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Original article

Very low birth weight infants in a Portuguese Neonatal Intensive Care Unit: a comparative study with the Vermont Oxford Network

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Abstract

Introduction: It is our goal to analyze the neonatal data from a Level III Unit and compare them with the overall data from the Vermont Oxford Network (VON).

Methods: It is an observational, retrospective study that included very low birth weight infants (VLBWI) born in this hospital or admitted in the first 24 hours of life between 2000 and 2013. Two periods, 2000-2006 and 2007-2013, were studied. Descriptive data and Chi-Square test were performed, and a value of $p < 0.05$ was considered statistically significant.

Results: A total of 607 VLBWI were studied, 51.1% male, mean weight 1,120 g and gestational age 29.3 weeks. Non-invasive ventilation in the Neonatal Intensive Care Unit (NICU) of Centro Hospitalar Universitário de São João (CHUSJ) was 63.5% in the 2000-2006 period and 70.2% in the 2007-2013 period, but still less than in the VON. Late-onset sepsis was 18.4% and 9.9% in the first and the second period, respectively, and 7.7% and 4.9% in the VON. Regarding mortality, it was higher in both periods in our NICU with respect to the VON, with a difference of 46.0% and 58.7% in the first and the second period, respectively.

Discussion: There were improvements regarding the use of mechanical ventilation and the incidence of late-onset sepsis. Both decreased between the two periods but were still having higher levels than those of the VON. Regarding morbidity and mortality, the difference may be explained by the fact that our NICU is Level III and a reference center for metabolic, oncological, cardiac and surgical pathologies.

Conclusion: It is very important for a NICU to know the characteristics of its population to assess the quality of healthcare and compare its results with other NICUs. VON allows us to identify the more and less positive aspects in order to improve the latter ones, and to promote better practices of healthcare.

Keywords

Very low birth weight infants, registry data, benchmarking analysis, morbidity, mortality.

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Introduction

In Neonatology, considerable progress has been made in recent decades with regard to neonatal and infant morbidity and mortality [1].

Higher survival rates followed improvements in prenatal and neonatal care, including surveillance of pregnancy, treatment of infections and other maternal diseases, antenatal corticosteroid therapy, non-invasive ventilatory support and administration of exogenous surfactant. In addition, the creation of referral centers has been shown to be associated with decreased mortality in very low birth weight infants (VLBWI) [2].

Several international groups have developed multidisciplinary collaborations focused on the search for better clinical practices, with the aim of improving the effectiveness and efficiency of neonatal care [3].

The Vermont Oxford Network (VON), founded in 1988, is a voluntary, non-profit group of health professionals committed to improving the effectiveness and efficiency of medical care for newborns and their families, through a coordinated research, education and quality program [4, 5]. In support of these activities, this network maintains a clinical database on VLBWI (birth weight from 401 to 1,500 grams) and/or from 22 to 29 weeks and 6 days of gestational age, born in member institutions or admitted within the first 24 hours after birth. The data record includes: place of birth, weight and head circumference, birth defects, maternal characteristics, initial resuscitation, respiratory care, surgery, neonatal mortality and morbidities [6].

The integration of the Units in this network allows benchmarking, which allows comparing their practices.

The Neonatal Intensive Care Unit (NICU) of the Centro Hospitalar Universitário de São João (CHUSJ) participated in VON between 2000 and 2013, registering all VLBWI.

The objective of this work is to compare the results of our Unit with the global data from the VON register to identify the benefits of participation in this international network.

Methods

It is an observational, retrospective study. Newborns with birth weight between 401 g and 1,500 g (VLBWI) and/or born between 22 weeks and 29 weeks and 6 days of gestation, born at CHUSJ or admitted until the first 24 hours of life, were studied. A period of 14 years was analyzed, between 2000 and 2013, divided into 2 periods, between 2000 and 2006 and between 2007 and 2013. The data were compared with the global data of the VON for the years 2008 and 2015, respectively. Records that did not meet these criteria were excluded.

