·文献综述·

阈值下微脉冲激光在中心性浆液性脉络膜视网膜病变中的作用机制

路 雪,谢 兵

引用:路雪,谢兵. 阈值下微脉冲激光在中心性浆液性脉络膜视网膜病变中的作用机制. 国际眼科杂志, 2024,24(5):749-752.

作者单位:(563000)中国贵州省遵义市,遵义医科大学附属医院眼科
作者简介:路雪,在读硕士研究生,住院医师,研究方向:眼底疾病。
通讯作者:谢兵,硕士,教授,主任医师,硕士研究生导师,研究方向:眼底疾病. panshi.xie@163.com
收稿日期: 2023-10-13 修回日期: 2024-03-26

摘要

中心性浆液性脉络膜视网膜病变(CSC)是发生在中青年患者中常见的黄斑病变,该病具有一定自限性,但治疗不及时也可致病情迁延、反复发作,进展为慢性 CSC、继发视网膜色素上皮(RPE)萎缩、脉络膜新生血管等,最终导致中心视力不可逆性损害。阈值下微脉冲激光(SMLP)是一种短促重复的脉冲激光,它不同于具有损伤性治疗作用的传统激光,在达到有效治疗效果的基础上,不会对 RPE 细胞和光感受器造成损伤和热损伤。在光动力治疗(PDT)缺乏维替泊芬的情况下,因其有效性、安全性和可重复性,SMLP 现已广泛应用于临床上 CSC 的治疗。本综述旨在阐述 SMLP 治疗 CSC 过程中涉及的效应细胞、细胞因子及作用机制,以期为 SMLP 在临床的推广和合理化应用提供更多理论依据。

关键词:中心性浆液性脉络膜视网膜病变;阈值下微脉冲激光;视网膜色素上皮;脉络膜毛细血管内皮细胞;作用机制
DOI:10.3980/j.issn.1672-5123.2024.5.16

Research progress on the mechanism of subthreshold micropulse laser photocoagulation in central serous chorioretinopathy

Lu Xue, Xie Bing

Department of Ophthalmology, Affiliated Hospital of Zunyi Medical University, Zunyi 563000, Guizhou Province, China
Correspondence to: Xie Bing. Department of Ophthalmology, Affiliated Hospital of Zunyi Medical University, Zunyi 563000, Guizhou Province, China. panshi.xie@163.com
Received:2023-10-13 Accepted:2024-03-26

Abstract

• Central serous chorioretinopathy (CSC) is a common macular degeneration that primarily affects young patients. While the disease may resolve on its own to some extent, delayed or inadequate treatment can result in recurrence and progression to chronic CSC. This can lead to complications such as retinal pigment epithelium (RPE) atrophy and choroidal neovascularization, ultimately causing irreversible damage to central vision. Subthreshold micropulse laser photocoagulation (SMLP) is a type of laser therapy that differs from traditional lasers in that it does not cause damage or thermal injury to RPE cells and photoreceptors. SMLP has become widely used in clinical treatment of CSC due to its effectiveness, safety, and reproducibility, particularly in cases where verteporfin is not available in photodynamic therapy (PDT). The purpose of this review is to explain the mechanism of SMLP in CSC and summarize the effector cells, cytokines, and mechanisms of action involved in its treatment. This will provide a theoretical basis for promoting and rationalizing the use of SMLP in clinical practice.

• KEYWORDS: central serous chorioretinopathy; subthreshold micropulse laser photocoagulation; retinal pigment epithelium; endothelial cells of the choroidal capillaries; mechanism

Citation: Lu X, Xie B. Research progress on the mechanism of subthreshold micropulse laser photocoagulation in central serous chorioretinopathy. Guoji Yanke Zazhi(Int Eye Sci), 2024,24(5):749-752.

