with nutrition, necrotizing enterocolitis and retinopathy of prematurity (3, 4, 5).

Currently, there are few data regarding the recommendations for stabilization and resuscitation in preterm infants in the delivery room. Usually, neonatology teams are guided by the Neonatal Resuscitation Program (NRP) whose fifth edition included guidelines for care of the premature infants (6).

Recent studies have established approaches to newborn care during the golden hour and have shown that the implementation of standardized protocols increases the stability of premature newborns and decreases the associated morbidity (4, 7, 8).

The concept "golden hour" was recently introduced in the literature and there is still little information about its impact on premature newborn infants.

The aim of our study was to evaluate the impact that golden hour has in the short-term outcomes of newborn infants with gestational age less than 32 weeks.

Methods

We performed a retrospective observational study of all newborns with less than 32 weeks of gestational age who born between December 2012 and December 2014 and admitted at our center, a Level III neonatal intensive care unit (NICU).

The inclusion criteria were: newborns with less than 32 weeks of gestational age, regardless of birth weight, born in our center and transferred after birth to the NICU. Those with major congenital anomalies, hydrops and chromosomal abnormalities were excluded as well as newborns transferred from another hospital or transferred to another hospital after birth.

Data was collected from medical records of the delivery room and the NICU.

We have included information about individual characteristics of the mother and prenatal period (maternal chronic diseases; maternal pregnancy diseases such as diabetes mellitus, hypertension, pre-eclampsia, Hellp syndrome, infectious risk; intrauterine growth restriction; abnormal umbical flow; placental abruption; premature membrane rupture; peripartum antibiotics and steroids), peripartum period (delivery type, infectious risk, Apgar score at 1^{st} and 5^{th} minute), demographic characteristics (gender, gestational age, birth weight, multiple gestation, diagnosis known at birth), procedures performed after birth including neonatal resuscitation (positive pressure ventilation, endotracheal tube, chest compression, medication with epinephrine, dopamine), ventilation devices (continuous positive airway pressure (CPAP), conventional mechanical ventilation), oxygen therapy , vascular catheterization (umbilical artery, umbilical vein, umbilical artery and vein) and other drugs (surfactant, antibiotics, steroids).

The laboratory data collected in the first hour of life included peripheral capillary oxygen saturation (%), systolic, diastolic and mean blood pressure (mmHg), temperature (ºC), umbilical cord pH, hemoglobin (g/dL) and blood glucose level (mg/dL).

Evolution during NICU stay was also recorded: need for surfactant, oxygen therapy (% and days of oxygen), days of mechanical ventilation**,** days of parenteral nutrition, days of mechanical ventilation, days of stay in NICU, data at discharge (deceased, transferred to another hospital or home) and neonatal morbidities such as sepsis (early or late), pneumothorax, hyaline membrane disease, bronchopulmonary dysplasia, patent ductus arteriosus and treatment (surgical, medical or both), necrotizing enterocolitis (if grade ≥2 according to Bell (9)), intraventricular hemorrhage (if grade≥3 according to Papile (10)), leukomalacia periventricular and retinopathy of prematurity (if grade≥2 according to the International Classification of Retinopathy of Prematurity (11)).

The outcomes were assessed at discharge by a multidisciplinary team including a neonatologist responsible for delivery care, physicians responsible in the NICU, nurses and pediatric surgery.

This study was approved by our institutional ethics committee and access to medical records was authorized by the office designated for this function.

Statistical analysis was performed using SPSS for Windows, version 20. Continuous variables were characterized by mean (± standard deviation) or median (medium-maximum) if they had symmetric or asymmetric distribution respectively and categorical variables by absolute and relative frequencies. A multivariate analysis by logistic regression was performed to evaluate the impact of golden hour in neonatal outcomes. A p value less than 0.05 was considered statistically significant.

Results

In the period study 84 newborns with less than 32 weeks of gestational age were eligible for this study.

The demographic characteristics and prenatal data are summarized in **Table 1**.