Statistical analysis was performed using the SPSS® program for Windows®, version 23. Continuous variables are characterized by the mean (± standard deviation) or median (minimum-maximum) if they have symmetric or asymmetric distribution, respectively, and categorical variables by relative or absolute frequencies. To compare continuous variables, we used the parametric test (t-Student for a sample). To compare categorical variables, we used the Chi-Square Independence test or Fisher's Exact test, when it was impossible to apply the first.

Ethical considerations

This study received the approval of both Ethics Committees involved: the Ethics Subcommittee for Life and Health Sciences and the CHUSJ Ethics Committee.

Results

In these 14 years, we treated 607 newborns with an average birth weight of 1,120 g and an average gestational age of 29.3 weeks. It was found that gestational age is higher in the NICU of CHUSJ compared to the VON in both periods. Induction of fetal maturation is more frequent in the NICU of CHUSJ, with an increase of approximately 6% between the two periods (**Tab. 1**).

The comparison of resuscitation in the Delivery Room (DR) and respiratory support in the NICU between CHUSJ and the VON is described in **Tab. 2**. The use of oxygen therapy in DR decreased when comparing the two periods (80.6% versus 63.0%) and was lower than that checked for the VON. Thus, about 25% of newborns did not require oxygen administration overall. The use of endotracheal intubation was still higher than in the VON, however with a downward trend.

As for the need for respiratory support in the NICU, there was a decrease in the use of oxygen therapy and, more importantly, a decrease in the use of invasive mechanisms that was accompanied by an increase in the use of nasal continuous positive airway pressure (nCPAP), being in the period from 2007 to 2013 of 70.2%. In fact, the use of nCPAP as the first ventilatory approach has been growing, but it still falls short of the use of the VON, which in 2015 was 77.6%.

The comparison of respiratory, cardiac and infectious morbidity and central nervous system (CNS) and ophthalmic pathology in the NICU between CHUSJ and the VON is described in **Tab. 3**. Regarding respiratory morbidity, there are overlapping or better results than those of the VON,

Table 1. Comparison of newborn characteristics, pregnancy and delivery data, between Centro Hospitalar Universitário de São João (CHUSJ) and Vermont Oxford Network (VON).

Variables	CHUSJ, 2000-2006 (n = 315)	VON, 2008 [a] (n = 48,887)	Δ%	p	CHUSJ, 2007-2013 (n = 292)	VON, 2015 [a] (n = 54,289)	Δ%	p
Male	167 (53.0%)	24,639 (50.4%)	+5.16%	p = 0.355	144 (49.3%)	27,145 (50.0%)	-1.40%	p = 0.815
Gestational age	29.2 ± 2.9	28	+4.29%	p = 0.001 [b]	29.4 ± 2.7	28	+5.00%	p = 0.005 [b]
Birth weigth	1,100	1,051	+4.66%	p = 0.098	1,113	1,056	+5.40%	p = 0.077
Multiple pregnancy	94 (29.8%)	14,226 (29.1%)	+2.41%	p = 0.773	106 (36.3%)	15,038 (27.7%)	+31.04%	p = 0.001 [b]
Cesarean section	208 (66.0%)	38,082 (77.9%)	-15.28%	p < 0.001 [c]	215 (73.6%)	39,572 (72.9%)	+0.96%	p = 0.777
Induction of fetal maturation	267 (84.9%)	34,710 (71.0%)	+19.58%	p < 0.001 [c]	265 (90.8%)	45,766 (84.3%)	+7.71%	p = 0.002 [b]

[a] Vermont Oxford Network Database of Very Low Birth Weight Infants. Burlington, VT: Vermont Oxford Network, 2018 – Unpublished data used with permission; [b] significant at 1%; [c] significant at 0.1%.
CHUSJ: Centro Hospitalar Universitário de São João; VON: Vermont Oxford Network.