0 引言

中心性浆液性脉络膜视网膜病变(central serous chorioretinopathy,CSC)是好发于青壮年男性、以黄斑区神经上皮浆液性脱离为特征的眼底疾病,可导致患者中心视力下降、视物变形、变暗,该病容易复发和慢性化,从而导致继发视网膜色素上皮(retinal pigment epithelium,RPE)萎缩、脉络膜新生血管等并发症,是具有代表性的肥厚型脉络膜谱系疾病之一。CSC 目前临床上的主要治疗手段有视网膜激光光凝、光动力治疗(photodynamic therapy,PDT)、药物治疗、微脉冲激光等。阈值下微脉冲激光(subthreshold micropulse laser photocoagulation,SMLP)是一种以长间歇为特征的短促高频的重复脉冲激光,不同于传统激光光凝是通过破坏失代偿 RPE 细胞来达到治疗 CSC 的作用,其是选择性作用于 RPE 细胞且不损伤周围正常

细胞,具有可重复治疗、安全性高的优点[1-4]。国内外多项临床研究指出,SMLP 治疗 CSC 疗效肯定,其临床疗效与其他治疗方式相同、远期疗效无显著差异且无明显副作用[5-6]。但其作用机制尚不完全明确,推测可能是通过调节视网膜细胞代谢活性的变化,从而引起基因和蛋白表达的改变达到治疗目的[4,7-8]。现就 SMLP 治疗 CSC 机制中可能的效应细胞、细胞因子及作用机制进行综述,以期探索更多微脉冲激光治疗 CSC 的病理生理机制,丰富微脉冲激光治疗 CSC 的理论基础。

1 SMLP 调节 RPE 细胞的代谢活性

CSC 的发生是由于脉络膜血管高通透性和高灌注所致,最终以 RPE 层及脉络膜功能异常表现为特征[9-10]。RPE 层的异常通常表现为局灶性或弥漫性功能障碍、RPE 斑块状萎缩、RPE 局部渗漏及视网膜下积液(subretinal fluid,SRF)的发生,SRF 导致 RPE 浆液性脱离[11]。RPE 细胞的一个关键功能是通过主动运输将视网膜下液体泵送到脉络膜来防止液体积聚,RPE 细胞作为血-视网膜屏障的一部分,同时负责回收感光细胞产生的视觉色素及代谢产物等,具有维持光感受器完整性的功能,RPE 层功能障碍及屏障功能的破坏是导致 CSC 发生的直接原因[12-13]。SMLP 刺激 RPE 细胞被认为是引起视网膜液体吸收的关键因素之一,但该过程的分子机制尚不清楚,其可能的机制如下。

1.1 刺激 RPE 细胞增殖和迁移 目前常用微脉冲激光波长有 810、577 nm 两种[14],微脉冲激光不会对目标靶组织造成损伤,不会造成可见的视网膜瘢痕、激光相关暗点以及视网膜敏感性降低,因此在各种脉络膜视网膜疾病中实现有效和安全的治疗反应[15-18]。已有研究证实 SMLP 治疗 CSC、糖尿病性黄斑水肿(diabetic macular edema,DME)以及视网膜静脉阻塞黄斑水肿治疗反应良好[16,19-20]。SMLP 能选择性作用于受损的 RPE 细胞,具有刺激、诱导 RPE 细胞的完整性和生理功能恢复的生物学效应,并最终促进视网膜神经上皮下浆液吸收[1,3]。Inagaki 等[7]利用 SMLP 照射 RPE 细胞 24 h,发现激光照射区域内的所有细胞均处于存活状态,但细胞较未照射区域稀疏,因此推断微脉冲激光可能刺激了照射区域 RPE 细胞甚至邻近的细胞,使其发生增殖和迁移。Colome 等[21]研究发现使用 810 nm SMLP 照射 RPE 细胞后,在与有丝分裂活动相关的治疗区域内出现了 RPE 细胞增殖,故认为 810 nm SMLP 能诱导 RPE 细胞的有丝分裂,且不会对相邻组织造成损伤。但 RPE 层的完整性和生理功能的恢复是否与有丝分裂后的 RPE 细胞增殖、迁移并覆盖在受损 RPE 细胞处有关目前还不清楚。

