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Original articles

Intracranial hemorrhage and central auditory disorders in neonates

Avaliação do sistema nervoso auditivo central em neonatos com Hemorragia peri intraventricular

Rosanna Giaffredo Angrisani[1]
Ana Micheline Costa Fagá[2]
Ana Lucia Goulart[3]
Marisa Frasson de Azevedo[4]

[1] Hospital São Paulo da Universidade Federal de São Paulo. São Paulo, SP - Brasil
[2] Universidade Federal de São Paulo - UNIFESP. São Paulo, SP - Brasil
[3] Departamento de Pediatria da Universidade Federal de São Paulo - UNIFESP. São Paulo, SP - Brasil.
[4] Departamento de Fonoaudiologia da Universidade Federal de São Paulo - UNIFESP. São Paulo, SP - Brasil.

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ABSTRACT

Purpose: to verify the occurrence of Intracranial hemorrhage in preterm infants undergoing neonatal intensive care, characterizing the occurrence of central hearing impairment in this population and its variation depending on the degree of hemorrhage.

Methods: a longitudinal retrospective study. Of the 719 premature infants, 46 (6.4%) had peri-intraventricular hemorrhage. 84 patients were selected, and divided into two groups: a study group, consisted of 42 with hemorrhage, and a control group, consisted of 42 without peri-intraventricular hemorrhage. All had transient evoked otoacoustic emissions present, and underwent brainstem auditory evoked potential investigation during hospitalization and were followed for two years, through behavioral assessment of hearing.

Results: there was a higher incidence of central alteration in the study group (33.4%) compared to the control group (4.8%), characterized by increased latency of waves III and V and interpeak interval IV. The auditory central alteration was higher in preterm infants with hemorrhage grade II, III and IV in the degree I, being significant.

Conclusion: The occurrence of peri-intraventricular hemorrhage was 6.4%. The occurrence of central alteration was 33.4% and varied with the hemorrhage degree: children with hemorrhage grades II, III and IV showed higher occurrence of central alteration in relation to the ones with hemorrhage grade I. In audiological follow-up, central hearing impairment remained at 51.85% of children who already had this alteration since birth.

Keywords: Intracranial Hemorrhages; Hearing; Infant, Newborn; Evoked Potentials, Auditory, Brain Stem

RESUMO

Objetivo: verificar a ocorrência de Hemorragia peri intraventricular em recém-nascidos prematuros submetidos a cuidados intensivos neonatais, caracterizando a ocorrência de alteração auditiva central nessa população e sua variação em função do grau de hemorragia.

Métodos: estudo longitudinal, retrospectivo. Dos 719 recém-nascidos prematuros, 46 (6,4%) apresentaram hemorragia peri-intraventricular. Foram selecionados 84 neonatos, distribuídos em Grupo Estudo formado por 42 com Hemorragia e Grupo Controle, com 42 sem Hemorragia Peri-intraventricular. Todos tiveram emissões otoacústicas evocadas por estímulo transiente presentes e foram submetidos à pesquisa do potencial evocado auditivo de tronco encefálico no período de internação e acompanhados durante dois anos, por meio de avaliação comportamental da audição.

Resultados: houve maior ocorrência de alteração central no Grupo Estudo (33,4%) em relação ao Grupo Controle (4,8%), caracterizada pelo aumento de latência das ondas III e V e intervalo interpico I-V. Houve maior ocorrência de alteração auditiva central nos prematuros com hemorragia graus II, III e IV em relação ao grau I.

Conclusão: A ocorrência de Hemorragia peri intraventricular foi de 6,4%. A ocorrência de alteração central foi de 33,4% e variou em função do grau da hemorragia: crianças com Hemorragia graus II, III e IV, apresentaram maior ocorrência de alteração central em relação às de grau I. No monitoramento audiológico, a alteração auditiva central manteve-se em 51,85% das crianças que já apresentavam tal alteração ao nascimento.