Thirty-seven newborns (44.4%) had an Apgar score at 1st minute less than 7 and 13 (15.5%) had an Apgar score at 5th minute less than 7; 53 (63.1%) newborns were resuscitated with positive pressure ventilation, 28 (33.3%) with endotracheal tube and 1 (1.2%) needed chest compressions; 28 newborns (33.3%) needed early CPAP and 28 (33.3%) needed mechanical ventilation after birth; vascular catheterization was used by 31 (37.3%) newborns, 3 (10.7%) of which used the umbilical artery, 11 (39.3%) umbilical vein and 14 (50%) umbilical artery and vein; medication was used in 3 (3.6%) newborns. Other delivery room and golden hour data are summarized in **Table 2**.

Twenty (23.8%) newborns had sepsis. Twenty-seven (32.1%) newborns had patent ductus arteriosus and 3 (11.1%) of them needed surgical ligation. The prevalence of hyaline membrane disease, bronchopulmonary dysplasia and retinopathy of prematurity ≥ grade 2 was, respectively, 47.6%, 13.1% and 13.1%. Intraventricular hemorrhage ≥ grade 3 occurred in 8 (9.5%) newborns, pneumothorax and cystic periventricular leukomalacia were diagnosed in 6 newborns (7.1%) and only 1 (1.2%) had necrotizing enterocolitis ≥ grade 2. Other neonatal intensive care unit data are summarized in **Table 3**.

In the multivariate analysis Apgar score at 5th minute < 7 was associated to sepsis (odds ratio (OR) 4.80; 95% confidence interval (95%CI) 1.3-18.7), hyaline membrane disease (OR 10.60; 95%CI 1.2-93.8), brochopulmonary dysplasia (OR 7.1; 95%CI 1.5-33.1) and patent ductus arteriosus (OR 7.7; 95%CI 1.8-33.4). Moreover, ventilation with positive pressure (OR 4.7; 95%CI 1.4-3) and mechanical ventilation in delivery room (OR 5.9; 95%CI 1.6-22.6) were associated hyaline membrane disease development. Higher mean arterial pressure was protective of hyaline membrane disease (OR 0.93; 95%CI 0.8-0.9). The needed of vascular catheters after birth was associated to bronchopulmonary dysplasia (OR 16.6; 95%CI 1.4-191.6). The odds of intraventricular hemorrhage ≥ grade 3 was 0.04 (95%CI, 0.002-0.08) in newborns who delivered by c-section. When we considered the diastolic arterial pressure, the odds of retinopathy of prematurity ≥ grade 2 was 0.9 (95%CI, 0.8-0.9).

The other golden hour variables did not show statistically significant association with the outcomes analyzed **(Table 4).**

Discussion

Our study showed that the Apgar score at 5th minute <7, one of the determinants of golden hour, is associated with an increased risk of developing sepsis, hyaline membrane

disease, brochopulmonary dysplasia, and patent ductus arteriosus, adjusted for the main risk factors. This association of low Apgar score with these various outcomes can be explained because it is a strong predictor of morbidity and neonatal mortality (12). Several studies have shown the relationship between low Apgar score and neonatal morbidities. A study aiming to identify risk factors for the development of sepsis had already showed that the low score of Apgar is a strong risk factor involved. (13). Another study whose objective was to study maternal and neonatal risk factors for the development of hyaline membrane disease also demonstrated this relationship. (14) A recent study demonstrated an association between low Apgar score at 5^{th} minute and patent ductus arteriosus. (15)

In addition to the Apgar score at 5^{th} minute <7, there is an association between the use of ventilation with positive pressure and mechanical ventilation at birth and hyaline membrane disease, when we adjusted variables to birthweight, gestational age and prenatal steroids. On the other hand, mean arterial pressure appears to be protective for this outcome. In fact, a recent study found that the prevalence of hyaline membrane disease is more frequent in patients requiring mechanical ventilation and conclude that CPAP may be a selected technique in the support of very low birth weight newborns with respiratory distress syndrome (16). The explanation we found for association between used of ventilation with positive pressure and hyaline membrane disease is that this type of ventilation is currently the preferred and most used in our center, furthermore is not without risks.