1.2 促进 RPE 细胞屏障功能修复 Luttrull 等[22]研究发现在 SMLP 刺激位点细胞间空间有稀疏的细胞群存在,从而推测这些细胞间空间的产生可能是由于 RPE 层中细胞间黏附的丧失所致,这可能导致血-视网膜屏障功能失调,直接增加了视网膜和脉络膜组织之间的液体和分子运动。目前已发现与 RPE 细胞黏附和紧密连接相关的蛋白质有 occludin、claudin 和 zonula occludens-1(ZO-1)。Ji Cho 等[23]研究发现,在糖尿病视网膜病变(DR)中炎性因子的刺激下,RPE 屏障完整性的破坏并不是由于细胞死亡,而是由于 ZO-1 磷酸化导致Ⅳ型胶原蛋白表达上调引起。SMLP 是否会直接促进 ZO-1 修复或重塑以达到恢复 CSC 患者 RPE 细胞屏障的作用,目前较为确切的证据是在 DME 中,血管内皮生长因子(vascular endothelial growth factor,VEGF)使 ZO-1 磷酸化而失去正常功能,SMLP 能通过下调 VEGF 的表达减少 ZO-1 的耗竭,从而恢复 RPE 细胞屏障功能[24]。

1.3 促进脉络膜毛细血管内皮细胞的修复 Pollack 等[25]研究发现,激光光凝后受损的 RPE 和脉络膜毛细血管修复,同时观察到再生 RPE 细胞的特定表型与新生血管形成之间存在一定关联,由此推断再生的 RPE 细胞可能具有刺激受损脉络膜血管内皮细胞增殖的功能。微脉冲激光亦具有相同作用,这已经得到了证实[26-27]。研究发现,使用阈值上激光照射体外培养的 RPE 细胞 30 min,并在照射后第 2、4、6、8 d 分别取出培养基进行分析,结果发现激光能重建 RPE 细胞产生的基质金属蛋白酶(matrix metalloproteinases,MMPs)和金属蛋白酶抑制剂(tissue inhibitors of metalloproteinases,TIMPs)之间的平衡,从而达到抑制新生血管生成的启动和维持程序[28]。Luttrull 等[29]使用 SMLP 治疗高危型年龄相关性黄斑变性发现脉络膜新生血管的发生率降低,提示微脉冲激光也具有一定的抑制脉络膜新生血管形成的作用,而此作用的产生是否和激光刺激后 MMPs 与 TIMPs 之间的平衡重塑有关,还需要进一步验证。由于 MMPs 在血管生成过程中作用机制复杂,可能涉及视网膜脉络膜血管内皮细胞的增殖和迁移以及毛细血管的形成。据此推测,微脉冲激光也具有促进脉络膜血管修复的作用。

1.4 上调热休克蛋白 70 的表达 SMLP 能上调 RPE 细胞中热休克蛋白 70(heat shock protein 70,HSP70)的表达,HSP70 能帮助变性的蛋白质复性,抑制蛋白质的错误聚集,具有抗炎和抗凋亡作用。研究表明,当组织内释放出略高于 20%的终点管理(endpoint management,EpM)能量时,HSP70 开始表达[30-31],SMLP 就可以实现 HSP70 最大限度的释放。视网膜组织的这种应激相关反应能诱导细胞功能的免疫调节,阻断导致细胞损伤的凋亡和炎症途径,同时触发修复过程,使某些细胞因子的表达正常化,从而减少存在于视网膜中的慢性炎症[32-34]。Inagaki 等[7]首次观察到应用 SMLP 照射体外培养的人 RPE(ARPE-19)细胞后 HSP70 表达上调,并提出 HSP70 的表达依赖于微脉冲的数量,但该观点有待更多实验验证。SMLP 上调 HSP70 表达,不仅对光感受器具有保护作用,也有助于改善 RPE 功能和减轻黄斑水肿[35-36]。Hirabayashi 等[37]研究发现 SMLP 照射小鼠 RPE 24 h 后,实验组水通道蛋白-3(aquaporin3,AQP3)较对照组升高 6 倍。Mahalka 等[38]进一步研究发现 HSP70 能激活磷脂酶 A2。Hollborn 等[39]研究证实人 RPE 细胞的渗透压变化和缺氧均会增加 AQP3 的表达,而磷脂酶 A2 抑制剂则会抑制 AQP3 的表达。SMLP 能上调 HSP70 的表达,从而激活磷脂酶 A2,进而提高 AQP3 的表达和视网膜下液的排出。因此推测,SMLP 可能通过增加 AQP3 的表达促进视网膜下液的排出,减轻视网膜水肿[37]。

