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Ocular sequelae of retinopathy of prematurity in Manaus, Amazonas

Sequelas oculares estruturais da retinopatia da prematuridade em crianças em Manaus, Amazonas

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ABSTRACT

Purpose: *To evaluate the structural ocular sequelae of retinopathy of prematurity in children at risk for the disease in Manaus, Amazonas, Brazil.* ***Methods****: A prospective, cohort-type, observational study was conducted. Fifty-seven children at risk for this retinopathy, who were born in the public health system facilities, were referred for ophthalmic evaluation at a secondary eye hospital. Inclusion criteria were gestational age ≤ 32 weeks and/or birth weight ≤ 1500 g.* ***Results:*** *Eighteen (31.6%) children were diagnosed with any stage of retinopathy of prematurity during the study period, and four (7.0%) of them needed treatment. Structural ocular sequelae were identified in 3 of 56 children (5.3%), consisting of peripheral retinal detachment with macular dragging in 3 eyes of 3 children and macular involving retinal detachment in 2 eyes of 2 children. Associations between occurrence of retinopathy of prematurity and birth weight, gestational age at birth and days in oxygen were observed (p<0.05). Indication of treatment was associated with birth weight (p<0.05).* ***Conclusion:*** *Retinopathy of prematurity stands out as an important cause of avoidable blindness in Amazonas, affected 31.6 % of children at risk in the present paper, which in this same context, led to ocular strucutral sequelae in about 5.3% of these infants, either peripheral or macular involving retinal detachment. A local program for screening and treatment of the population at risk is necessary in order to avoid blindness from this disease, providing care to the public health system users that contemplates equality and universality of access.*

Keywords: *Retinopathy of prematurity/complications; Blindness; Very low birth weight; Premature*

RESUMO

Objetivo: Avaliar as sequelas oculares estruturais da retinopatia da prematuridade em crianças com risco para a doença em Manaus, Amazonas, Brasil. **Métodos:** Foi conduzido um estudo observacional prospectivo, do tipo coorte. Cinquenta e sete crianças que nasceram em um hospital público, com risco desta retinopatia, foram referênciadas para avaliação oftamológica em um hospital de olhos secundário. Critérios de inclusão foram idade gestacional ≤ 32 semanas e/ou peso ao nascer ≤ 1500 g. **Resultados:** Dezoito (31.6%) crianças foram diagnosticadas com retinopatia da prematuridade em qualquer estágio durante o período de estudo, quatro (7.0%) delas precisaram de tratamento. Sequelas oculares estruturais foram identificadas em 3 de 56 (5.3%) crianças, consistindo de descolamento de retina periférico com tração macular em 3 olhos de 3 crianças e descolamento de retina envolvendo a mácula em 2 olhos de 2 crianças. Associações entre a ocorrência de retinopatia da prematuridade e peso, idade gestacional e dias em oxigênio foram observadas (p<0.05). Indicação de tratamento foi associada com peso ao nascer (p<0.05). **Conclusão:** A retinopatia da prematuridade constitui uma importante causa de cegueira prevenível no Amazonas, acometeu 31.6% das crianças em risco no presente estudo, que neste mesmo contexto, levou a seqüelas estruturais oculares em cerca de 5.3% destas, tanto descolamento de retina periférico quanto envolvendo a mácula. Um programa local de triagem e tratamento da população de risco é necessário a fim de evitar a cegueira por esta comorbidade em Manaus, proporcionando cuidados aos usuários do sistema público de saúde que contemplem a igualdade e universalidade de acesso.

Descritores: Retinopatia da prematuridade/complicações; Cegueira; Muito baixo peso ao nascer; Prematuro

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Introduction

Retinopathy of prematurity (ROP) has been recognized for more than 50 years.[1] It's a vasoproliferative disease of the retina of multifactorial etiology in which neovascular tissue formation occurs in the incompletely vascularized retina.[2] Improvement of socioeconomic status and of health care assistance allowed the survival of more preterm newborns (PTNB) of very low birth weight thus raising the frequency of ROP.[3,4] ROP is amongst the most frequent preventable causes of childhood blindness, accounting for 50.000 blind children in the world.[1] One-third of children weighing less than 1,500 grams may present retinopathy of prematurity and 81.6% with less than 1000 grams are affected. 2,2% of newborns with weighting between 1001-1500 grams, will have sequelae as a complication of prematurity and 0.5% will be blind.[5] However, early detection of the disease and appropriate treatment can avoid blindness.[4,6]

In Brazil, the impact of ROP as a cause of childhood blindness is not clearly known. In Amazonas, a large state in the brazilian Amazon region, the public health system does not have a well established ROP screening and treatment program according to Brazilian Guidelines[7] and there isn't data regarding ROP frequency. So, this study was performed aiming to evaluate the occurrence of structural ocular sequelae due to ROP in children at risk in Manaus, Amazonas.

