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Observation of hyaloid artery remnants in premature infants

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早产儿中玻璃体动脉残留的临床观察

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摘要

目的:观察早产儿中玻璃体动脉残留的情况。

方法:回顾性研究。使用双目间接检眼镜观察 2018-05/11 在同济医院进行早产儿视网膜病变(ROP)筛查的患儿。

结果:最终 60 例早产儿被纳入此项观察。根据玻璃体动脉是否残留分为两组:玻璃体动脉残留阳性组(49 例)和玻璃体动脉残留阴性组(11 例)。结果显示,玻璃体动脉残留阳性组的胎龄和出生体质量明显低于玻璃体动脉残留阴性组(P<0.05)。两组患儿在性别、产程、ROP 发生概率方面无差异(P>0.05)。玻璃体动脉残留阳性患儿随访期间的玻璃体动脉残留均完全消退。玻璃体动脉残留消退的时间约为矫正胎龄 37~44wk。

结论:早产儿玻璃体动脉的残留多为生理性残留。较小胎龄或体质量较轻的早产儿玻璃体动脉残留的阳性检出率较高。玻璃体动脉的残留与 ROP 无明显相关性。当矫正胎龄超过 43wk 时,如果残留的玻璃体动脉没有消退,将有可能发生病变,应根据病情的严重程度选择适当的干预措施。

关键词:玻璃体动脉;早产儿;早产儿视网膜病变

Abstract

• AIM: To observe the hyaloid artery remnants in the eyes of premature infants.

• METHODS: This retrospective study recruited premature infants who consecutively attended the Tongji Hospital for retinopathy of prematurity (ROP) screening from May 2018 to November 2018. The binocular indirect ophthalmoscope was used for examination.

• RESULTS: In total, 60 cases were pulled for data analysis. The cases were categorized as having the following condition: hyaloid artery remnants positive (49 cases) or hyaloid artery remnants negative (11 cases). It was showed that the remnants positive group had significant lower gestational age and birth weight than those of the negative group (P< 0.05). There was no significant difference in gender, labor presentation and ROP between the two groups (P>0.05). The hyaloid artery remnants completely regressed in all the follow-up cases. The range of disappearing time of hyaloid artery remnants was 37-44wk of corrected gestational age.

• CONCLUSION: The hyaloid artery remnants in preterm infants are most likely to be physiological residues. Younger or lower weight premature infants will have higher positive detection rates of hyaloid artery remnants. It seems like co-existence with ROP has no significant association with the detection of hyaloid artery remnants. When the corrected gestational age extends over 43wk, if the hyaloid artery remnants don't regress, there is a possibility of pathological changes, and appropriate interventions should be selected according to the severity of the lesions.

• KEYWORDS: hyaloid artery; premature infant; retinopathy of prematurity

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INTRODUCTION

Hyaloid artery (HA) is a temporary intraocular blood vessel system in fetal period[1-3]. This vessel is the branch of the main ophthalmic artery, and extends from the optic disc to the embryo lens *via* the primitive vitreous[1-3]. It is prominent around ninth week of gestation period and regresses by the seventh month[1]. The regression of the vessel begins from posterior region, gradually progresses toward the anterior part, and then the transparent remnant lies in the canal of cloquet[1]. Conclusion from a series of studies suggested that vascular endothelial growth factor (VEGF) might be one of the important factors that trigger the

development of HA[2,4-5]. If HA does not fully regress or even not regress, leading to the condition persistent HA, which may cause adverse effects on the visual function. The more serious is that the failure regression of the primary hyaloidal vasculature system may lead to persistent hyperplastic primary vitreous (PHPV), which will cause worse vision[6-7]. With the continuous improvement of medical and neonatal intensive care level, the survival rate of premature infants gradually increased[8-11]. The HA of some premature infants was not completely regressed at birth. Jones[1] reported that HA remnants could be observed in 95% of premature infants, but less than 3% of full-term infants. The purpose of this study is to observe the HA remnants in premature infants and explore its regression rule.

SUBJECTS AND METHODS

Patients This retrospective study included premature infants who consecutively attended the Tongji Hospital for retinopathy of prematurity (ROP) screening from May 2018 to November 2018. The review board of the Tongji Hospital approved our study, and the study followed the tenets of the Declaration of Helsinki. As it was a retrospective assessment and all the data were obtained during routinely taking care of the patients, the necessity of an informed consent by the participants was waived by the Ethics Committee.