2 促进脉络膜血管内皮细胞间紧密连接恢复

Schubert 等[40]研究发现钙黏着蛋白-5(cadherin 5,CDH5)与 CSC 的发生显著相关,CDH5 的遗传变异是男性

占 CSC 人群中相当大比例的基础。CDH5 存在于内皮细胞连接处,包括人脉络膜脉血管内皮细胞,是脉络膜血管内皮细胞内聚和细胞间连接组织的重要蛋白,对维持内皮细胞-细胞间连接很重要,其表达异常与 CSC 中所见的脉络膜高渗透性相关[40]。该结论进一步证实了 CSC 的发生与脉络膜血管通透性增加有关。有学者推测该基因通过促进脉络膜血管内皮细胞之间的连接从而达到修复脉络膜高通透性的作用。而微脉冲激光是否会直接促进 CDH5 的表达从而修复或重塑脉络膜血管内皮细胞间紧密连接还需要进一步验证,目前较为确定的证据是,类固醇激素可抑制 CDH5 的表达,从而使脉络膜血管内皮细胞间紧密连接减少,增加脉络膜血管系统的通透性,导致视网膜下液体渗漏。研究发现,接受皮质类固醇治疗的患者发生 CSC 的风险更高,这与类固醇激素抑制 CDH5 的表达,从而导致 CSC 发生的观点相一致[41-42]。

3 影响细胞因子的表达

促血管生成因子和抗血管生成因子之间的动态平衡在维持视网膜脉络膜内皮细胞的正常生理功能方面起着关键作用[27]。应用 810 nm SMLP 照射小鼠 RPE 细胞后可改变 RPE 细胞的代谢活性,调节血管生成和通透性的生长因子和细胞因子的表达,上调色素上皮衍生因子(pigment epithelium-derived factor, PEDF)表达,下调 VEGF 等通透性因子的表达[43]。Hattenbach 等[44]研究也发现接受视网膜激光光凝后人 RPE 细胞中 PEDF 表达增加。Matsumoto 等[45]研究表明视网膜激光光凝后 RPE 细胞内转化生长因子-β2(transforming growth factor β2, TGF-β2)表达增加,通过对这些因子的上调或下调恢复病理失衡。相反,平衡破坏会导致 PEDF 减少和 VEGF 增加,这些均可促使脉络膜新生血管(choroidal neovascularization,CNV)的病理状态[45]。同时,研究表明 SMLP 能抑制促脉络膜新生血管因子的表达,并上调血管生成抑制剂 PEDF 的表达,但仍然需要进一步研究以了解其机制[26]。上述研究结果表明,微脉冲激光可能通过调节血管生成调节因子的平衡来逆转或减少 CNV 的发生。

4 减轻视网膜炎症反应

CSC 与全身炎症之间的联系尚未明确,但鉴于脉络膜高通透性和渗漏的基本病理机制,有学者对这一病理过程中的炎症标志进行研究发现,单核细胞与高密度脂蛋白(high-density lipoprotein, HDL)的比率(monocyte to HDL ratio,MHR)以及中性粒细胞与淋巴细胞的比率(neutrophil-to-lymphocyte ratio,NLR)可以作为急性 CSC 全身炎症的观察指标,且 MHR 是急性 CSC 的独立预测因子[46]。同时,也有研究显示,纤维蛋白原/白蛋白比值可作为监测急性 CSC 患者治疗和随访期间全身炎症状态的生物标志物[47]。Matet 等[48]研究显示,与健康对照组相比,急性和慢性 CSC 患者血清脂钙蛋白 2(一种具有抗炎和促炎作用的急性时相反应物)明显下降。尽管 CSC 与视网膜炎症的关系目前尚未阐明,但较为确定的是视网膜胶质细胞(retinal ganglion cells,RGC)是视网膜炎症过程中的重要参与者[49-50]。RGC 的稳态是调节视网膜血流、水平衡和维持屏障功能的前提条件[51]。既往认为 RGC 是主要的结构性细胞,而最近研究发现其对维持视网膜环境的稳态至关重要[52]。另有研究证实,微脉冲激光治疗后 RGC(如 Müller 细胞)的形态功能得到恢复,与之相关的炎症病理生物标志物显著降低[8]。这提示微脉冲激光可能通过减弱 RGC 的异常活化,减轻视网膜的炎症反应和神经细胞的损伤等途径从而减轻黄斑区液体的产生,以达到治疗目的。