In this study, we showed that the use of vascular catheters, besides the previously mentioned Apgar score 5^{th} minute <7, were associated with an increased risk of developing brochopulmonary dysplasia, when the variables are adjusted to birthweight and gestational age. A study showed that the risk of brochopulmonary dysplasia is not only associated with low Apgar score but also with prelabour preterm rupture of membranes, small for gestational age and comorbidities that may increase the need for vascular access, such as patent ductus arteriosus, persistent pulmonary hypertension pulmonary, interstitial emphysema, pneumothorax, late onset infections, intubation, chest compressions and mechanical ventilation (17).

We also found that some variables of golden hour were associated with decreased risk of adverse outcome. On the one hand, c-section delivery seems to be associated with a decreased risk of intraventricular hemorrhage ≥ grade3, when variables are adjusted to birthweight and gestational age. This association between c-section delivery and the lower risk of intraventricular hemorrhage is already documented in the literature (18), and nowadays vaginal delivery is considered one of the risk factors for this outcome (19). Furthermore, diastolic arterial pressure seems to decrease the risk of retinopathy of prematurity ≥grade2, when variables are adjusted to birthweight, gestational age and oxygen therapy. This result seems to be justified by the fact of considering the hemodynamic instability, with tension variations, as a possible risk factor for retinopathy (20).

In this study, there was no statistically significant association between the variables studied the golden hour and the following outcomes: pneumothorax, necrotizing enterocolitis ≥ grade 2 and cystic periventricular leukomalacia. One possible reason is that golden hour cannot be a determining factor for the development of these outcomes, that is, perhaps these outcomes are more dependent on other determinants that may occur later.

By reviewing the literature, it is clear that the concept of golden hour in neonatology is relatively recent (1) (2). Studies have been conducted to establish the determinants of the first hour of life and major complications in newborns (4), as well as the importance of the application of a specific protocol for golden hour to standardize care and increase the stability of newborns (7) (8). A recent study sought to study the impact of the golden hour in some of the outcomes but it only demonstrate that the implementation of the golden hour protocol is associated with marked decreased in intraventricular hemorrhage and faster time for umbilical catheter insertion (21).

The main limitation of our study consists in its design. As it is a retrospective observational study, it mainly relies on information from medical records, with possible inaccuracies and loss of data. Another limitation is the fact that our population sample (n) is small, since we include only infants with gestational age less than 32 weeks and born in our center and transferred after birth to the NICU.

Conclusion

In this study, determinants of golden hour showed association with some outcomes in newborns with less than 32 weeks of gestational age, such as Apgar score at 5^{th} minute < 7 and development of sepsis, hyaline membrane disease, brochopulmonary dysplasia and patent ductus arteriosus. Also, there was an association between ventilation with positive pressure and mechanical ventilation at birth and hyaline membrane disease, and use of vascular catheters and brochopulmonary dysplasia.

These results confirm our hypothesis that golden hour has an impact on newborn outcomes with less than 32 weeks old. We should be aware to this critical period and optimize all variables to minimize neonatal morbidity.

Declaration of interest

The Authors declare that there is no conflict of interest.

