Systemic steroids as an aid to the management of Idiopathic Polypoidal Choroidal Vasculopathy (IPCV): A descriptive analysis

Aditya Sudhalkar; Divya Balakrishnan *; Subhadra Jalali; Raja Narayanan

Abstract

Purpose: To determine the role of systemic steroids in improving visual acuity, preventing recurrence and hastening pigment epithelial detachment resolution in IPCV patients.

Methods: Retrospective computer assisted comparative case series of consecutive patients with documented IPCV who did and did not receive systemic steroids as part of their treatment regimen between 2007 and 2012. Patients who had systemic contraindication to steroid therapy were excluded from the steroid arm. Data collected included demographics, the best corrected visual acuity, details of the ocular and systemic exam, the treatment offered, the follow-up period and the final visual and anatomic outcomes. Outcome measures included the final BCVA, the time to resolution of the associated pigment epithelial detachment (PED, if present), the recurrence rate and the associated side effects, if any. Appropriate statistical analysis was done.

Results: 14 patients (14 eyes) had received systemic steroids in the stated period; these were compared with 26 consecutive patients (26 eyes) who did not. Mean age: 59.24 vs 62.38 years (A vs B). Mean baseline BCVA: 1.86 ± 1.24 logMAR vs 2.12 ± 1.48 logMAR (A vs B). 8 females in Group A and 14 in Group B. 11 patients in group A and 19 in group B had associated systemic hypertension. Therapy consisted of laser photocoagulation, anti-vascular endothelial growth factor therapy, photodynamic therapy or a combination of these. Mean follow-up: 43.21 ± 11.32 months (Group A) vs 48.24 ± 9.75 months (Group B). BCVA at three months was significantly better (0.84 ± 0.74 logMAR vs 1.16 ± 0.89 (p = 0.039). Final BCVA: 0.86 ± 0.78 logMAR (Group A) vs 1.29 ± 0.92 (Group B, p = 0.042). 7 patients in group A and 12 in Group B had a recurrence (insignificant difference). 1 patient in Group A and 7 in Group B had unresolved disease (persistent PED) at the end of follow-up (OR: 4.60; 95% CI 1.7–11.10).

Conclusion: Steroids appear to improve visual acuity and accelerate the resolution of the PEDs in patients with IPCV and large PEDs, but do not seem to influence recurrence.

Keywords: Polypoidal choroidal vasculopathy, Steroids, Systemic, Recurrence, Pigment epithelial detachment

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http://dx.doi.org/10.1016/j.sjopt.2015.08.001

Introduction

Idiopathic Polypoidal Choroidal Vasculopathy (IPCV) is considered to be a variant of neo-vascular Age Related Macular Degeneration (AMD).1–4 The disease is characterized by polypoidal dilatations of the choroidal vasculature in the foveal or extrafoveal region, which results in hemorrhagic or exudative pigment epithelial detachments. In the natural history of PCV, half of the patients had persistent leakage or repeated bleeding and a poor visual outcome.4 Sho et al. also reported severe visual loss in 35% of eyes5 with IPCV.

There is a lack of evidence regarding the most appropriate therapy or a combination thereof for treatment of polyps.6–11 The role of anti-VEGF monotherapy in IPCV is unclear, and...
studies show that photodynamic therapy is more effective in terms of aiding IPCV closure, whereas anti-VEGF therapy acts mainly to reduce macular edema and improve vision. The EVEREST trial showed that photodynamic therapy, alone or combined with anti-VEGF therapy was better than anti-VEGF monotherapy alone. Argon laser photoacoagulation has also been attempted successfully in effecting the closure of polyps. Combination therapy often yields favorable results.

Thus, while treatment of these lesions is desirable, there is no clear consensus regarding the optimal management strategy. Also, patients with IPCV tend to have large serous or hemorrhagic pigment epithelial detachments (PEDs) which may rupture leading to break through vitreous hemorrhage and RPE rips and can severely affect vision. Inflammation is said to play a role in the pathogenesis of wet AMD (although it is still considered inconclusive). There is a report of the use of local steroids as an adjunct to treatment for IPCV. The role of oral steroids in IPCV, however, is unclear and, to an extent controversial, mentioned in an earlier publication from our institute, wherein a patient with a large, tense pigment epithelial detachment was treated with steroids prior to further treatment. The underlying basis is of course that IPCV is possibly an inflammatory process and may respond to steroids.