Descritores: Hemorragia Intracraniana; Audição; Recém-Nascido; Potenciais Evocados Auditivos do Tronco Encefálico

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Mailing address:
Rosanna Giaffredo Angrisani
Rua Botucatu, 802
São Paulo - SP – Brasil
CEP: 04023-900
E-mail: roangrisani@gmail.com

INTRODUCTION

Peri-intraventricular hemorrhage (PIVH) is a neurological disease that mainly affects low birthweight preterm newborns (PN). Several studies show that gestational age lower than 32 weeks and very low birth weight are risk factors for the occurrence of this disease.[1] The incidence of PIVH is higher in newborns with birth weight below 750g (32.6%), and lower (11.6%) in those with birthweights between 1,251 and 1,499g. Over the years there is a significant drop in incidence of PIVH for all weight ranges.[2]

PIVH occurs from the subependymal germinal matrix, the site of neuronal proliferation and origin of the tissue that support the brain. It is a highly vascularized region, but with vessels which present a fragile morphology. These characteristics, associated to immaturity, make these vessels vulnerable to the action of peri and postnatal aspects that occurs in some situations, such as: perinatal asphyxia, mechanical ventilation, birthweight inferior to 1500g, gestational age inferior to 34 weeks, among others.[3,4]

The most widely PIVH classification used was established by Papile et al. (1978)[5] based on skull CT scans. According to this classification the PIVH can be subdivided into: grade I which is limited to the area of the germinal matrix (subependymal hemorrhage); grade II, when there is a extension to ventricles without ventricular dilatation; grade III when there is an enlargement of the ventricles; and grade IV when it compromises the brain parenchyma.

The prognosis for PIVH varies according to the degree of injury. For the grade I and II hemorrhage, the infant often progresses without any noticeable neurological abnormalities; the grade III may develop into ventriculomegaly or hydrocephalus, with an incidence of 40% for cerebral palsy and mental retardation. PIVH grade IV has a high mortality rate, especially when major injuries occur in low gestational age infants.[6]

PIVH is one of the causes of peripheral and central auditory disorders in premature,[7] which may cause changes in the development of hearing and language.[8]

Hearing and language are interrelated functions, which makes the anatomical and functional integrity of audio system crucial for the development and improvement of various hearing abilities which are performed by the peripheral and central auditory system.[8,9]

In a retrospective study, the medical records of 27 newborns with PIVH treated in ICU were analyzed in respect to audiological evaluation with Transient-evoked otoacoustic emission tests, and brainstem evoked auditory potential. The authors found 11.11% of central change in grade I PIVH; 57.14% in grade II PIVH, and 50% in grade III PIVH. The authors concluded that infants with PIVH present high occurrence of central auditory disorders, especially neonates with grades II and III PIVH, justifying the need for inclusion of Brainstem Auditory Evoked Potential (BAEP) in audiological diagnosis of this population.[10]

Based on these, this study aims at verifying the occurrence of peri-intraventricular hemorrhage (PIVH) in premature infants treated in neonatal ICU, featuring the occurrence of central hearing impairment in this population and its variation depending on the degree of hemorrhage.

METHODS

This study was reviewed and approved by the Federal University of São Paulo Ethics Committee, protocol 195. 777.

The study was retrospective, longitudinal and developed from a survey of 719 newborn medical records from a public hospital between 2009 and 2012, from which 84 met the inclusion criteria for this study. Although the study is retrospective, all assessment was held by the authors.

Inclusion criteria adopted were: preterm newborns from the maternity ward in the institution, with or without the presence of PIVH according to ultrasound examination; and presence of otoacoustic emissions by transient stimulus at birth, who regularly attended the multidisciplinary monitoring program in the same institution.

Term infants and/or preterm neonates born in other hospitals were excluded from the study.