Table 2. Comparison of resuscitation in the Delivery Room (DR) and respiratory support in the Neonatal Intensive Care Unit (NICU) between Centro Hospitalar Universitário de São João (CHUSJ) and Vermont Oxford Network (VON).

Variable	CHUSJ, 2000-2006 (n = 315)	VON, 2008 [a] (n = 48,887)	Δ%	p	CHUSJ, 2007-2013 (n = 292)	VON, 2015 [a] (n = 54,289)	Δ%	p
Oxygen in DR [b]	254 (80.6%)	41,603 (85.1%)	-5.29%	p = 0.025 [b]	184 (63.0%)	44,680 (82.3%)	-23.45%	p < 0.001 [d]
Endotracheal intubation in DR	204 (65.0%)	24,590 (50.3%)	+29.22%	p < 0.001 [d]	124 (42.5%)	22,313 (41.1%)	+3.41%	p = 0.636
Oxygen in NICU	265 (84.1%)	43,461 (88.9%)	-5.40%	p = 0.007 [c]	196 (67.1%)	46,634 (85.9%)	-21.87%	p < 0.001 [d]
Conventional ventilation	234 (74.3%)	30,114 (61.6%)	+20.62%	p < 0.001 [d]	163 (55.8%)	29,099 (53.6%)	+4.10%	p = 0.448
High-frequency ventilation	11 (3.5%)	8,457 (17.3%)	-79.77%	p < 0.001 [d]	12 (4.1%)	10,912 (20.1%)	-79.60%	p < 0.001 [d]
nCPAP in NICU	200 (63.5%)	39,745 (81.3%)	-21.89%	p < 0.001 [d]	205 (70.2%)	42,128 (77.6%)	-9.53%	p = 0.003 [c]

[a] Vermont Oxford Network Database of Very Low Birth Weight Infants. Burlington, VT: Vermont Oxford Network, 2018 – Unpublished data used with permission; [b] significant at 5%; [c] significant at 1%; [d] significant at 0.1%.
BPD: bronchopulmonary dysplasia; CHUSJ: Centro Hospitalar Universitário de São João; DR: Delivery Room; nCPAP: nasal continuous positive airway pressure; NICU: Neonatal Intensive Care Unit; ROP: retinopathy of prematurity; VON: Vermont Oxford Network.

namely regarding respiratory distress syndrome (RDS) and the need for oxygen therapy on day 28 (23.5% in the 2000-2006 period and 15.4% in the 2007-2013 period). In addition, there is a positive evolution, with a decrease in these rates.

Regarding late-onset sepsis, there was a very significant decrease between the two periods (18.4% in the 2000-2006 period and 9.9% in the 2007-2013 period), however, in both cases, it was much higher than that observed for the VON.

It should be noted that there is a much higher incidence of intraventricular hemorrhage (IVH) and cystic periventricular leukomalacia (cPVL) in the NICU of CHUSJ in relation to the VON, in both periods. Retinopathy of prematurity (ROP) saw an increase between the two periods that was naturally accompanied by an increase in surgery.

The comparison of data on discharge from the NICU between CHUSJ and the VON is described in **Tab. 4**. The length of stay was on average 54.2

Table 3. Comparison of respiratory, cardiac and infectious morbidity, pathology of the central nervous system (CNS), ophthalmic, gastrointestinal and major birth defect in the Neonatal Intensive Care Unit (NICU) between Centro Hospitalar Universitário de São João (CHUSJ) and Vermont Oxford Network (VON).