Methods

A prospective, cohort type, observational study was conducted in a sampling for free demand from referral of pediatricians to children under conditions to go to a secondary eye hospital for ophthalmic evaluation in Manaus, Amazonas, Brazil. A total of 57 premature infants at risk for ROP were followed from 2016 to 2018. Five children were not included due to non-addressing of inclusion criteria. Signing the TCLE by the responsible was required and the study adhered to tenets of the Helsinki Declaration. The research was approved by the ethics committee of Universidade do Estado do Amazonas (CAAE: 66729917.7.0000.5016).

The sample size was based on the number of PTNBs at risk for ROP between 2011 and 2016 (6478 PTNBs, 1079.66/year) in Amazonas, whom a mean of 75.0/year would need treatment and 48.4 infants /year (4,5%) would progress to unfavorable visual acuity outcomes considering data from DATASUS and CRYO-ROP study.[6] With 95% confidence level and error 5%, it is estimated that a sample of 61 children.

Premature newborns at risk were defined as weighing ≤ 1500 g (very low birth weight) and/or ≤ 32 weeks of gestational age, based on ROP screening and treatment Brazilian Guidelines, which recommends screening of all newborn with birth weight ≤1.500 g and/or with ≤32 weeks of gestational age and the examination was considered in newborns with presence of risk factors, such as respiratory distress syndrome, sepsis, blood transfusions, multiple gestation and intraventricular hemorrhage.[7]

Scheduling of subsequent exams were determined by the findings of the first examination: a) Mature retina (complete vascularization): evaluation at 1 year old. b) Immature retina (non-complete vascularization) with no ROP: evaluation at 4 weeks weeks; c) ROP less than type 2 ROP: evaluation of 2/2 weeks; d) ROP zone I any stage or ROP 3: evaluation at 1 week; g) Exams may be discontinued when retinal vascularization is complete, ROP completely regressed; h) ROP type 1: treatment was indicated. The ophthalmic examination was performed under mydriasis (tropicamide 0.5% and phenilefrine 5% solution) and topical anesthesia (tetracaine solution) with indirect binocular ophthalmoscope and 28 diopter lens, blepharostat and scleral depressor.

Results

The study included a total of 57 preterm infants, 29 males (50.8%) and 28 females (49.2%). Mean gestational age at birth was 29.9 weeks, and the mean birth weight of this population was 1286 g. The occurence of ROP was 18 cases (31.6%), four had indication of treatment and 3 presented a structural sequelae (one of the patients who needed treatment lost clinical follow-up) (Table 1). Ocular sequelae included peripheral retinal detachment with macular dragging in 3 eyes of 3 children and macular involving retinal detachment in 2 eyes of 2 children.

Statistically significant association ($p<0.05$) was observed between occurrence of ROP and gestational age (GA) at birth, birth weight and oxygen use. Indication of treatment was associated with birth weigth. (Table 2).

Discussion

Retinopathy of prematurity is a ischemic disease that has great potential for blindness.[8] In about 85% of affected patients, the neovascular tissue growth induced by ischemia undergoes spontaneous involution,[9,10] while in the remaining patients the fibrovascular proliferation progress towards the vitreous creating membranes and retinal traction, thus indicating the need of treatment.[11]

According to Brazilian guidelines for screening and treatment of ROP, proposed in 2007,[7] all premature infants with a birth weight of 1500 g or less and/or with a gestational age of 32 weeks or less, or that have risk factors for ROP development, must be examined between the fourth and sixth weeks of life by an ophthalmologist who is experienced in the examination of preterm infants for ROP, aiming to identify the cases, follow and, if necessary, treat those patients. In the CRYO-ROP study, at 15 years of follow-up, the treatment of threshold ROP reduced the occurrence of tractional retinal folds or retinal detachment by more than 40% and reduced the frequency of unfavorable visual outcome (visual acuity equal to or worse than 20/200) by 30%, as compared with control eyes.[6] Also, the incidence of blindness was reduced from 55.1% in control eyes to 36.3% in treated eye.[6]

