ORIGINAL ARTICLE

PERI-INTRAVENTRICULAR HEMORRHAGE IN NEWBORNS WEIGHING LESS THAN 1500 GRAMS: COMPARATIVE ANALYSIS BETWEEN 2 INSTITUTIONS

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PURPOSE: This study aims to characterize the peri-intraventricular hemorrhages in the neonatal period in very low birth weight newborns in 2 institutions that provide neonatal tertiary assistance.

METHOD: This was a comparative and observational study in 2 neonatal intensive care units, the Maternity Hospital of Campinas and the "Centro de Atenção Integrada à Saúde da Mulher" of the State University of Campinas, from December 01, 1998 to November 30, 1999. We examined 187 newborns for peri-intraventricular hemorrhages, using transfontanel ultrasound (76 and 11 respectively at the first and second unit), and classified them into 4 grades. We observed their gender, intrauterine growth, weight, and gestational age at birth.

RESULTS: We diagnosed 34 cases of peri-intraventricular hemorrhages (13 and 21, respectively), and both groups differed as to the birth weight and the adequacy of weight to the gestational age at birth. There was no difference in the prevalence or extent of peri-intraventricular hemorrhages among cases. There was a statistically significant occurrence of lower birth weight at gestational ages of less than 30 weeks.

CONCLUSIONS: The prevalence of peri-intraventricular hemorrhages in our study was compared to that reported in the world literature. Although the cases of the second institution had a smaller mean birth weight, the prevalence of peri-intraventricular hemorrhages was similar to that at the first institution, probably because in the first one, 69% of the gestational ages of the neonates with hemorrhage were less than 30 weeks as compared to 48% in the second one. We stress the importance of the ultrasonographic method for diagnosing peri-intraventricular hemorrhages in very low birth weight newborns.

DESCRIPTORS: **Intracranial hemorrhage. Intraventricular hemorrhage. Preterm newborn. Transfontanellar ultrasonography.**

Peri-intraventricular hemorrhage (PIVH) is a common event among very low birth weight (VLBW) infants (newborns weighing less than 1500 grams at birth). Its incidence varies in several reports, probably due to the difference between the studied populations or to the availability of the diagnostic means, as well as the differences in study protocols. Among our institutions, the incidence of PIVH varies from 15% to 51%[1,2]. A reduced incidence has been described in the past few decades, especially regarding more severe hemorrhages. However, PIVH remains a concern among neonatologists, since it is related to elevated mortality indexes and directly related to the neurological future of these children[3-5].

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Peri-intraventricular hemorrhage has its origin in the germinal matrix, an area of the lateral ventricular floor that is constituted of spongioblasts and neuroblasts and is responsible for the formation of the cerebral cortex, basal nuclei, and the cerebral support tissue. This structure involutes progres-

sively with the progression of gestational age, becoming less frequent in newborns with gestational age over 34 weeks and/or birth weight over 1500 grams[5].

The germinal matrix is irrigated by immature vessels of thin and friable walls that experience great variations in their blood flow, secondary to the newborn's pressure changes. Therefore, fluctuations in the cerebral blood flow were described as being capable of causing the rupture of these vessels, thus favoring the appearance of PIVH[5].

Therefore, several factors have been related to PIVH in premature newborns weighing less than 1500 grams, since PIVH could be caused by changes in the cerebral blood flow induced by factors such as vaginal delivery, the use of assisted ventilation in respiratory insufficiency, apnea, pneumothorax, asphyxia, hypercapnia, convulsions, cardiopathies, sepsis with shock, and rapid fluid infusions, as well as stressful invasive procedures, including the manipulation of the newborn, venoclysis, and respiratory physical therapy[5-8]. Measures such as the use of antenatal corticosteroids can prevent the occurrence of PIVH by contributing to the occurrence of fewer severe respiratory conditions as well as by acting directly in the maturation of the cerebral vessels[5].