The study group (SG) consisted of 42 preterm newborns (PN) that presented peri-intraventricular hemorrhage (PIVH) at birth. The control group (CG) consisted of 42 preterm infants who did not have peri-intraventricular hemorrhage at birth, and matched by sex and age. Gestational age for both groups ranged from 28 to 31 weeks. The post-conceptual age at first assessment varied from 33 to 36 weeks in both groups.

The PIVH classification (I, II, III and IV) was conducted by the maternity neonatology medical staff, using the classification of Papile et al., 1978.[4] For the demographic characteristics of the children included in the study, data related to gender, gestational age and birthweight were collected.

The first stage of the study consisted of an analysis of transient evoked otoacoustic emissions (TEOE) and brainstem auditory evoked potential (BAEP) performed in 84 preterm infants in the predischarge. In the second stage of the study, we analyzed the medical records of children who attended the hearing monitoring visits during the first two years of life in the Children's Audiology Clinic at the institution. From the 84 preterm infants, 46 (54.8%) regularly attended the follow-up assessment for auditory development: 27 (58.7%) from the study group; and 19 (41.3%) from the control group.

The behavioural assessment included a survey of the development of the hearing abilities of sound localization and audiometry with visual reinforcement for children aged between six and 18 months; recognition of commands for children aged nine months or more; and the test of cochlear-palpebral reflex, following the recommendation and suggested criteria by Azevedo.[8] It was considered an alteration of development when a delay of the responses for sound localization or recognition of verbal commands were observed, with minimum response levels superior to the expected for their age in visual reinforcement audiometry, or non-response to pure tone for standard hearing sensitivity.[9]

The comparison of the results between the two groups was performed to test the hypothesis that the PTNB group with PIVH would present a higher incidence of central auditory alterations and delayed development. For comparison between groups we used the chi-square test with Yates's continuity correction.[11]

RESULTS

The incidence of PIVH in the studied population was 6.4%.

The analysis of the brainstem auditory evoked potential (BAEP) made at birth showed a higher incidence of central alterations in the group with PIVH (Table 1).

The alterations observed in the SG were an increased latency for waves III and V and an interpeak interval I-V, suggesting impairment of the high brainstem portion.

Table 1. Results for Brainstem Auditory Evoked Potential at birth for both groups

	Normal		Altered		Total	
	n	%	n	%	n	%
GE	28	66,6	14	33,4	42	100
GC	40	95,2	02	4,8	42	100
Total	68	80,9	16	19	84	100

Chi-square test (p)=0,002*. Significant.
SG – Study group; CG- Control Group; N – number of children; % - percentage

There was a significant association between BAEP and the grade of PIVH in the study group (SG), presented in Table 2.

There was a higher occurrence of central abnormality for grade II, III and IV PIVH children, as compared to the degree I, statistically significant (Table 3).

Table 2. Results for Brainstem Auditory Evoked Potential in relation to the peri-intraventricular haemorrhage in the study group.

PIVH	Normal		Altered		Total	
Grade I	22	84,7%	04	15,3%	26	100%
Grade II	04	44,4%	05	55,5%	09	100%
Grade III	0	0%	03	100%	03	100%
Grade IV	02	50,0%	02	50%	04	100%
Total	28	66,7%	14	33,3%	42	100%

Chi-square test - p=0,002*. Significant.
PIVH - Peri-intraventricular hemorrhage

Table 3. Results for Brainstem Auditory Evoked Potential in relation to the peri-intraventricular haemorrhage grade in the study group

PIVH	Normal		Altered		Total	
Grade I	22	84,7%	04	15,3%	26	100%
Grades II+III+IV	06	37,5%	10	62,5%	16	100%
Total	28	66,7%	14	33,3%	42	100%

Chi-square test - p=0,005*. Significant.
PIVH - Peri-intraventricular hemorrhage

From the 27 children followed in the SG, the ability for sound localization were preserved in 21 (77%) and abnormal for six infants (23%). In the control group (19 children), location was adequate in 16 (84.2%) and abnormal in three (15.8%). However, there was no significant difference (p = 0.389) in relation to this ability.