Variable	CHUSJ, 2000-2006 (n = 315)	VON, 2008 [a] (n = 48,887)	Δ%	p	CHUSJ, 2007-2013 (n = 292)	VON, 2015 [a] (n = 54,289)	Δ%	p
RDS	184 (58.4%)	35,688 (73.0%)	-20.00%	p < 0.001 [d]	151 (51.7%)	38,980 (71.8%)	-28.00%	p < 0.001 [d]
Pneumothorax	11 (3.5%)	2,151 (4.4%)	-20.45%	p = 0.433	13 (4.5%)	2,226 (4.1%)	+9.76%	p = 0.762
Steroids for BPD	13 (4.1%)	3,960 (8.1%)	-49.31%	p = 0.010 [b]	14 (4.8%)	5,157 (9.5%)	-49.47%	p = 0.006 [c]
Oxygen on day 28	74 (23.5%)	23,075 (47.2%)	-50.21%	p < 0.001 [d]	45 (15.4%)	23,887 (44.0%)	-65.00%	p < 0.001 [d]
PDA	76 (24.1%)	9,680 (19.8%)	-50.21%	p = 0.055	78 (26.7%)	14,875 (27.4%)	-2.55%	p = 0.793
Indomethacin/ ibuprofen	65 (20.6%)	11,928 (24.4%)	-16.80%	p = 0.121	92 (31.5%)	11,075 (20.4%)	+54.41%	p < 0.001 [d]
Early-onset sepsis	4 (1.3%)	1,222 (2.5%)	-48.00%	p = 0.203	6 (2.1%)	1,792 (3.3%)	-36.36%	p = 0.234
Late-onset sepsis	58 (18.4%)	3,745 (7.7%)	+138.96%	p < 0.001 [d]	29 (9.9%)	2,660 (4.9%)	+102.04%	p < 0.001 [d]
IVH	41 (13.0%)	3,764 (7.7%)	+68.86%	p < 0.001 [d]	36 (12.3%)	3,583 (6.6%)	+86.36%	p < 0.001 [d]
cPVL	26 (8.3%)	1,418 (2.9%)	+186.21%	p < 0.001 [d]	24 (8.2%)	1,466 (2.7%)	+203.70%	p < 0.001 [d]
Severe ROP	22 (7.0%)	3,520 (7.2%)	-2.77%	p = 0.882	26 (8.9%)	3,040 (5.6%)	+58.93%	p = 0.014 [b]
ROP surgery	10 (3.2%)	1,955 (4.0%)	-20.00%	p = 0.456	13 (4.4%)	1,088 (2.0%)	+120.00%	p = 0.003 [c]
NEC	23 (7.3%)	2,982 (6.1%)	+19.67%	p = 0.375	13 (4.4%)	2,443 (4.5%)	-2.22%	p = 0.939
NEC surgery	7 (2.2%)	1,320 (2.7%)	-18.52%	p = 0.602	13 (4.4%)	1,412 (2.6%)	+69.23%	p = 0.052

[a] Vermont Oxford Network Database of Very Low Birth Weight Infants. Burlington, VT: Vermont Oxford Network, 2018 – Unpublished data used with permission; [b] significant at 5%; [c] significant at 1%; [d] significant at 0.1%.
BPD: bronchopulmonary dysplasia; CHUSJ: Centro Hospitalar Universitário de São João; cPVL: cystic periventricular leukomalacia; IVH: intraventricular hemorrhage; NEC: necrotizing enterocolitis; NICU: Neonatal Intensive Care Unit; RDS: respiratory distress syndrome; ROP: retinopathy of prematurity; VON: Vermont Oxford Network.

Table 4. Comparison of data on discharge from the Neonatal Intensive Care Unit (NICU) between Centro Hospitalar Universitário de São João (CHUSJ) and Vermont Oxford Network (VON).