This study was undertaken with the aim of determining the role of oral steroids in IPCV, specifically whether it alters visual recovery, IPCV recurrence and PED resolution. Complications, if any, were to be noted as well.

Methods

A retrospective data search was made for all patients diagnosed to have IPCV between January 2007 and 2012. The data collected included demographics, details of the ocular exam, the special investigations performed (such as fluorescein and indocyanine green angiography, and ocular coherence tomography scans), the treatment given and whether steroids were used. The baseline and final corrected distance visual acuity were measured using a logMAR chart and noted. Patients of IPCV who presented with breaks were excluded from the analysis. The review adhered to previously set guidelines for retrospective reviews. The institutional review board for LV Prasad Eye Institute, Hyderabad, approved the study. The study adhered to the tenets of Helsinki. Patient consent for possible academic use of data had been obtained at the time of the first visit.

All patients received one or a combination of the following treatment modalities: anti-VEGF injections, frequency doubled Nd:Yag laser photoacoagulation to polyps that were extrafoveal and photodynamic therapy to polyps that were <200 µm away from the foveal center. Photodynamic therapy was also offered to patients who did not respond to the aforementioned modalities.

Patients with large, tense hemorrhagic or serous pigment epithelial detachments near the polyp (as identified on indocyanine green angiography) at risk for a retinal pigment epithelium rip (RPE rip) were given oral steroids (after a physician consult) for a fortnight at 0.5 mg/kg body weight followed by a weekly taper of 10 mg prior to any ocular intervention (such as laser photoacoagulation or intravitreal injections). Administration of oral steroids was with informed consent from the patient. If the lesion identified on angiography was away from the fovea and the pigment epithelial detachment, laser photoacoagulation was performed first, followed a week later by intravitreal ranibizumab. If the lesion showed no signs of reduction on serial ocular coherence tomography (i.e. less than 10 µm reduction in size of PED observed on serial OCT scans for two consecutive months), the patient was either started on oral steroids (0.5 mg/kg body weight) or observed (investigator discretion; subsequently described as Group A and Group B). If the polyp was identified to be less than 200 µm from the foveal center, photodynamic therapy was offered, with or without anti-VEGF agents (as decided by the treating physician). Care was taken to include the fine vascular network in the treatment diameter during photodynamic therapy.

Patients were followed up monthly for 6 months after treatment, and then 3 monthly thereafter. Indocyanine angiography was repeated at months 3, 6, 9 and 12 after completion of therapy and then as needed. OCT raster and macular cube scans were repeated at each follow-up. The change in PED dimensions, the subretinal fluid and retinal thickening was monitored on serial OCT scans.

The patients were divided into two groups: Those that received oral steroids as an adjunct to oral therapy (Group A) and those that did not (Group B). Descriptive statistics were used to analyze the results. The paired t-test was used to analyze the change in visual acuity with treatment within both groups. The odds ratio was used to analyze whether there was a difference in resolution of the PED and/or the disease process between the two groups. The number of patients who came back with a recurrence in each group was noted. Complications, both ocular and systemic, if any, were noted for both groups. The time to resolution of PED was compared using the unpaired t-test. Statistical significance was set at p < 0.05.

The primary outcome measure was the proportion of patients with resolved PEDs at the end of the follow-up period in each group. Secondary outcome measures were the (1) corrected visual acuity at three months after completion of therapy and at final follow-up in both groups, (2) the recurrence rate in both groups and (3) the complications noted in both groups.

Results

A total of 14 patients (Group A) had received steroids as an adjunct to therapy for IPCV in the said period. These patients were compared to 26 consecutive patients of IPCV undergoing treatment in the same period who did not receive oral steroids (Group B).