The visual reinforcement audiometry was considered appropriate to the age in 20 (74%) and abnormal in seven (26%) of 27 children from the SG. It was adequate in 18 (95.2%) and abnormal in one (4.8%) of the 19 children in the CG, with no significant difference between groups (p = 0.055).

The recognition of verbal commands, considering children over the age of nine months, showed changes in 52.2% of children in the SG and 37.5% for the CG, with no significant difference (p = 0.342).

The occurrence of hearing loss obtained in audiologic follow-up is presented in Table 4.

Table 4. Audiologic assessment during follow-up for both groups

	Normal		Altered		Total	
SG	09	33,3%	18	66,7%	27	100%
CG	12	63,2%	07	36,8%	19	100%
Total	21	45,7%	25	54,3%	46	100%

Qui-square test - p=0,072#. Não significante.
SG – Study Group; GC - Control Group

DISCUSSION

In the three-year period studied, the occurrence of PIVH in premature infants was 6.4%, similar to the data obtained in previous national study, which found 5%.[12] Surveys with very low birthweight preterm infants observed an occurrence of PIVH varying from 11% to 44.68%.[2,13]

However, literature has been signalling a decrease in the occurrence of PIVH in children with very low birthweight, from 50.9% in 1991 to 11.9% in 2005,[13] for the Brazilian population, the study noted significant reduction in PIVH during the four years analyzed.[12] The decrease in the incidence of hemorrhage can be attributed to an improvement in the overall care of newborns in intensive care units, such as treatment with surfactant and prenatal steroids, modernization of mechanical ventilation equipment and reduction of the newborn manipulation.[2,13]

Intracranial hemorrhage in preterm newborns may occur due to the immaturity of cerebral blood vessels. PIVH is a common complication in premature, especially those with very low birthweight, and it may lead to important consequences, among them, peripheral and central auditory disorders, including auditory processing disorders that interfere with language development, school learning and subsequent social performance. Based on the principle that hearing and language are interrelated, it is believed that it is essential to evaluate and monitor the auditory and language development in children who have had this type of hemorrhage at birth, confirming the conclusion of previous study.[14]

In this study there was a higher occurrence of central hearing loss for the group with PIVH, reinforcing previous research findings.[14] These data indicate that PIVH can be considered a significant risk indicator for central alteration. Thus, it is believed that premature infants who suffered PIVH in the neonatal period

present a higher risk of alterations in auditory pathway in its central portion when compared to those who did not suffer such complications.

In this study there was a higher incidence of grade I PIVH, which presents a better prognosis, with chance of resorption. In contrast, research that evaluated 28 children with cerebral palsy, found a higher incidence of grades III and IV PIVH (21%) as compared to grade I (14%). This difference was probably due to the type of population, which included exclusively children with cerebral palsy, a frequent sequel of grades II, III and IV PIVH.[15]

Although it was not the objective of this study, it was observed that 59.4% of the SG infants were born with gestational age inferior to 30 weeks, while 76.2% of children had a birthweight inferior to 1500g. Indeed, previous study found a statistically significant correlation between weight and the occurrence of PIVH, being proportional to lowest average weight, a fact that led the authors to conclude that the PIVH is a frequent event and can be associated to a birthweight inferior ton 1500g.[16] On the other hand, in a longitudinal study with 847 children born with gestational age inferior to 33 weeks, it was observed that the presence and severity of developmental changes were directly related to the occurrence and intensity of PIVH, regardless of the child's gestational age. The authors found that multifactorial etiology of PIVH is frequent and is an important risk factor for developmental delays.[17]

Therefore, it is confirmed the urge for monitoring the overall development of the child, including hearing and language.