Variable	CHUSJ, 2000-2006 (n = 315)	VON, 2008 [a] (n = 48,887)	Δ%	p	CHUSJ, 2007-2013 (n = 292)	VON, 2015 [a] (n = 54,289)	Δ%	p
Length of stay	54.2 ± 5.6	62	-12.58%	p < 0.001 [c]	49.9 ± 10.5	64	-22.03%	p < 0.001 [b]
Discharge	217 (68.9%)	35,639 (72.9%)	-5.49%	p = 0.110	177 (60.6%)	40,337 (74.3%)	-18.44%	p < 0.001 [c]
Death	69 (21.9%)	7,333 (15.0%)	+46.00%	p = 0.001 [b]	64 (21.9%)	7,492 (13.8%)	+58.70%	p < 0.001

[a] Vermont Oxford Network Database of Very Low Birth Weight Infants. Burlington, VT: Vermont Oxford Network, 2018. Unpublished data used with permission; [b] significant at 1%; [c] significant at 0.1%.
CHUSJ: Centro Hospitalar Universitário de São João; VON: Vermont Oxford Network.

± 5.6 in the 2000-2006 period and 49.9 ± 10.5 in the 2007-2013 period, below that observed for the VON. The overall mortality of the NICU of CHUSJ was 21.9% in the two studied periods, compared with 15.0% and 13.8% in the first and the second period of the study for the VON, respectively.

Discussion

It is very important for a NICU to know the characteristics of the population it treats and to promote its dissemination. A register such as the VON allows us to compare our data with those of other Units with the same characteristics and to identify the most and least positive aspects in order to improve the latter. In this way, it is possible to measure the quality of their care and evolve in improving care practice. This study provides an overview of the evolution of neonatal care and the outcomes that result from it.

Our VLBWI population has a higher gestational age and greater weight in relation to the VON. It also presents a higher rate of multiple pregnancies and an increasing number of cesarean sections when comparing the two temporal groups.

Regarding induction of fetal maturation, it is observed that this is more frequent in CHUSJ than in the VON and that it has been growing over the years.

RDS has a high incidence in VLBWI and remains an important complication of prematurity as well as a major factor in the mortality and morbidity associated with these newborns, despite the great advances in their prevention and treatment (namely the use of perinatal corticosteroids and surfactant) [7]. The RDS still affects about half of the VLBWI of CHUSJ (despite a downward trend), however a much lower value than that verified for the VON.

One of the negative aspects that urgently needs to be improved is the infection rate associated with healthcare (represented by late-onset sepsis), in which there is a significant deviation from the results of the VON (18.4% in the first period and 9.9% in the second time period in CHUSJ). These numbers will have to be studied and the reasons for such a discrepancy identified, even though we saw a reduction to about half in the second period. On the basis of this reduction will be increased attention to hygiene care (namely hand hygiene), feeding with breast milk, standardizing catheter insertion practices and discontinuing the use of invasive techniques when they are no longer needed [8-10]. Since previous studies associate late-onset sepsis with an increased risk of sequelae, its decrease is essential to improve the long-term outcomes of these newborns [11].

The most important CNS and ophthalmic morbidities associated with this population of VLBWI are IVH, cPVL and ROP.

The IVH registered a decrease between the 2 periods, however still much higher than that observed for the VON. Currently, cPVL is the most important cause of brain damage in premature infants, determining sequels in their neurodevelopment. It is a parameter that is also increased in our NICU. Among the causes of cPVL, invasive mechanical ventilation, twin pregnancy, antepartum hemorrhage and chorioamnionitis are factors where one can act in order to reduce its incidence. Regarding the ROP, it increased when comparing the 2000-2006 period with the 2007-2013 period, which puts us at a higher rate than the VON. Prematurity and low weight are the main risk factors for ROP. In addition, Apgar at the 1st and 5th minute, the oxygen therapy time, the max FiO_2, and the need for surfactant are parameters that also influence ROP and that will have to be analyzed.

The analysis concluded that there is more pathology of the CNS, ophthalmic, gastrointestinal and malformative, as well as higher mortality in the population of VLBWI of the NICU of CHUSJ than in the VON. The main justification seems to be related to the fact that it is a Level III NICU and it is, therefore, a geographic reference center for cardiac and neonatal surgical pathology. This characteristic means that satellite hospitals in the region, whenever they are unable to respond, make the referral of patients to this NICU. However, this inference needs further studies.