References

1) Annibale DJ, Bissinger RL. The golden hour. Adv Neonatal Care. 2010; 10(5):221-3.
2) Chatterjee J, Gullam J, Thornton S. The management of preterm labour. Arch Dis Fetal Neonatal Ed. 2007; 92 (2): F88-F93.
3) Bissinger RL, Annibale DJ. Thermoregulation in very low-birth-weight infants during the golden hour: results and implications. Adv Neonatal Care. 2010; 10(5):230-8.
4) Reynolds RD, Pilcher J, Ring A, Johnson R, McKinley P. The Golden Hour: care of the LBW infant during the first hour of life one unit's experience. Neonatal Netw. 2009; 28(4):211-9.
5) Flamant C, Gascoin G. [Short-term outcome and small for gestational age newborn management]. J Gynecol Obstet Biol Reprod. 2013;42(8):985-95.
6) AHA/AAP (2006). Textbook of neonatal resuscitation (^{5th} ed.) Elk Grove Village, IL: Author.
7) Castrodale V, Rinehart S. The golden hour: improving the stabilization of the very low birth-weight infant. Adv Neonatal Care. 2014;14(1):9-14.
8) Wyckoff MH. Initial resuscitation and stabilization of periviable neonate: The Golden Hour approach. Elsivier. 2014;(38)12-16.
9) Lin PW, Stoll BJ. Necrotising enterocolitis. Lancet. 2006; 368(9543):1271-83.
10) Papile LA, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500gm. J Pediatr. 1978; 92:529-534.
11) International Classification of Retinopathy of Prematurity. Arch Ophthalmol 102:1130-5. 1984.
12) Casey BM, McIntire DD, Leveno KJ. The continuing value of the Apgar score for the assessment of newborn infants. N Engl J Med. 2001;344:467-71.
13) Shah GS, Budhathoki S, Das BK, Mandal RN. Risk factors in early neonatal sepsis. Kathmandu Univ Med J (KUMJ). 2006; 4(2):187-91.
14) Pérez Molina JJ, Blancas Jacobo O, Ramírez Valdivia JM. [Hyaline membrane disease: mortality and maternal and neonatal risk factors]. Ginecol Obstet Mex. 2006; 74(7):354-9.
15) Chen YY, Wang HP, Chang JT, Chiou YH, Huang YF, Hsieh KS. Perinatal factors in patent ductus arteriosus in very low-birthweight infants. Pediatr Int. 2014; 56(1):72-6.

16) Tavares PN, Flor-de-Lima F, Soares H, Guimarães H. Early nCPAP versus intubation in very low birth weight infants. Journal of Pediatric and Neonatal Individualized Medicine. 2013; 2(2):e020201.
17) Eriksson L, Haglund B, Odlind V, Altman M, Ewald U, Kieler H. Perinatal conditions related to growth restriction and inflammation are associated with an increased risk of bronchopulmonary dysplasia. Acta Paediatr. 2015; 104(3):259-63.
18) Philip AG, Allan WC. Does cesarean section protect against intraventricular hemorrhage in preterm infants? J Perinatol. 1991; 11(1):3-9.
19) Ballabh P. Intraventricular Hemorrhage in premature infants: Mechanism of disease. Pediatr Res. 2010; 67(1): 1–8.
20) Henriques G, Brito C, Clemente F, Breda J, Teixeira S. Retinopatia da Prematuridade. Consensos em Neonatologia. 2014.
21) Reuter S, Messier S, Stevens D. The Neonatal Golden Hour – Intervation to Improve Quality of Care of the Extremely Low Birth Weight Infant. S D Med. 2014; 67(10):397-403, 405.

Table 1. Demographic characteristics and prenatal data

	Total (n=84)
Male gender, n (%)	51 (60.7)
Gestational age (wk), median (min-max)	30 (23-32)
Birth weight (g), mean (± SD)	1229 (±414)
Multiple gestation, n (%)	29 (34.5)
Maternal chronic diseases, n (%)	30 (35.7)
Maternal pregnancy diseases, n (%)	70 (83.3)
Gestational diabetes	8 (9.5)
Hypertension	2 (2.4)
Pre-eclampsia	16 (19.0)
Hellp syndrome	3 (3.6)
Infection risk	48 (57.1)
Intrauterine growth restriction, n (%)	16 (19.0)
Abnormal umbilical flow, n (%)	15 (18.3)
Placental abruption, n (%)	7 (8.3)
Steroids, n (%)	75 (89.3)
Premature membrane rupture, n (%)	22 (26.2)
Peripartum antibiotics, n (%)	22 (26.2)