From May 2018 to November 2018, 94 premature infants with different gestational age (GA) underwent fundus examination. Informed consent for each infant was obtained from its guardian. The premature infants with genetic disorders or other ocular abnormalities were excluded from the observation. Usually the eyes were first examined when the infants were 2-4 weeks old. But some of them who were examined later than this time were excluded from our study, in order to make the study more reliable. Since the HA remnants in most premature infants are both eyes[1], single premature infant with HA remnants involving both eyes were considered as one case. At last, 60 premature infants were included in our retrospective observation.

Fundus Examination All the infants were in the supine position. Tropicamide and topical anesthetic drops were applied for pupil enlargement and anesthesia. The eyelid speculum was placed for opening eyelid. The HA and retinal condition of premature infants were observed by the same ophthalmologist with binocular indirect ophthalmoscope.

Statistical Analysis SPSS software version 25.0 was used for statistical analysis. Analysis of variance (t - test) for continuous measurement data and Chi - squared test for enumeration data were used for multi - group comparison, respectively. The measurement data are presented as the mean± standard error of mean (SEM). A P value < 0.05 was considered to be statistically significant.

RESULTS

In total, 60 cases were pulled for data analysis. The cases were categorized as having the following condition: HA remnants positive or HA remnants negative. There were 49 cases in remnants positive group, 11 cases in negative group, respectively. The HA remnants positive detection rate is 81.3%. The basic characteristics that included GA, birth weight (BW), gender, labor presentation (LP) and the co-existence with ROP between remnants positive and negative groups were presented in Table 1.

Table 1 Comparison of baseline characteristics between HA remnants positive and negative groups

Parameters	HA remnants	
	Positive	Negative
Number of cases, n (%)	49 (81.7)	11 (18.3)
Gestational age, wk	30.69±0.04	31.91±0.11
Birth weight, kg	1.38±0.04	1.61±0.15
Gender		
M	27	6
F	22	5
Labor presentation		
Cesarean section	35	10
Natural labor	14	1
ROP		
Positive	3	1
Negative	46	10

HA: Hyaloid artery; ROP: Retinopathy of prematurity; Values are represented as mean±standard error of mean or numbers (n).

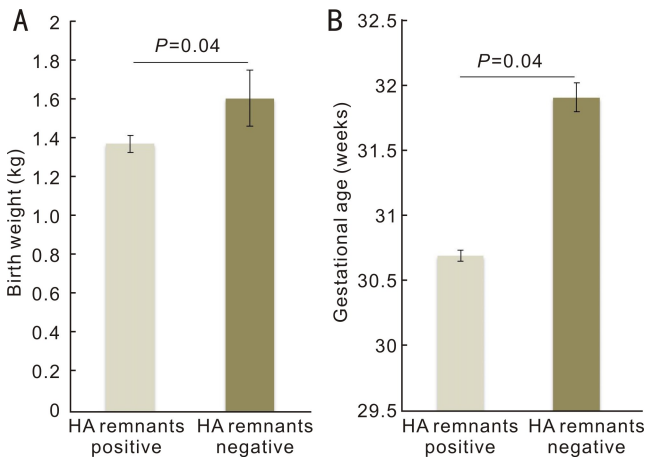

Figure 1 Comparison of birth weight and gestational age between HA remnants positive and negative groups A: The differences of birth weight between the HA remnants positive and negative groups; B: The differences of gestational age between the HA remnants positive and negative groups.

There were significantly different in GA and BW between the two groups, respectively (Figure 1; $P<0.05$). The positive detection rate of HA remnants is correlated with the GA and BW: younger or lower weight premature infants will have higher detection rate.

The forest plot of other confounding variables (gender, LP and co-existence with ROP) associated with the detection rate of HA remnants was presented in Figure 2. It shows that the investigated factors such as gender, LP, and co-existence with ROP had no significant association with the detection rate of HA remnants.

