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.

sively with the progression of gesta-
tional age, becoming less frequent in
newborns with gestational age over 34
weeks and/or birth weight over 1500
grams\(^3\).

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 in-
duced by factors such as vaginal de-
ivery, the use of assisted ventilation
in respiratory insufficiency, apnea, pneu-
mothorax, 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\(^5\,^6\). 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 asympto-
matic, and when it presents symptoms,
it can be slight, with changes of
conscientiousness level, a decrease
in the spontaneous activity, hypotonia,
and discrete changes in the ocular po-
sition and movements. Severe condi-
tions are more rarely described, such
as profound stupor/coma, hypoventilation and apnea, general-
ized 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 glu-
cose 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 di-
agnosis even in asymptomatic cases. In
addition to its high sensitivity, ultra-
sonography 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 un-
available\(^5\).

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 fac-
tors related to the occurrence of the dis-
ease.

**METHOD**

A comparative study was per-
formed in VLBW infants to check the
frequency of PIVH, to compare the
studied groups, and to identify the fac-
tors related to the diagnosis of the dis-
ease 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
(CAIMS/UNICAMP), assists exclu-
sively SUS patients with about 300
deliveries/month, presenting LBW and
VLBW indexes of 17% and 3.3% re-
spectively.

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. There-
fore, 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 hos-
pital and a university hospital.

The diagnostic method chosen was
transfontanel ultrasound. It was per-
formed around the seventh day of life
by neonatologists trained at the
CAISM/UNICAMP and capable of per-
forming 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 re-
view of the pathologic cases by a sec-
don observer. The criterion utilized for
the PIVH diagnosis followed the rat-
ing 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 ven-
tricular dilatation, III – PIVH occurs
with dilatation, and IV – the PIVH
compromises the cerebral parenchyma.

We characterized the population by:
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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 (Capurro10 in the conceptuses older than 29 weeks and New Ballard11 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 Lubchenco12.

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.

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

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.

<table>
<thead>
<tr>
<th>PIVH</th>
<th>MC</th>
<th>%</th>
<th>CAISM/UNICAMP</th>
<th>n</th>
<th>%</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>MC</td>
<td>%</td>
<td>N</td>
<td>n</td>
<td>%</td>
<td></td>
</tr>
<tr>
<td>Grade I</td>
<td>6</td>
<td>46</td>
<td>12</td>
<td>57</td>
<td>0.94</td>
<td></td>
</tr>
<tr>
<td>Grade II</td>
<td>1</td>
<td>7.6</td>
<td>1</td>
<td>4.7</td>
<td>0.94</td>
<td></td>
</tr>
<tr>
<td>Grade III</td>
<td>2</td>
<td>15.3</td>
<td>3</td>
<td>14.2</td>
<td>0.94</td>
<td></td>
</tr>
<tr>
<td>Grade IV</td>
<td>4</td>
<td>30.7</td>
<td>5</td>
<td>23.8</td>
<td>0.94</td>
<td></td>
</tr>
</tbody>
</table>

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. 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.

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 reference curve, which reflects part of the American population in the 1960s, when the ideal would be to use curves reflecting the Brazilian population. 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 and a GA less than 30 weeks were variables that were significantly related to the occurrence of PIVH, which had already been reported in the literature. 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. Gestational age was the variable that showed a higher correlation to the pathology.
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. 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. 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. 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, the literature begins to infer that the precocious treatment of some conditions related to the pathology is a differential in the reported incidence. The established diagnosis makes possible the verification of the related problems, thus enabling interventions for improvement of the quality of life of these children. 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


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 observational 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). Destacam a importância do método ultra-sonográfico para o diagnóstico das hemorragias perintraventriculares em recém-nascidos de muito baixo peso.


REFERENCES