The shorter hospital stay is also a consequence of our NICU's high level of differentiation. The need to create vacancies for the hospitalization of newborns with more severe pathology means that those who are not in a critical condition are quickly transferred to hospitals in their area of residence.

This study allowed us to verify that the Service has followed the evolution that Neonatology has had over the years with regard to, for example, less invasive respiratory practices and therapies.

One possible explanation for the improvements observed is the development and dissemination of evidence-based antenatal and obstetric care and the application of best practices in the routine of clinical practice [12].

Induction of fetal maturation with cortico-steroids [11, 13], the adoption of less invasive

ventilatory support techniques [14], standardized care for VLBWI and improved feeding management for newborns, especially the recognition of the importance of feeding with breast milk in these babies [15], are examples of practices that can have measurable effects on these outcomes. The increasing use of Evidence-Based Medicine and its implementation using methods with proven quality have contributed to less mortality and morbidity; this approach has effects only if it is carried out by multidisciplinary groups of NICUs from various hospitals around the world [16, 17]. Late-onset sepsis has been one of the main focuses of the efforts carried out by NICUs, with evidence that neonatal [18, 19], pediatric [10] and adult [20] infections in Intensive Care Units can be reduced by participation in quality improvement programs. Neonatology has been at the forefront in applying science to daily care for newborns.

We can see from this register that, currently, VLBWI are a heterogeneous population. The level of neonatal care required for a newborn with 600 g or 1,400 g, for example, is completely different, as well as the respective mortality and morbidity in its overall. Thus, it will never be overemphasized the need to practice excellent perinatology avoiding as far as possible preterm delivery.

Many of the consequences of prematurity, especially in the most immature ones, are not evident at the time of discharge from the NICU, as was well established in the EPICure studies [12]. It is known that even VLBWI without complications during hospitalization can later have multiple problems that will have to be addressed in a timely manner to minimize them [21, 22]. Thus, the need for a long-term follow-up of these children is evident, which is usually done until entry into compulsory schooling, in order to actually be able to assess the quality of medical practice performed at the Neonatology Service of CHUSJ.

Another aspect we would like to discuss is that we compared our results from the first period (2000-2006) with the VON 2008 and the second period (2007-2013) with the VON 2015. This means that the improvement trend observed in CHUSJ could likely have been greater if we had compared the same years.

Conclusion

Over the past few decades, many things in the healthcare in perinatology have changed. VLBWI are particularly vulnerable, requiring special and highly specialized care.

If, on the one hand, there has been a decrease in mortality, on the other hand, morbidity is still far from what is observed in term newborns, so the road to travel is still long.

The existence of data recording networks such as the VON is extremely important because it allows comparing clinical practices and results among several Neonatal Units with the same characteristics (medical and surgical care), always aiming to improve neonatal outcomes.

This work allowed us to compare our VLBWI population with those registered in the VON. We found that we followed the evolution that Neonatology has undergone over the years and identified areas that could be improved.

Abbreviations

BPD: bronchopulmonary dysplasia
CHUSJ: Centro Hospitalar Universitário de São João
CNS: central nervous system
cPVL: cystic periventricular leukomalacia
DR: Delivery Room
IVH: intraventricular hemorrhage
nCPAP: nasal continuous positive airway pressure
NEC: necrotizing enterocolitis
NICU: Neonatal Intensive Care Unit
RDS: respiratory distress syndrome
ROP: retinopathy of prematurity
VLBWI: very low birth weight infants
VON: Vermont Oxford Network

Disclaimer

The Vermont Oxford Network had no role in the concept, design, analysis, or formulation of this research report. The discussion and views belong solely to the Authors and do not represent the opinions of the Vermont Oxford Network.

Declaration of interest

The Authors declare that there is no conflict of interest.

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