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Original Article

Comparison of the effect of reduced-fluence photodynamic therapy with intravitreal bevacizumab and standard-fluence alone for polypoidal choroidal vasculopathy

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Abstract

Background: Photodynamic therapy (PDT) has previously been reported to be effective in treating polypoidal choroidal vasculopathy (PCV), with satisfactory polyp regression. However, the optimum treatment protocol remains controversial. This study compared the effect of reduced-fluence PDT combined with intravitreal bevacizumab (rPDT/IVB) and standard-fluence PDT (sPDT) alone for treating symptomatic PCV in Chinese patients.

Methods: A retrospective review was carried out of the medical records of patients with PCV who were treated with rPDT/IVB (14 eyes of 13 patients) or sPDT (12 eyes of 12 patients) with at least 6 months of follow-up.

Results: The mean best-corrected visual acuity of the rPDT/IVB group improved significantly at the 6-month follow-up ($p = 0.041$). Only one eye (7.1%) in the rPDT/IVB group showed a decrease in visual acuity, compared with four eyes (33.3%) in the sPDT group. A total of 40.0% of eyes in the sPDT group showed increased lipid exudate at follow-up 1 month after treatment, whereas no increase in lipid exudate was observed in the rPDT/IVB group ($p = 0.015$). The mean maximum area of post-treatment hemorrhage in the rPDT/IVB group was smaller than that in the sPDT group (2.57 ± 2.74 mm^2 vs. 12.69 ± 10.28 mm^2, $p = 0.042$).

Conclusion: Combination therapy with rPDT/IVB for patients with PCV showed encouraging results in vision improvement, a lower decrease in visual acuity, significantly less post-treatment lipid exudate and a smaller area of post-treatment hemorrhage at the 6-month follow-up than patients treated with sPDT.

Keywords: combination therapy; intravitreal bevacizumab; photodynamic therapy; polypoidal choroidal vasculopathy; reduced-fluence photodynamic therapy

1. Introduction

Polypoidal choroidal vasculopathy (PCV) has a distinctive choroidal appearance characterized by an abnormal vascular network terminating in polypoidal structures. The disease is more prevalent in Asian populations, with an incidence ranging from 22.3% to 40%, compared with a reported incidence of 4−13.9% in Caucasian patients diagnosed with presumed age-related macular degeneration (AMD).[1−5]

Polypoidal choroidal vasculopathy often follows a remitting−relapsing course associated with subretinal hemorrhage, macular edema and retinal pigment epithelial (RPE) detachment. Although the natural course of PCV is reported to be more favorable than exudative AMD, about 35% to 50% of patients develop a loss of vision due to recurrent bleeding or leakage and RPE atrophy after a longer follow-up period.[1,2,6]

The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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The optimum treatment for PCV remains controversial. Several studies have shown encouraging results with standard-fluence photodynamic therapy (sPDT) with verteporfin (50 J/cm^2 delivered as 600 mW over 83 seconds) in the regression of the polypoidal lesions (85−95%) and vision stabilization or improvement (80.9−95%) at the 1-year follow-up.[3,7,8] However, some studies have shown that sPDT damages the physiological choriocapillary layer beyond the irradiated area and that repeat sPDT results in persistent choriocapillary nonperfusion and can lead to a decrease in vision.[9−11] The vascular endothelial growth factor (VEGF) surge secondary to choriocapillary ischemia may be related to the recanalization of choriocapillaries, which may lead to post-treatment retinal hemorrhage in PCV.[12,13] Furthermore, 19% to 30.8% of patients with PCV experienced retinal hemorrhage or even massive subretinal hemorrhage and vitreous hemorrhage after sPDT.[3,7,14−17] Several studies have shown that the reduced-fluence PDT (rPDT, 25 J/cm^2 delivered as 600 mW over 42 seconds or 300 mW over 83 seconds) resulted in less choriocapillary nonperfusion than sPDT,[18,19] with a similar choroidal neovascularization closure rate.[20] Yamashita et al[21] reported 1-year results of rPDT on patients with PCV and showed improved visual outcome and fewer treatment sessions compared with the results of sPDT from other studies.[22,23]