Often, PIVH is clinically asymptomatic, and when it presents symptomatology, it can be slight, with changes of conscientiousness level, a decrease in the spontaneous activity, hypotonia, and discrete changes in the ocular position and movements. Severe conditions are more rarely described, such as profound stupor/coma, hypoventilation and apnea, generalized tonic convulsions, and pupils and eyes nonreactive to luminous stimuli. These clinical signs can be followed by hypotension, fontanelle vault, bradycardia, thermal unbalance, hematocrit fall, metabolic acidosis, changes in the fluid balance and glucose homeostasis, and, more rarely, the syndrome of inappropriate secretion of antidiuretic hormone[5].

Therefore, ultrasonography has been considered the method of choice for the detection and follow-up of PIVH, thus enabling a precocious diagnosis even in asymptomatic cases. In addition to its high sensitivity, ultrasonography does not use radiation, thus being a noninvasive procedure that is performed easily and quickly by apt physicians. Additionally, nurses can perform the procedure when other intracranial imaging methods are unavailable[4].

In this study, we aimed to find the prevalence of PIVH and to compare the data obtained in the analyses of 2 populations of VLBW infants from 2 neonatal care institutions that are structurally different from one another, trying to identify epidemiological factors related to the occurrence of the disease.

METHOD

A comparative study was performed in VLBW infants to check the frequency of PIVH, to compare the studied groups, and to identify the factors related to the diagnosis of the disease in 2 neonatal tertiary institutions from December 01, 1998 to November 30, 1999.

The first institution, the Maternity Hospital of Campinas (MC), is the largest maternity hospital in the region and provides assistance to about 800 deliveries/month. Approximately, 64% of its newborns are covered under the Unique Health System (SUS), with the others being covered by health plans or being covered under private payers. The MC patients present a low birth weight (LBW), infant index (infants under 2500 grams at birth) of 8.8%, and VLBW index of 1.3%. The other institution, the "Centro de Atenção Integrada à Saúde da Mulher" of the State University of Campinas (CAISM/UNICAMP), assists exclusively SUS patients with about 300 deliveries/month, presenting LBW and VLBW indexes of 17% and 3.3% respectively.

As to the existing resources for the care of preterm newborns, MC has 54 beds distributed between high-risk and medium-risk care and others financed by the township. The CAISM/UNICAMP has a capacity of 30 beds, also distributed among high-risk and medium-risk care, but with a university structure financed by the State. Therefore, both maternity hospitals present similar therapeutic infrastructures, but it is important to consider that access to the diagnostic procedures and to multiprofessional teams are different between a private philanthropic hospital and a university hospital.

The diagnostic method chosen was transfontanel ultrasound. It was performed around the seventh day of life by neonatologists trained at the CAISM/UNICAMP and capable of performing the exam. At the MC, the equipment utilized was the Aloka SSD-500, with a 5MHz microconvex electronic transducer, and at the CAISM/UNICAMP, an Aloka SSD-630 with a sectorial mechanical transducer with equal frequency was used. The exams were recorded on black and white film through a Sony UP - 890MD Video Printer, which allowed for a review of the pathologic cases by a second observer. The criterion utilized for the PIVH diagnosis followed the rating proposed by Papile[9] in 1978, which consists of 4 grades: I – the bleeding is confined to the germinal matrix, II – PIVH occurs with no ventricular dilatation, III – PIVH occurs with dilatation, and IV – the PIVH compromises the cerebral parenchyma.

We characterized the population by:

1) gender;
2) birth weight, measured using electronic scales with grading at each 5 grams;
3) gestational age (GA), calculated as definitive utilizing amenorrhea if compatible with a precocious fetal ultrasonographic criterion (FUC), or the latter if these conflicted. If no fetal ultrasound (FUC) was performed until the 20th week of GA, we utilized the amenorrhea criterion if it was corroborated by the physical exam (Capurro[10] in the conceptuses older than 29 weeks and New Ballard[11] in those younger than 29 weeks), or the latter criterion if the difference was greater than 2 weeks.
4) intrauterine growth, evaluated by the curves of Battaglia and Lubchenco[12] .