5 小结

综上所述,SMLP 作为一种完全不同于传统视网膜激光的新的治疗方式,RPE 细胞是其作用的主要靶标细胞,其以低于细胞死亡阈值能量水平刺激 RPE 细胞、促进 RPE 细胞增殖和迁移及屏障功能修复、上调 HSP70 的表达,促进视网膜下液排出、改善脉络膜血管内皮细胞间紧密连接、影响其分泌细胞因子,并能减轻视网膜炎症反应,从而达到修复血-视网膜屏障、消除视网膜下液、降低脉络膜通透性及促使脉络膜功能恢复的作用,有望在临床上得到更广泛的应用。

参考文献

[1] Zhao TT, Li JN, Wang YB, et al. Intravitreal injections with anti-VEGF agent aflibercept versus subthreshold micropulse laser for chronic central serous chorioretinopathy: the alternative treatment regimens for verteporfin-shortage in China. Ann Med, 2023,55(1):2227424.

[2] Sabal B, Teper S, Wylęgała E. Subthreshold micropulse laser for diabetic macular edema: a review. J Clin Med, 2022,12(1):274.

[3] Framme C, Alt C, Schnell S, et al. Selective targeting of the retinal pigment epithelium in rabbit eyes with a scanning laser beam. Invest Ophthalmol Vis Sci, 2007,48(4):1782-1792.

[4] Arora S, Sridharan P, Arora T, et al. Subthreshold diode micropulse laser versus observation in acute central serous chorioretinopathy. Clin Exp Optom, 2019,102(1):79-85.

[5] Wu ZZ, Wang HX,An JS. Comparison of the efficacy and safety of subthreshold micropulse laser with photodynamic therapy for the treatment of chronic central serous chorioretinopathy. Medicine, 2021, 100(17):e25722.

[6] Li X, Long H,Hu QH. Efficacy of subthreshold micropulse laser for chronic central serous chorioretinopathy: a meta-analysis. Photodiagnosis Photodyn Ther, 2022,39:102931.

[7] Inagaki K, Shuo T, Katakura K, et al. Sublethal photothermal stimulation with a micropulse laser induces heat shock protein expression in ARPE-19 cells. J Ophthalmol, 2015,2015:729792.

[8] Midena E, Bini S, Martini F, et al. Changes of aqueous humor Müller cells' biomarkers in human patients affected by diabetic macular edema after subthreshold micropulse laser treatment. Retina, 2020,40(1):126-134.

[9] Jeong S, Kang W, Noh D, et al. Choroidal vascular alterations evaluated by ultra-widefield indocyanine green angiography in central serous chorioretinopathy. Graefes Arch Clin Exp Ophthalmol, 2022,260(6):1887-1898.

[10] Zarnegar A, Ong J, Matsyaraja T, et al. Pathomechanisms in central serous chorioretinopathy: a recent update. Int J Retina Vitreous, 2023,9(1):3.

[11] Spitznas M. Pathogenesis of central serous retinopathy: a new working hypothesis. Graefes Arch Clin Exp Ophthalmol, 1986,224(4):321-324.

[12] Dvoriashyna M, Foss AJE, Gaffney EA, et al. Fluid and solute transport across the retinal pigment epithelium: a theoretical model. J R Soc Interface, 2020,17(163):20190735.

[13] Pollack JS, Kim JE,Pulido JS, et al. Tissue effects of subclinical diode laser treatment of the retina. Arch Ophthalmol, 1998,116(12):1633-1639.