Table 2. Delivery room and golden hour data

	Total (n=84)
Delivery, n (%)	
Vaginal	33 (39.3)
C-section	51 (60.7)
Apgar score, n (%)	
1^{st} min <7	37 (44.4)
5^{th} min <7	13 (15.5)
Resuscitation, n (%)	
Positive pressure ventilation	53 (63.1)
Endotracheal tube	28 (33.3)
Chest compressions	1 (1.2)
CPAP, n (%)	36 (42.9)
Mechanical ventilation, n (%)	28 (33.3)
Vascular catheterization, n (%)	31 (37.3)
Umbilical artery	3 (10.7)
Umbilical vein	11 (39.3)
Umbilical artery and vein	14 (50.0)
Medication, n (%)	3 (3.6)
Epinephrine	2 (66.7)
Dopamine	1 (33.3)
Umbilical cord pH, mean (±SD)	7.25 (±0.1)
Hemoglobin (g/dL), mean (±SD)	16.5 (±3.0)
Blood glucose level (mg/dL), mean (±SD)	83.3 (±52.5)
Peripheral capillary oxygen saturation, median (min-max)	96 (19-100)
Blood pressure (mmHg), mean (±SD)	
Systolic	53.4 (±11.8)
Diastolic	31.7 (±9.7)
Mean	37.9 (±8.8)

Temperature (°C), mean (±SD)	36.3 (±0.9)

Table 3. Neonatal Intensive Care Unit data

	Total (n=84)
Neonatal morbidities, n (%)	
Sepsis	20 (23.8)
Early	3 (15.0)
Late	17 (85.0)
Pneumothorax	6 (7.1)
Hyaline membrane disease	40 (47.6)
Brochopulmonary dysplasia	11 (13.1)
Patente ductus arteriosus	27 (32.1)
Surgical ligation	3 (11.1)
Necrotizing enterocolitis ≥ grade 2	1 (1.2)
Intraventricular hemorrhage ≥ grade 3	8 (9.5)
Cystic periventricular leukomalacia	6 (7.1)
Retinopathy of prematurity ≥grade 2	11 (13.1)
Surfactant, n (%)	44 (53.0)
Steroids, n (%)	10 (11.9)
Oxygen (%), median (min-max)	25 (21-100)
Parenteral nutrition, n (%)	75 (89.3)
Days of parenteral nutrition, median (min-max)	11 (1-46)
Mechanical ventilation (days), median (min-max)	5 (1-59)
Stay in NICU (days), median (min-max)	28 (1-148)
Deceased, n (%)	16 (19.0)

Table 4. The impact of golden hour in neonatal outcomes

Outcomes	**OR*§**	**95% CI**	**P value**
Sepsis			
Apgar score 5th min <7	4.80	1.3-18.7	0.022*
Other golden hour variables			NS
Pneumothorax			
All golden hour variables			NS
Hyaline membrane disease			
Apgar score 5th min <7	10.60	1.2-93.8	0.033**
Ventilation with positive pressure at birth	4.7	1.4-3	0.014**
Mechanical ventilation in delivery room	5.9	1.6-22.6	0.009**
Mean arterial pressure	0.93	0.8-0.9	0.016**
Other golden hour variables			NS
Brochopulmonary dysplasia			
Apgar score 5th min <7	7.1	1.5-33.1	0.012***
Vascular catheter	16.6	1.4-191.6	0.025***
Other golden hour variables			NS
Patent ductus arteriosus			
Apgar score 5th min <7	7.7	1.8-33.4	0.006****

Other golden hour variables			NS
Necrotizing enterocolitis ≥ grade 2			
Golden hour variables			NS
Intraventricular hemorrhage ≥ grade3			
C- section	0.04	0.002-0.08	0.032*****
Other golden hour variables			NS
Cystic periventricular leukomalacia			
Golden hour variables			NS
Retinopathy of prematurity ≥ grade 2			
Diastolic arterial pressure	0.9	0.8-0.9	0.046******
Other Golden hour variables			NS

[§]Logistic regression

* Adjusted to birthweight, gestational age, premature membrane rupture and infectious risk)

** Adjusted to birthweight, gestational age and prenatal steroids

*** Adjusted to birthweight and gestational age

******** Adjusted to birthweight and gestational age

********* Adjusted to birthweight and gestational age

********** Adjusted to birthweight, gestational age and oxygen therapy

NS- non significant

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À Dra. Filipa Flor-de-Lima.

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Presidente da Comissão de Ética para a Saúde do
Centro Hospitalar de S. João – EPE

Assunto: Pedido de apreciação e parecer para estudo/projecto de investigação

Nome do Investigador Principal: Joana Maria Soares Ferreira

Título do projecto de investigação: The golden hour in infants <32 weeks gestational age.