A total of 211 neonates were selected (80 at MC and 131 at CAISM/UNICAMP), with 24 newborns being excluded because they presented a birth weight less than 500 grams, malformation of the central nervous system, precocious neonatal death, or because they had not been evaluated by the ultrasonographic method at the proposed time. Therefore, 76 newborns from MC and 111 from CAISM/UNICAMP were admitted in this study, a total of 187 children.

The frequency of PIVH was observed in both hospitals, and the results were analyzed according to the characteristics of each population. Frequency tables for the categorical variables as well as measurements of position and dispersion for the continuous variables were designed for the descriptive analysis. The chi-square test or the Fisher's exact test were utilized for the comparison of proportions when needed. The Shapiro-Wilk test was utilized to check the normality of the distributions of the continuous variables. The Mann-Whitney test was utilized for the comparison of continuous variables or the ordinal ones between 2 groups. Logistic regression analysis was utilized for the dichotomous response – logit model, in order for the variables that determine the PIVH to be checked. All the analyses were carried out with the use of the SAS System for Windows (Statistical Analysis System) program.

The protocol of the study was approved by the Ethics Committee of both institutions, and all the newborns were included after the consent of their parents.

RESULTS

The CAISM/UNICAMP hospital exhibited a smaller mean birth weight of their newborns, whose population consisted of a significantly higher number of infants who were small for gestational age (SGA), as shown on table 1. The prevalence of PIVH and the distribution of the different grades was identical for MC and CAISM/UNICAMP, and both institutions presented a higher frequency of parenchymatous hemorrhage than intraventricular hemorrhage (Table 2).

At the CAISM/UNICAMP, the population with hemorrhage was constituted mainly of infants who were SGA, a difference from the MC. We observed that at the CAISM/UNICAMP, 62% of the newborns with PIVH weighed less than 1000 g as compared with 46% at MC, whereas at CAISM/UNICAMP only 48% of newborns with PIVH had a GA of <30 weeks, as compared to 69% of the newborns with PIVH at MC (Table 3).

Regarding the related studied factors, we observed a positive correlation of the birth weight less than 1000 g and the GA less than 30 weeks with the occurrence of PIVH (Table 4). Regarding the epidemiological variables related to PIVH to the place studied, we found a tendency, although not significant, of more hemorrhage at the CAISM/UNICAMP. There was a statistically significant correlation between GA <30 weeks and occurrence of PIVH (Table 5).

Table 1 - Epidemiological characteristics of the 187 newborns.

Characteristic	MC (n=76)	CAISM/UNICAMP (N=111)	*p* value
Male (n)	33	41	0.33
Weight (mean)	1178 ± 227 g	1061 ± 252 g	**0.002**
Gestational age (mean)	30.4 ± 2.6 weeks	30.7 ± 2.7 weeks	0.24
Small for gestational age (n)	24	62	**0.001**

MC - Maternity Hospital of Campinas; CAISM/UNICAMP - "Centro de Atenção Integrada à Saúde da Mulher" of the State University of Campinas.

Table 2 - Frequency of peri-intraventricular hemorrhage (PIVH) and its extent in each institution.

	MC		CAISM/UNICAMP		*p* value
	N	%	n	%	
PIVH	**13**	**17.1**	**21**	**18.9**	**0.75**
Grade I	6	46	12	57	0.94
Grade II	1	7.6	1	4.7	0.94
Grade III	2	15.3	3	14.2	0.94
Grade IV	4	30.7	5	23.8	0.94

MC - Maternity Hospital of Campinas; CAISM/UNICAMP - "Centro de Atenção Integrada à Saúde da Mulher" of the State University of Campinas.

Table 3 - Epidemiological characteristics of newborns with peri-intraventricular hemorrhage.

Characteristics	MC	CAISM/UNICAMP	*P* value
Male (%)	53.8	38	0.36
Weight (mean)	1059 ± 262 g	939 ± 241 g	0.14
Weight < 1000 g (%)	46	62	0.36
Gestational age (mean)	28.9 ± 2.4	29.1 ± 2.4	0.70
Gestational age < 30 weeks (%)	69	48	0.21
Small for gestational age (%)	15.3	57.1	**0.02**

MC - Maternity Hospital of Campinas; CAISM/UNICAMP - "Centro de Atenção Integrada à Saúde da Mulher" of the State University of Campinas.