Intravitreal injection of an anti-VFGF agent is found to reduce exudation in the eyes of patients with PCV, but has a limited effect on the regression of polypoidal lesions.[24,25] The combination therapy of sPDT and intravitreal anti-VEGF injection into the eyes of patients with PCV was found to reduce the incidence of post-treatment subretinal hemorrhage, resulting in a better visual outcome with a similar polyp regression rate to sPDT monotherapy.[13] A recent study of Chinese patients showed that the treatment effect of PDT combined with intravitreal bevacizumab injection was superior to PDT monotherapy within 1 year of follow-up.[26]

Theoretically, the combination of rPDT, which has a reduced extent of physiological choriocapillary closure, and the anti-VEGF, which has both antiangiogenic and antipermeability effects, may result in less post-treatment exudation and hemorrhage, and reduced additional vision loss due to choriocapillary and RPE degeneration. The purpose of this study was to investigate the efficacy and safety of rPDT combined with intravitreal bevacizumab injection (IVB) and sPDT monotherapy in Chinese patients with symptomatic PCV.

2. Methods

This retrospective comparative case series included patients with symptomatic PCV treated with sPDT monotherapy or rPDT and IVB (rPDT/IVB) at Taipei Veterans General Hospital, Taiwan from June 2002 to August 2008. The diagnosis of PCV was based on the presence of characteristic aneurysmal polypoidal lesions with a branching network of choroidal vessels observed in indocyanine angiography (ICGA). The criteria for enrollment were: (1) an absence of evidence suggesting choroidal neovascularization associated with AMD, pathological myopia, idiopathic choroidal neovascularization, presumed ocular histoplasmosis, angioid streak, and other secondary choroidal neovascularization; (2) the absence of other maculopathies, such as diabetic maculopathy; (3) no previous retinal surgery within the last 6 months; (4) no previous PDT treatment within 1 year; and (5) a completed 6-month follow-up after treatment. The Institutional Review Board for Human Research of Taipei Veterans General Hospital approved this study. Informed consent was obtained from each of the participants.

All patients received a comprehensive ocular examination including best-corrected visual acuity (BCVA), intraocular pressure measurement, indirect ophthalmoscopy, slit-lamp biomicroscopy with noncontact lens, color fundus photography before treatment (baseline), and at months 1 and 3 and then at 3-month intervals after treatment. The BCVA was measured with the standard Snellen chart at 6 m. To quantify the visual changes, all Snellen BCVAs were converted to a logarithm of the minimum angle of resolution (logMAR) BCVA. Vision tested with counting fingers was assigned with logMAR 2.0. An increase in BCVA of more than two lines (logMAR BCVA change $\geq$2 lines) was considered an improvement, and a decrease of more than two lines was considered a worsening. The ICGA and/or fluorescein angiography (FA) were evaluated at baseline and at 3-month intervals after treatment. The ICGA was performed with a scanning laser ophthalmoscope (HRA2, Heidelberg Engineering, Heidelberg, Germany) and fundus photography and FA were taken by a digital fundus camera (Canon CF-60UD, Tokyo, Japan) at a 60° view. The presence of hemorrhage and lipid exudate was documented by fundus photography.

Photodynamic therapy with verteporfin (Novartis, Basel, Switzerland) was performed with 6 mg per square meter of body surface area via an intravenous infusion of 30 mL over 10 minutes. Five minutes after complete infusion, the patients received an irradiance of 600 mW/cm^2 with a laser light at 689 nm delivered over 42 seconds (reduced-fluence) or 83 seconds (standard-fluence). The intravitreal bevacizumab injection was performed in an operating room under sterile conditions. For the patients who received rPDT before the injection, the light was dimmed to avoid further photoactivation of verteporfin. Topical anesthesia with 0.5% proparacrine hydrochloride was applied three times before disinfection of the ocular surface and periocular skin with a 5% povidone−iodine solution. Bevacizumab (0.1 mL, 2.5 mg) (Avastin, Roche, Basel, Switzerland) was injected through the inferior pars plana into the vitreous cavity using a 30-gauge needle. Anterior chamber paracentesis was performed before the injection to avoid an intraocular pressure spike. A topical antibiotic was prescribed as prophylaxis against infection. The treatment choice of rPDT/IVB or sPDT was based on the discretion of the retinal specialists (L.I.L., S.J.C., F.L.L., Y.C.S.). Repeat treatments were administered every 3 months to the eyes of patients with either persistent or new hyperfluorescence on ICGA or the presence of leakage on FA suggesting an active lesion. Additional IVB was given during the follow-up period between the 3-month treatment interval of PDT when optical coherent tomography demonstrated cystoid macular edema and/or subretinal fluid.