Pretendendo realizar no(s) Serviço(s) de Neonatologia do Centro Hospitalar de S. João – EPE o estudo/projecto de investigação em epígrafe, solicito a V. Exa., na qualidade de Investigador/Promotor, a sua apreciação e a elaboração do respectivo parecer.

Para o efeito, anexo toda a documentação referida no dossier dessa Comissão respeitante a estudos/projectos de investigação.

Com os melhores cumprimentos.

Porto, 2 / Maio / 2014

O INVESTIGADOR/PROMOTOR

Joana Ferreira

7. SEGURO

a. *Este estudo/projecto de investigação prevê intervenção clínica que implique a existência de um seguro para os participantes?*

SIM ☐ (Se sim, junte, por favor, cópia da Apólice de Seguro respectiva)
NÃO ☒
NÃO APLICÁVEL ☐

8. TERMO DE RESPONSABILIDADE

Eu, Joana Maria Soares Ferreira,
abaixo-assinado, na qualidade de Investigador Principal, declaro por minha honra que as informações prestadas neste questionário são verdadeiras. Mais declaro que, durante o estudo, serão respeitadas as recomendações constantes da Declaração de Helsínquia (com as emendas de Tóquio 1975, Veneza 1983, Hong-Kong 1989, Somerset West 1996 e Edimburgo 2000) e da Organização Mundial da Saúde, no que se refere à experimentação que envolve seres humanos. Aceito, também, a recomendação da CES de que o recrutamento para este estudo se fará junto de doentes que não tenham participado em outro estudo no decurso do actual internamento ou da mesma consulta.

Porto, ____ / _____ / 20____

Joana Ferreira
O Investigador Principal

PARECER DA COMISSÃO DE ÉTICA PARA A SAÚDE DO CENTRO HOSPITALAR DE S. JOÃO

emitido na reunião plenária da CES de 20 / fevereiro / 2012

A Comissão de Ética para a Saúde APROVA por unanimidade o parecer do Relator, pelo que nada tem a opor à realização deste projecto de investigação.

Prof. Doutor Filipe Almeida
Presidente da Comissão de Ética

Parecer

Título do Projecto: The golden hour in infants < 32 weeks gestational age

Nome do Investigador Principal: Joana Maria Soares Ferreira

Serviço onde decorrerá o Estudo: Serviço de Neonatalogia e Serviço de Obstetrícia e Ginecologia do Centro Hospitalar de São João

Objectivo do pedido de parecer:

É objectivo deste estudo conhecer o impacto a curto prazo da "*Golden Hour*" nos *outcomes* nos RN com <32 semanas de idade gestacional

Concepção e Pertinência do Estudo:

Trata-se de um estudo prospectivo, observacional, desenvolvido no âmbito do Projecto Opção do Curso de Mestrado Integrado em Medicina, incidindo em RN nascidos no CHSJ entre 1 Junho e 31 Dezembro 2014. Serão recolhidos dados demográficos, clínicos e laboratoriais dos RN, inclusive dados sobre a transferência dos RN.
Os Srs. Directores dos Serviços anuíram à realização do estudo.

Benefício/risco: Sem benefícios nem riscos directos com a participação no estudo.

Respeito pela liberdade e autonomia do sujeito de ensaio: Será solicitado consentimento informado aos representantes legais dos participantes a envolver.

Confidencialidade dos dados: Na metodologia prevista para a realização do estudo, a recolha de dados será anonimizada, garantindo assim a respectiva confidencialidade.

Elo de ligação: Dr. Henrique Soares e Dr. Marina Moucho

Indemnização por danos: NA

Continuação do tratamento: NA

Propriedade dos dados: Os dados serão objecto de divulgação à comunidade científica

Curriculum do investigador: Adequado ao perfil da investigação

Data previsível da conclusão do estudo: Janeiro de 2015

Conclusão: Proponho um parecer favorável à realização deste projecto de investigação, na sua actual definição metodológica.

Porto e C.H.S.João, 2014.06.20

O Relator

Doutor Filipe Almeida