Table 4 - Observation of factors related to peri-intraventricular hemorrhage (PIVH).

Variable	With PIVH (34)	Without PIVH (153)	*p* value
Weight < 1000 g (%)	55.8	30	**0.005**
Gestational age < 30 weeks (%)	55.8	27	**0.001**
Male (%)	44	38	0.56
Small for gestational age (%)	41	47	0.49

Table 5 - Final model of multivariate logistic regression.

Variable	Estimate	*p* –value	Odds Ratio	Gestational age 95%
Intercept	-0.1402	<0.0001	-	-
Place MC x CAISM/UNICAMP	-0.1407	0.4876	0.755	(0.341 - 1.671)
Gestational age < 30 x ≥ 30 weeks	0.6245	**0.0016**	3.487	(1.607 - 7.569)

MC - Maternity Hospital of Campinas; CAISM/UNICAMP - "Centro de Atenção Integrada à Saúde da Mulher" of the State University of Campinas.

DISCUSSION

The prevalence of PIVH in our study is in accordance with the data reported in the literature, which vary from 15% to 37% in more recent years, with the higher frequency being associated with smaller birth weight and younger GA[3,7,13]. The frequency of PIVH was similar in both institutions, which was not expected, because there was a significant difference with regard to the weight of the newborns between these institutions. Therefore, we had predicted a higher prevalence of PIVH at the CAISM/UNICAMP due to a smaller ponderal mean, which was not observed. Consequently, a hypothesis was proposed that the higher frequency of newborns with fetal growth restriction found at the CAISM/UNICAMP could have neutralized the expected tendency, since the literature has suggested that fetal malnutrition confers protection through the acceleration of the cerebral maturity, with a still undefined consensus[3,7,14] .

However, when analyzing the newborns with PIVH, we observed that at the CAISM/UNICAMP there was a higher occurrence of bleeding in SGA, following the distribution of the nutritional classification of its population. Therefore, the hypothesis that cerebral maturation could be induced by the restriction of intrauterine growth, conferring protection to the central nervous system, could not be supported. In order to obtain the nutritional classification, we utilized the Battaglia and Lubchenco[12] reference curve, which reflects part of the American population in the 1960s, when the ideal would be to use curves reflecting the Brazilian population[15]. This strategy could have affected our results. Nevertheless, the reference curve is valid, since we utilized the same curve in both analyzed services. Another problem associated with the nutritional classification is the determination of GA, since the weight is a easily measurable variable. Gestational age, in the absence of the precocious fetal ultrasonographic data, is a variable subject to bias, since it depends on natural physiological variations of the ovulatory cycle in calculating the amenorrhea or on a subjective evaluation of the physical and neurological characteristics of the newborn. Finally, we have to consider that the small and disproportional number of SGA with PIVH at MC in comparison with CAISM/UNICAMP (2 and 14 respectively) could possibly compromise this analysis.

In an attempt to explain the statistical parity of PIVH between both institutions, we observed the hemorrhages together and verified that a weight less than 1000 g (p = 0.005) and a GA less than 30 weeks (p = 0.001) were variables that were significantly related to the occurrence of PIVH, which had already been reported in the literature[3,5,7,14]. Based upon these findings, we applied the multivariate logistic regression model, rating the institution, the weight, the GA, and the nutritional classification as independent variables. Gender was excluded, since it did not modify the results when present or not in the analysis. We established the variable *institution* for correction of the odds ratio, and we observed that at the CAISM/UNICAMP there was a higher tendency for bleeding, although this finding was not significant (p = 0.75). Gestational age was the variable that showed a higher correlation to the pathology (p = 0.02) in the complete

model, with a 3.5 times chance of bleeding being noted in the newborns less than 30 weeks in the final model, which speaks to the physiopathology of the disease. Although we had observed a higher tendency for the occurrence of PIVH at the CAISM/ UNICAMP, this finding was not corroborated in our findings, possibly due to a higher frequency of newborns less than 30 weeks with hemorrhage at the MC.

