·临床报告·

早产儿视网膜病变激光术后嵴前无血管区的临床观察

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Clinical outcome of nonvascularization area after laser photocoagulation in patients with retinopathy of prematurity

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Abstract

• AIM: To observe the clinical outcome of non-vascularization area after laser photocoagulation in the patients with retinopathy of prematurity (ROP) to lay the foundation for the clinical treatment of ROP.

• METHODS: For a prospective follow-up observation from June 2014 to June 2016, 186 cases (372 eyes) underwent retinal laser photocoagulation were screened out in the ROP screening clinic and neonatal intensive care unit (NICU) bedside screening by the cooperative group of screening for ROP in our hospital. Non-vascularization area were exist in 26 cases (32 eyes). There were 17 male patients (18 eyes) and 9 females (14 eyes), the gestational age at birth was 29.4±0.4wk, and the average birth weight was 1222.8±70.3g. Among these cases, 10 patients (12 eyes) developed pre-threshold type 1 ROP, 12 patients (14 eyes) developed threshold ROP, and 4 cases (6 eyes) developed aggressive posterior-ROP. The Retcam fundus photography was performed at 1, 3, 8 and 12wk after laser surgery respectively. The changes of the non-vascularization area, the lesions and the additional lesions were observed. During following-up, if the lesions were found to increase, retinal laser photocoagulation or intravitreal injection of anti-vascular endothelial growth factor (VEGF) would be performed, until the lesions were completely under control.

• RESULTS: In the all 26 patients, non-vascularization areas were found in 1wk after laser resection, but the lesions ridge dissipated from the stage 3 to stage 2 and stage 1. The dissipation were more obviously in patients with ROP of pre-threshold type 1. The range of non-vascularization areas was narrowed at 3wk in 27 eyes (84%), and the retinal vessels continued to develop to the surrounding areas, but in the other 5 eyes (16%), the non-vascularization areas were not significantly narrowed, the lesion ridge developed stage 3-4, with bleeding and proliferation phenomenon, then we timely to gave additional retinal laser photocoagulation. In these 5 eyes, 3 (9%) developed threshold ROP, and 2 developed aggressive posterior-ROP. At the 8th week, 3 eyes (9%) of the 5 eyes were found with additional photocoagulation, the condition was controlled and stable. In 2 eyes (6%), the neovascularization disappeared in the ridge and the lesion was not found, then intravitreal injection of anti-VEGF were given. At the 12th week, the additional lesions in the 2 eyes had subsided, the ridge subsided, and the retinal blood vessels to the temporal shaped slightly stiff.

• CONCLUSION: Retinal laser photocoagulation is an effective method for the treatment of retinopathy in premature infants. Most retinal blood vessels would develope in missing areas after the laser photocoagulation. A small proportion of patients need timely replenishment of laser photocoagulation treatment, if necessary, combined with intravitreal injection of anti-VEGF.

• KEYWORDS: retinopathy of prematurity; retinal laser photocoagulation; non-vascularization; threshold period

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摘要

目的:观察早产儿视网膜病变(retinopathy of prematurity, ROP)激光光凝术后嵴前部分无血管化区的临床转归,为ROP的临床治疗提供依据。

方法:前瞻性随访观察2014-06/2016-06由我院ROP筛查协作组在门诊以及NICU床旁筛查发现并进行视网膜激光光凝治疗的患儿186例372眼,激光光凝术后嵴前存在部分无血管区的患儿26例32眼,其中男17例18眼,

女 9 例 14 眼,平均出生胎龄(29.4 ± 0.4)周,平均出生体质量 1222.8 ± 70.3g,阈值前 1 型 10 例 12 眼,阈值期 12 例 14 眼、急性进展性后极部型 4 例 6 眼,分别于激光术后 1、3、8、12wk 行 Retcam 眼底照相复查,观察病变嵴、嵴前无血管区以及附加病变的消退情况。随访中如发现病变嵴或附加病变加重,则给予补充视网膜激光光凝或行玻璃体腔抗 VEGF 治疗,直至病变嵴和附加病变完全消退,病情稳定。

结果:患儿 26 例均在激光术后 1wk 复查时发现病变嵴前无血管区,但附加病变减轻,病变嵴由 3 期向 2 期、1 期消退,阈值前 1 型消退最明显;3wk 复查时 27 眼(84%)病变嵴为 1 期或不明显、无血管区逐渐缩小,视网膜血管向周边发育;5 眼(16%)无血管区缩小不显著,附加病变(+~++),病变嵴 3~4 期、或伴有出血,其中 3 眼(9%)为阈值期病变患儿,2 眼(6%)为急性进展性后极部型患儿,遂及时给予补充视网膜光凝;8wk 复查,未补充视网膜光凝的 27 眼嵴前无血管区已血管化,嵴及附加病变消退;补充光凝中 3 眼(9%)病情得到控制、稳定,其中阈值期 2 眼、急性进展性后极部型 1 眼,2 眼(6%)嵴上新生血管消退不明显、附加病变依然存在,其中阈值期 1 眼、急性进展性后极部型 1 眼,故给予玻璃体腔抗 VEGF 治疗,12wk 复查时见附加病变、病变嵴消退,视网膜血管向颞侧走形稍僵直。