[14] Ambiya V, Goud A, Mathai A, et al. Microsecond yellow laser for subfoveal leaks in central serous chorioretinopathy. Clin Ophthalmol, 2016,10:1513-1519.
[15] Bansal M. Commentary: Subthreshold micropulse yellow laser in diabetic macular edema. Indian J Ophthalmol, 2020,68(1):151-152.
[16] Hu XY, Cao L, Gao Y, et al. Comparative efficacy of subthreshold micropulse laser photocoagulation versus conventional laser photocoagulation for diabetic macular edema: a meta-analysis. Ophthalmic Res, 2023,66(1):611-619.
[17] Lee SH, Lee J, Kim M, et al. The effect of nondamaging subthreshold laser therapy in patients with chronic central serous chorioretinopathy. Graefes Arch Clin Exp Ophthalmol, 2023[Epub ahead of print].
[18] Lois N, Campbell C, Waugh N, et al. Diabetic macular edema and diode subthreshold micropulse laser: a randomized double-masked noninferiority clinical trial. Ophthalmology, 2023,130(1):14-27.
[19] Guo J, Li X, Wan J. Efficacy and safety of subthreshold micropulse laser in the treatment of acute central serous chorioretinopathy. Internat J Ophthalmol, 2023,16(6):921-927.
[20] Uzlu D, Erdöl H, Kola M, et al. The efficacy of subthreshold micropulse yellow laser (577 nm) in chronic central serous chorioretinopathy. Lasers Med Sci, 2021,36(5):981-988.
[21] Colome J, Ruiz-Moreno JM, Montero JA, et al. Diode laser-induced mitosis in the rabbit retinal pigment epithelium. Ophthalmic Surg Lasers Imaging, 2007,38(6):484-490.
[22] Luttrull JK, Dorin G. Subthreshold diode micropulse laser photocoagulation (SDM) as invisible retinal phototherapy for diabetic macular edema: a review. Curr Diabetes Rev, 2012,8(4):274-284.
[23] Ji Cho M, Yoon SJ, Kim W, et al. Oxidative stress-mediated TXNIP loss causes RPE dysfunction. Exp Mol Med, 2019,51(10):1-13.
[24] Wang JJ,Xu XL, Elliott MH, et al. Müller cell-derived VEGF is essential for diabetes-induced retinal inflammation and vascular leakage. Diabetes, 2010,59(9):2297-2305.
[25] Pollack A, Korte GE. Repair of retinal pigment epithelium and choriocapillaries after laser photocoagulation: correlations between scanning electron, transmission electron and light microscopy. Ophthalmic Res, 1997,29(6):393-404.
[26] Li ZY, Song YP, Chen X, et al. Biological modulation of mouse RPE cells in response to subthreshold diode micropulse laser treatment. Cell Biochem Biophys, 2015,73(2):545-552.
[27] Ohno-Matsui K, Morita I, Tombran-Tink J, et al. Novel mechanism for age-related macular degeneration: an equilibrium shift between the angiogenesis factors VEGF and PEDF. J Cell Physiol, 2001, 189(3):323-333.
[28] Flaxel C, Bradle J, Acott T, et al. Retinal pigment epithelium produces matrix metalloproteinases after laser treatment. Retina, 2007,27 (5):629-634.
[29] Luttrull JK, Sinclair SH, Elmann S, et al. Low incidence of choroidal neovascularization following subthreshold diode micropulse laser (SDM) in high-risk AMD. PLoS One, 2018,13(8):e0202097.
[30] Dorin G. Evolution of retinal laser therapy: minimum intensity photocoagulation (MIP). Can the laser heal the retina without harming it? Semin Ophthalmol, 2004,19(1-2):62-68.
[31] Lavinsky D, Wang J, Huie P, et al. Nondamaging retinal laser therapy: rationale and applications to the macula. Invest Ophthalmol Vis Sci, 2016,57(6):2488-2500.
[32] Gawęcki M. Micropulse laser treatment of retinal diseases. J Clin Med, 2019,8(2):242.