Regarding the severity of the bleeding, the majority of the articles found showed a higher prevalence of less severe hemorrhages[7,8,16,17]. Our study was in accordance with these findings regarding Grade I hemorrhage, but disagreed with the other distributions, due to the higher frequency of the parenchymatous hemorrhage. This finding can be explained by the lower mortality rate of these newborns, which previously could not express this condition[5,18]. Currently in the developed countries, the higher survival of severe cases is also followed by the reduction of morbidity, since the technological infrastructure enables preventive actions for the pathology[5].

Through the studies of the incidence of PIVH in the different neonatal intensive care units, it is possible to obtain a profile of the disease and to propose control measures. Even though the factors implied in the genesis of PIVH are obscure with regard to providing data that would enable interventions for the reduction of its occurrence[5,6], the literature begins to infer that the precocious treatment of some conditions related to the pathology is a differential in the reported incidence[19]. The established diagnosis makes possible the verification of the related problems, thus enabling interventions for improvement of the quality of life of these children[20]. The diagnostic method utilized in this study is in accordance with these proposals, and all the concerns are justified because of the extensive number of preterm infants that survive today, enhancing the social impact that the cerebral lesions cause. Therefore, our results indicate the need for precocious ultrasonographic diagnosis of PIVH in all centers for tertiary neonatal assistance in the Brazil and also provide indirect indicators for the quality of the assistance to be provided to the fetus and to the newborn. The resources spent on the implementation of the method in all neonatal intensive care units, when analyzed only in light of the preterm newborn hemorrhages, can be considered a good investment. These institutions serve 20% of this population of newborns with risk for the disease, and they provide actions for the prevention of the pathology, a priority issue for the developed countries with regard to public health strategies. These factors should rule the policy of distribution of resources to mother/fetal assistance.

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RESUMO

PONTE MD da e col. - Hemorragia periintraventricular em recém-nascidos menores de 1500 gramas: análise comparativa entre duas instituições. **Rev. Hosp. Clín. Fac. Med. S. Paulo 58**(6):299-304, 2003.

OBJETIVO: Caracterização das hemorragias periintraventriculares no período neonatal, em recém-nascidos de muito baixo peso (<1500g), em duas instituições de atendimento terciário neonatal.

MÉTODOS: O estudo foi observacional e transversal, em duas unidades de terapia intensiva neonatais, a da Maternidade de Campinas e a do Centro de Atenção Integrada à Saúde da Mulher da Universidade Estadual de Campinas, no período de 01 de Dezembro de 1998 a 30 de Novembro de 1999. Rastreamos 187 recém-nascidos para a pesquisa de hemorragias, através de ultra-sonografia transfontanelar (76 e 111, respectivamente, na primeira e segunda unidade) e as classificamos em 4 graus. Verificamos o sexo, crescimento intra-uterino, peso e idade gestacional ao nascimento.

RESULTADOS: Diagnosticamos 34 casos de hemorragias (13 e 21, respectivamente) e os dois grupos diferiram no peso de nascimento e adequação do peso à idade gestacional. Não existiu diferença na prevalência ou extensão das hemorragias entre ambos. Houve correlação do peso e da idade gestacional com a sua ocorrência, e a idade gestacional inferior a 30 semanas mostrou significativa associação.

CONCLUSÃO: A prevalência das hemorragias periintraventriculares em nosso estudo foi comparável à da literatura mundial. Embora os recém-nascidos da segunda instituição tivessem menor média de peso, sua prevalência de hemorragias foi semelhante à da primeira, provavelmente porque nessa,

69% dos neonatos com hemorragia tinha uma idade gestacional inferior a 30 semanas (e 48% na segunda). Destacamos a importância do método ultra-sonográfico para o diagnóstico das hemorragias periintraventriculares em recém-nascidos de muito baixo peso.

DESCRITORES: **Hemorragia intracraniana. Hemorragia intraventricular. Recém-nascido pré-termo. Ultra-sonografia transfontanelar.**

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