结论:视网膜激光光凝是 ROP 治疗的有效方法,光凝术后嵴前部分无血管区多可自行发育完善。对于少数激光术后病情活动的阈值期及急性进展性后极部型嵴前部分无血管区需及时补充激光光凝治疗,必要时可联合玻璃体腔抗 VEGF 治疗。

关键词:早产儿视网膜病变;视网膜激光光凝;无血管化;阈值期
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0 引言

早产儿视网膜病变(retinopathy of prematurity, ROP)是一类发生于早产、低体重儿的视网膜血管异常增殖性致盲眼病[1]。ROP 激光治疗由于受各种因素影响,术后嵴前常常残留部分无血管区,本文对 ROP 激光术后嵴前无血管区的转归进行了随访、观察,现将结果报告如下。

1 对象和方法

1.1 对象 收集 2014-06/2016-06 由暨南大学附属深圳市眼科医院 ROP 筛查协作组在门诊以及 NICU 床旁筛查发现并进行视网膜激光光凝治疗后,病变嵴前存在部分无血管区的患儿26 例32 眼,其中男 17 例 18 眼,女 9 例 14 眼,平均出生胎龄 29.4 ± 0.4 周,平均出生体质量 1 222.8 ± 70.3g,阈值前 1 型 10 例 12 眼,阈值期 12 例 14 眼、急性进展性后极部型(AP-ROP)4 例 6 眼纳入前瞻性随访观察。

1.2 方法 筛查标准按照 2004 年我国原卫生部颁发的《早产儿用氧和视网膜病变防治指南》[2]筛查。所有患儿筛查均由深圳市眼科医院儿童眼底病专业组具备筛查经验的医生采用双目间接眼底镜和 RetCam Ⅱ(Ⅲ)完成。治疗指征:32 眼 ROP 均达到国际诊断标准(图 1A),符合激光光凝治疗指征。手术均在 NICU 床旁镇静下完成,并有新生儿医生监护。步骤如下:常规术前 1h 复方托吡卡胺滴眼液散瞳,术前 30min 静脉注射苯巴比妥 10mg/kg,术前 5min 静脉注射地西泮 0.4mg/kg 及结膜囊滴 5g/L 盐酸丙美卡因滴眼液表面麻醉,儿童开睑器开睑,激光使用半导体 810nm 波长激光机,在双目间接眼底镜下对患眼视网膜无血管区进行光凝,曝光时间 0.2s,能量大小以视网膜产生灰白色反应为宜,相邻光斑之间相隔半个光斑距离,眼位固定或巩膜顶压借助小斜视钩完成,光凝后局部使用糖皮质激素、抗生素和散瞳药物 7d,以减轻眼部术后反应及预防感染的发生。并分别于激光术后 1、3、8、12wk 行 Retcam 眼底照相复查,观察嵴前无血管化范围大小的变化,病变嵴、附加病变的消退情况。随访中如发现病变未控制或加重,则给予补充视网膜激光光凝或行玻璃体腔抗 VEGF 治疗,直至病变完全控制稳定。

2 结果

所有患儿术后均无葡萄膜炎或视网膜脱离等严重并发症出现,术后 1wk 复查发现病变嵴前无血管区(图 1B),但附加病变减轻,病变嵴由 3 期向 2 期、1 期消退,阈值前 1 型消退最明显;3wk 复查时 27 眼(84%)病变嵴为 1 期或不明显、无血管区逐渐缩小,视网膜血管向周边发育(图 1C);5 眼(16%)无血管区缩小不显著,附加病变(+~++),病变嵴 3~4 期、或伴有出血,其中 3 眼(9%)为阈值期病变患儿,2 眼(6%)为急性进展性后极部型患儿,遂及时给予补充视网膜光凝;8wk 复查,未补充视网膜光凝的 27 眼嵴前无血管区已血管化,嵴及附加病变消退;补充光凝中 3 眼(9%)病情得到控制,其中阈值期 2 眼、急性进展性后极部型 1 眼,2 眼(6%)嵴上新生血管消退不明显、附加病变依然存在,其中阈值期 1 眼、急性进展性后极部型 1 眼,故给予玻璃体腔抗 VEGF 治疗,12wk 复查时见附加病变、病变嵴消退,视网膜血管向颞侧走形稍僵直。

3 讨论

ROP 是导致儿童盲的重要原因之一,约占儿童盲的 6%~18%[1],其发病率为 5.5%~47%[3-4]。对于阈值期 ROP 和 AP-ROP,如不及时接受治疗,43% 会发生预后不良。伴随围产医学和新生儿医学水平的提高,早产儿和低出生体重儿的存活率明显上升,ROP 的发病率亦随之增加。