The purpose of the multidisciplinary monitoring program of the institution responsible for the present study is to provide support and guidance to families of newborns who are at risk for peripheral and/or central hearing loss, either temporary or permanent, particularly for the language delay risk and the importance of early stimulation. However, because of poor adherence (drop-out rate of 45.2% in the SG), monitoring of PIVH patients was impaired, even considering that 15% had presented central hearing loss at birth. This evasion was probably due to the low socioeconomic level of the children treated at the public hospital. In addition, the hospital serves people from various regions of Brazil, which makes it often difficult to follow. These findings are consistent to those found in longitudinal studies that show rates of 46% evasion.[18-20]

After analyzing the audiological evaluation performed during follow-up, it was found that from the 27 neonates of the SG participating in the monitoring program, 18 (66.7%) had central hearing impairment. From these, 14 (51.85%) had already presented such alteration at birth. In four cases the change was only identified in the monitoring, which demonstrates the importance of following the auditory development for high risk newborns.

In fact, the audiological assessment periodically conducted during the first years of life allows checking the progress of response skills to acoustic stimuli with increasing age which, in turn, reflects the central nervous system maturation process. [8] Alterations in hearing development may reflect auditory processing disorders with repercussions on school learning.

The sound localization ability can be observed from six months of age.[8] The average age of these children in the evaluation of sound localization was six to 10 months. According to the literature, a difficulty for sound localization has been observed both for premature infants without PIVH[8-14] and in preterm infants with PIVH[14]. These results are similar to those of the present study with the highest occurrence of delay of sound localization in children with PIVH, although the difference is not significant probably due to the sample restriction as a consequence of evasion.

In this study, two children in the control group presented a reduction in the sound localization ability. In fact, another study also found delay sound localization in premature infants treated in neonatal intensive care unit, without specifying the presence of PIVH.[21]

The Visual Reinforcement Audiometry (VRA) is recommended from six months old. Children at this age who do not respond in VRA are considered delayed. In this study, the responses in the visual reinforcement audiometry were age appropriate for 72% of the study group and 95.2% for the control group, with a tendency to a significant difference between the groups. In general, children with central hearing alterations, with difficulty in responding to pure tones, fail to achieve the minimum levels of expected responses for the age.[8,14] Zanchetta, (1997)[14] found a lower incidence of responses to pure tones in children with PIVH. This result was similar to what was found in the present study, in which seven children (26%) with PIVH presented alterations in their VRAs, while only one child (4.8%) without PIVH had such difficulty.

The verbal command recognition skills appear at the end of the first year of life, between nine and 12 months. At 12 months 92.3% of children born at term and with proper development can recognize simple

verbal commands.[8] In the follow-up, 41 children aged from nine months could be evaluated in relation to the ability to recognize verbal commands. Such ability was compromised in more than half of children with PIVH (52.2%), although the statistical analysis could not be considered significant, probably due to the restrictive sample. In fact, studies found a lower performance in the recognition of verbal commands in group of preterm infants in relation to the group of children born at term.[21,22] Thus, prematurity alone could explain the speech recognition delay presented in the children studied, a fact that would mean a higher risk for language delay.[22]

Recent research found that children who do not recognize verbal orders between 12 and 18 months are 12.5% more likely to have language delay between two and four years of age.[23] Another study found that the absence of speech recognition in the first year increases in 66.7% the chance of presenting altered neurological examination at the age of three.[24] These results demonstrate the importance of monitoring the preterm and high-risk children, including those with PIVH.

The alterations identified during the first two years of life could be related to the process of maturation and / or transient central nervous system alterations resulting from neonatal clinical events. A periodic and systematic monitoring of the development of hearing, interfere favourably and allows early identification of delays and hearing disorders allowing immediate intervention.[8]

CONCLUSION

The occurrence of peri-intraventricular hemorrhage was 6.4%. The occurrence of central change was 33.4% and ranged according to the hemorrhage degree: children with hemorrhage grades II, III and IV showed higher occurrence of central change in relation to grade I. In audiological monitoring, central hearing impairment remained at 51.85% for children who already had such impairment at birth.

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