[33] Beckham JT,Wilmink GJ, Mackanos MA, et al. Role of HSP70 in cellular thermotolerance. Lasers Surg Med, 2008,40(10):704-715.
[34] Du SS, Zhang Q, Zhang SS, et al. Heat shock protein 70 expression induced by diode laser irradiation on choroid-retinal endothelial cells *in vitro*. Mol Vis, 2012,18:2380-2387.
[35] Yenari MA, Liu JL, Zheng Z, et al. Antiapoptotic and anti-inflammatory mechanisms of heat-shock protein protection. Ann N Y Acad Sci, 2005,1053:74-83.
[36] Sramek C, Mackanos M, Spitler R, et al. Non-damaging retinal phototherapy: dynamic range of heat shock protein expression. Invest Ophthalmol Vis Sci, 2011,52(3):1780-1787.
[37] Hirabayashi K, Kakihara S, Tanaka M, et al. Investigation of the therapeutic mechanism of subthreshold micropulse laser irradiation in retina. Graefes Arch Clin Exp Ophthalmol, 2020,258(5):1039-1047.
[38] Mahalka AK, Code C, Jahromi BR, et al. Activation of phospholipase A2 by Hsp70 *in vitro*. Biochim Biophys Acta, 2011,1808 (10):2569-2572.
[39] Hollborn M, Ulbricht E, Reichenbach A, et al. Transcriptional regulation of aquaporin-3 in human retinal pigment epithelial cells. Mol Biol Rep, 2012,39(8):7949-7956.
[40] Schubert C,Pryds A, Zeng SM, et al. Cadherin 5 is regulated by corticosteroids and associated with central serous chorioretinopathy. Hum Mutat, 2014,35(7):859-867.
[41] Tsai DC, Chen SJ, Huang CC, et al. Risk of central serous chorioretinopathy in adults prescribed oral corticosteroids: a population-based study in Taiwan. Retina, 2014,34(9):1867-1874.
[42] Ge G, Zhang Y, Zhang YC, et al. Corticosteroids usage and central serous chorioretinopathy: a meta-analysis. Graefes Arch Clin Exp Ophthalmol, 2020,258(1):71-77.
[43] Su D, Hubschman JP. A review of subthreshold micropulse laser and recent advances in retinal laser technology. Ophthalmol Ther, 2017, 6(1):1-6.
[44] Hattenbach LO, Beck KF, Pfeilschifter J, et al. Pigment-epithelium-derived factor is upregulated in photocoagulated human retinal pigment epithelial cells. Ophthalmic Res, 2005,37(6):341-346.
[45] Matsumoto M, Yoshimura N, Honda Y. Increased production of transforming growth factor-beta 2 from cultured human retinal pigment epithelial cells by photocoagulation. Investig Ophthalmol Vis Sci, 1994, 35(13):4245-4252.
[46] Sirakaya E, Duru Z, Kuçuk B, et al. Monocyte to high-density lipoprotein and neutrophil-to-lymphocyte ratios in patients with acute central serous chorioretinopathy. Indian J Ophthalmol, 2020,68(5): 854-858.
[47] Limon U, Bozkurt E, Bulut S, et al. Elevated serum fibrinogen/albumin ratios in patients with acute central serous chorioretinopathy. Eur J Ophthalmol, 2022,32(3):1735-1742.
[48] Matet A, Jaworski T, Bousquet E, et al. Lipocalin 2 as a potential systemic biomarker for central serous chorioretinopathy. Sci Rep, 2020, 10(1):20175.
[49] Midena E, Bini S. Multimodal retinal imaging of diabetic macular edema: toward new paradigms of pathophysiology. Graefes Arch Clin Exp Ophthalmol, 2016,254(9):1661-1668.
[50] Grigsby JG, Cardona SM, Pouw CE, et al. The role of microglia in diabetic retinopathy. J Ophthalmol, 2014,2014:705783.
[51] Bringmann A, Wiedemann P. Müller glial cells in retinal disease. Ophthalmologica, 2012,227(1):1-19.
[52] Telegina DV, Kozhevnikova OS, Kolosova NG. Changes in retinal glial cells with age and during development of age-related macular degeneration. Biochemistry, 2018,83(9):1009-1017.