2004 年我国卫生部颁布《早产儿治疗用氧和视网膜病变防治指南》[2],双目间接眼底镜配合巩膜顶压的方法在国际上被认为是 ROP 筛查的"金标准"[5-7]。双目间接眼底镜下激光光凝治疗仍是 ROP 早期治疗的"金标准"[8]。美国多中心 ROP 冷凝治疗研究[9]将 ROP 早期治疗指证确定为阈值期 ROP,2003 年 ROP 早期治疗研究[10]将 ROP 治疗指证调整为高危阈值前 1 型病变,视网膜激光光凝治疗主要机制是破坏外周视网膜未血管化区、减轻无血管区对缺血、缺氧的刺激,延缓或阻断新生血管纤维化增殖,有效率可达 91%。目前对于阈值期、阈值前 1 型 ROP 的治疗仍以视网膜激光光凝治疗为主[8],其效果肯定,常常需要 1~2 次完成激光治疗。

ROP 激光光凝治疗过程中,由于受到各种因素的影响,常常出现病变嵴前部分无血管化区域激光斑难以完全覆盖,常见原因主要包括:(1)镇静效果不佳,患儿活动剧烈,视网膜周边无血管化区域难以完全窥清;(2)ROP 轻重不一,"岛状、舌状"无血管化区域存在;(3)长时间巩膜顶压,角膜水肿,屈光间质不清,周边病变窥不清;(4)巩膜顶压"嵴"遮挡视网膜病变嵴及边界;(5)嵴上及嵴前出血,

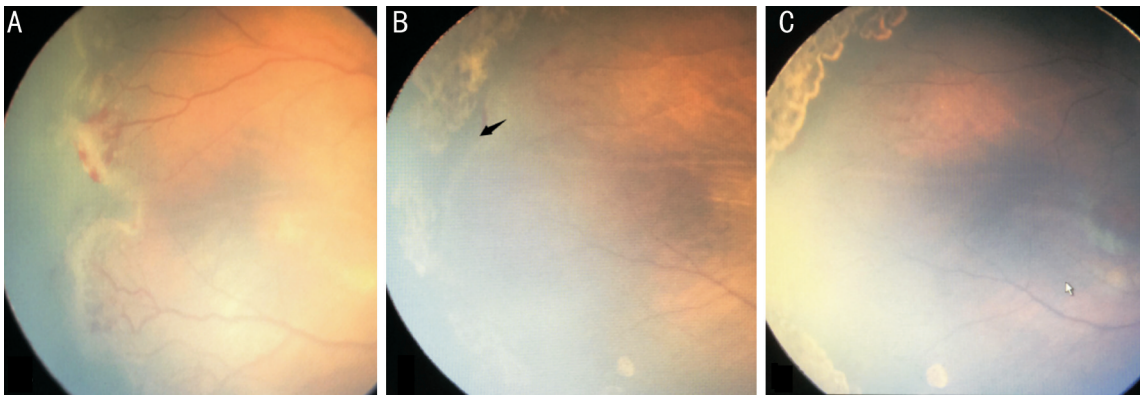

图 1　病历资料　A:患者发病时病变轻重不一,诊断 ROPⅢ区 3 期(plus+)阈值期病变;B:视网膜激光光凝术后 1wk 随访见周边激光斑围绕,plus 病变减轻,嵴部分消退,颞侧嵴前部分无激光斑覆盖(箭头所指);C:激光术后 4wk 随访见残留部分无血管区已消失、发育完善,plus 病变及嵴均已消退。

边界模糊不清等。本文中所有观察对象一次光凝后随访时所见嵴前残留无血管区存在的因素均与以上因素有关,但残留的无血管区 84% 可自行发育完善,无需再次补充视网膜激光光凝治疗,对随访中少数病变活动的病例可给予补充激光光凝或抗 VEGF 治疗。

此外,视网膜激光治疗为破坏性治疗,在控制病情的同时也限制了视网膜的进一步发育,尤其对于Ⅰ区病变者影响更大。有文献报道[10],对于阈值期或阈值前期 1 型 ROP 尽管及时给予完全的视网膜光凝,仍有 9.1% ~ 15.4% 患儿病变继续进展。对 AP-ROP 即使早期实施光凝治疗,仍有 58.0% 患儿在 3.5a 内发生视网膜全脱离[11]。国内外曾有学者使用贝伐单克隆抗体玻璃体腔注射治疗 AP-ROP 取得良好效果[12-13]。因此,对于Ⅰ区病变和 AP-ROP 患儿,首选抗 VEGF 治疗效果会优于视网膜光凝治疗;同时也有报道[14],玻璃体腔注射雷珠单克隆抗体治疗 AP-ROP 后仍有 36.8% 患儿周边视网膜残留无血管区,附加病、病变嵴再次形成,故需再次行视网膜光凝治疗控制病情。

总之,ROP 需要早发现、早诊断、早治疗。视网膜激光光凝是 ROP 治疗的有效方法,对于阈值期、阈值前 1 型患儿应尽早激光手术治疗,防止病变的进一步加重带来严重不良后果。ROP 光凝术后嵴前残留部分无血管区多可自行发育完善;对于少数激光术后病情活动的阈值期及 AP-ROP 嵴前残留的无血管区需及时补充激光光凝治疗,必要时可联合玻璃体腔抗 VEGF 治疗。由于本观察组病例数量较少,ROP 激光术后嵴前部分无血管区的临床转归仍需进一步大样本、多中心、前瞻性随访观察。

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