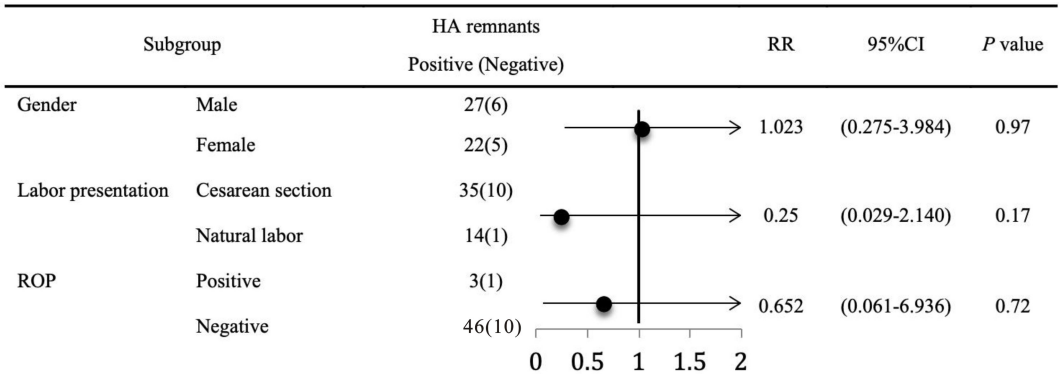

Figure 2 The forest plot of factors associated with the detection rate of HA remnants HA: Hyaloid artery; ROP: Retinopathy of prematurity.

About the follow up, many of the premature infants could not be followed because of many reasons, but still 14 cases were followed until the hyaloid remnants had completely disappeared. In those cases, the range of gestational age was 27-34wk, and the range of disappearing time of hyaloid artery remnants was 37 - 43wk. Since the infants were not seen frequently, usually at intervals of about one month or more, so the recorded time of disappearance may have been over-estimated in some cases.

DISCUSSION

HA could regress spontaneously during the development of embryo eye. Human embryology shows that HA extend from optic disc to the embryo lens *via* the primitive vitreous at 5wk of gestation period, begin to regress at 12wk, and completely disappear after 8-9mo[12]. Some *vivo* ultrasound studies show HA could be detected around 16wk, and the regression of HA could be started at 18wk, and disappear completely after 29wk[13-15]. Our observation results show that 81. 7% premature infants could be detected with HA remnants. This percentage is a little lower than Jones[1] study, which showed the percentage was 95%. The different results may be due to the different time of the first examination. In Jones[1] study, eyes were first examined when the infants were 1 - 2wk. However, the first screening time in our study was 2-4wk that is later than Jones[1] study, and some HA remnants had spontaneously regressed during this gap period. Our study also indicated that the detection rate of HA remnants in preterm infants was related to the GA and BW, but gender, LP, and co-existence with ROP had no significant association with the detection rate of HA remnants. Younger or lower weight premature infants will have higher detection rate of HA remnants. From the follow up cases, the range of disappearing time of HA remnants was 37 - 44wk of corrected GA. The disappearing time of we found is similar with Jones[1] reported, but is later than the ultrasound studies. We speculated that there have some reasons attributed to the differences: 1) After delivery, the effects of rescue and treatment interventions on the growth and development of premature infants are not as good as the physiological environment in utero, which will also affect intraocular microenvironment. Thus, the spontaneous regression of HA is also been delayed; 2) The sensitivity and specificity between the different study methods such as using ultrasound or ophthalmoscope for examinations are differences.

The mechanism of spontaneous regression of HA is not yet clear. There is a reciprocal relationship between the regression of the hyaloid system and the development of the retinal vasculature. The hyaloid artery itself does not regress completely until the middle of the eighth month of gestation, at the time the retinal vasculature is almost fully developed[16]. Studies have shown that VEGF plays an important regulatory role in HA regression, and the decrease of VEGF in eyes can promote HA regression[3,17]. As a severe ocular disease of premature infants, ROP has been shown to increase the level of plasma and intraocular VEGF in premature infants[18-20]. It is speculated that the high level of VEGF associated with ROP may affect the process of HA regression. However, our study indicated that if whether or not co-existence with ROP had no significant association with the detection rate of HA. The ROP may not be the cause of affecting the regression of HA, but it may be have some intrinsic relationship which need further study.

In conclusion, the HA remnants in preterm infants are most likely to be physiological residues. When the corrected GA extends over 43wk, if the HA remnants don't regress, there is a possibility of pathological changes, and appropriate interventions should be selected according to the severity of the lesions.

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