In Brazil, there aren't country-level studies that allow for the comprehension of the impact of ROP in the country,[12] however, there are studies investigating ROP prevalence in some areas of the country that contribute to estimate the impact of this disease, although different inclusion criteria and study settings may limit comparison. Data from studies conducted in some places in Brazil show a prevalence of ROP ranging from 24.2% to 53.4% in the population of premature infants at risk of this comorbidity[4,13–16] and the frequency of treatment ranged from 5.3% to 10%, considering all children in the same group.[4,14,15]

In Amazonas, there isn't a ROP screening and treatment program implemented in the public health system facilities, as established by Brazilian Guidelines for ROP. Premature newbor-

Table 1
Demographic characteristics for all infants

	n (%)	Mean (SD)	CI 95%
Gender (Male:Female)	29:28 (50.8:49.2)	-	-
Birth weigth (g)	-	1286 (388)	1182.8-1389.2
Birth place (Interior: Capital)	6:47 (11.3:88.7)	-	-
Gestational age at birth (weeks)	-	29.9 (2.7)	29.1-30.6
Oxygen use (days)	-	29.9 (27.9)	22.5-37.3
Occurrence of ROP	18 of 57 (31.6)	-	21-44.4
Indication of treatment	4 of 57 (7.0)	-	2.7-16.7
Structural sequel	3 of 56 (5.3)	-	1.8-14.6

Table 2
Demographic data of all infants and statistical associations

		ROP occurrence	Indication of treatment	Structural sequel
Gender	Male	12 of 29 (41.4%)	1 of 29 (3.4%)	1 of 29 (3.4%)
	Female	6 of 28 (21.4%)	3 of 28 (10.7%)	2 of 27 (7.4%)
Birth weigth (g)	Mean (Std Dev)	1009 (238.6)*	917 (146)*	972.6 (115.6)
Gestational age at birth (weeks)	Mean (Std Dev)	27.5 (2.1)*	27 (2.1)	27.3 (2.5)
Oxygen use (days)	Mean (Std Dev)	48.7 (27.4)*	52.7 (29.8)	60.3 (31.5)

* Indicates statistical significance with $p < 0.05$

ns at risk for ROP that survive more than 4 weeks of life represented 1,37% of live births in the State during 2011 and 2016, a number that constitutes more than (6.478 of 470.622 children), which should be examined according to Brazilian Guidelines for ROP. Considering data obtained by our study extrapolated to population numbers, it's estimated that 341 children, each year, would have ROP at any stage, and 75 children would need treatment. However, without adequate screening and treatment, a great proportion of these 75 children/year, will progress to blindness and severe visual impairment, and these individuals will have a lifetime of blindness ahead, consequently implicating in an enormous socioeconomic impact, as seen in the cases of our study that needed prompt treatment but could not have access to it, consequently developing structural ocular sequelae. In our study, 3 of 4 children who needed treatment progressed to structural ocular sequelae, one of these four children was lost to follow-up, and only one of the 3 who needed treatment was treated, although it presented peripheral retinal detachment in one eye. Retinal detachment was the main debilitating condition either directly involving the macula or causing macular traction, which was a bilateral condition in 2 children and unilateral in the whom who was treated. However, other conditions may also limit visual capacity in these children such was central nervous system diseases causing optic atrophy, strabismus and uncorrected refractive errors.

Therefore, the opportunity for preventing visual incapacity due to ROP may be lost, meaning that, in spite of ROP affects marked less individuals than cataract, for example, it will generate severe socioeconomic and psychological impact, as childhood blindness depicts as the second most important cause of blind--years, second only to cataract at global level.[17]

However, there are some pitfalls in our study: patients from the interior of Amazon state that were born in Manaus, were generally directed home after discharge from hospital and these were not available to evaluation at a secondary eye hospital setting and treatment in Manaus. Also, our study was conducted in an eye hospital and not in the maternity hospital due to logistical questions, and many patients may not have been able to attend to ophthalmic evaluation.

Conclusion

Retinopathy of prematurity stands out as an important cause of avoidable blindness in Amazonas and, in the current context, it may led to serious ocular strucutral sequelae in these children at risk for ROP, either peripheral or macular involving retinal detachment. So, it should be adopted measures that address the universality and equality of access for screening and treatment for ROP in the State, in order to reduce the estimated impact on childhood blindness.

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