9 patients in Group A and 14 in Group B had received laser photoacoagulation to the polyp followed one week later with intravitreal anti-VEGF injections, which were repeated as required, depending on the response. The remaining patients received photodynamic therapy for subfoveal or juxtafoveal polyps (as described earlier). The mean number of injections in Group A was 2.85 ± 1.23 vs 2.60 ± 1.32 in Group B. All patients in Group A and 23 patients in Group B had associated large PEDs. The median PED height as measured on ocular coherence tomography scans was 412 ± 108 µm vs 429 ± 122 µm in Groups A vs B respectively.
There were eight female patients in Group A and 14 in Group B. The median age of the patients in Group A was 59.24 (52–73) years vs 62.38 (53–70) years in Group B (p = 0.31). 9 patients in Group A and 12 in Group B were pseudophakic. 11 patients in Group A and 19 in Group B had associated systemic hypertension, and a total of 4 patients in each group had type II diabetes mellitus, without evidence of diabetic retinopathy. The median follow-up was 43.21 ± 11.32 months (Group A) vs 48.24 ± 9.75 months (Group B). 1 patient in Group A had persistent PED at the end of the follow-up period vs 7 in Group B. The median baseline visual acuity was 1.86 ± 1.24 logMAR vs 2.12 ± 1.48 logMAR (A vs B). The median visual acuity at three months after treatment completion was 0.84 ± 0.74 logMAR (Group A) vs 1.16 ± 0.89 (Group B; p = 0.039). The visual acuity was thus significantly better in both groups as compared to baseline (Group A: 0.033; Group B: 0.047). The median final visual acuity was 0.82 ± 0.78 logMAR (Group A) vs 1.19 ± 0.92 (Group B, A vs B: p = 0.042). Group A showed better visual acuity. There was also significant improvement in the visual acuity in both groups (Group A: 0.03, Group B: 0.043). The odds that a patient from Group B would have persistent PEDs at the end of the follow-up period were 4.60 (95% CI 1.7–11.10). 4 patients in Group B and none in Group A had breakthrough bleeds during the course of treatment; 3 of these had submacular hemorrhage and one had vitreous hemorrhage. These occurred a median of 3.56 ± 1.24 months after completion of therapy. The median time to resolution of the PED was 2.64 ± 1.25 months in Group A vs 8.15 ± 2.42 months in Group B (p = 0.012, significant difference).

7 patients in Group A and 12 in Group B had a recurrence. The difference was statistically insignificant (p = 0.28). All were offered photodynamic therapy as a second line of treatment except 1 patient in Group B who was advised repeat laser photocoagulation.

None of the patients in either group had treatment related adverse reactions. None of the patients in Group A had any systemic side effects secondary to steroids and no patient required discontinuation of therapy because of steroids.
Discussion

A tailored approach to each patient with IPCV is recommended. This study shows good results in terms of PED resolution in patients who have otherwise received local therapy appropriate to the clinical and angiographic picture.

A troublesome complication of large tense serous or hemorrhagic PEDs is pigment epithelial rip and/or breakthrough hemorrhage, be it suprachoroidal, subretinal or vitreal. Additionally, local therapy in the form of laser photocoagulation or intravitreal injections may actually initiate RPE rip or breakthrough hemorrhage, especially in patients with large...
PEDs. A predictive factor for such an event is determined by the size of the PED, and a positive correlation has been noted between PED size and the occurrence of a RPE rip.

The role of inflammation in the pathogenesis of AMD in general and IPCV in particular has been to an extent, analyzed. Authors have used triamcinolone injections, intravitreally or subtenon, as a combination therapy with PDT in AMD. Authors have found that non-PCV lesions do show some benefit with local steroid injection with respect to reduced recurrence rates. An earlier publication from our institute describes a patient of IPCV who responded to oral steroids with respect to reduction in PED size.

This study shows greater visual benefit in patients of PCV who received steroids as an adjunct to local therapy, contrary to other studies; it should, however, be borne in mind that our analysis was retrospective. We too did not notice any significant difference with respect to recurrence in both groups. But oral steroids appeared to help accelerate the fluid/hemorrhage reabsorption process. We speculate that this probably is a consequence of reducing inflammation and subsequent leakage. As has been shown in an earlier publication, subretinal fluid resolution precedes PED reduction, and PED reduction may be influenced by PCV persistence and/or recurrence. A persistent, tense PED can give rise to breakthrough hemorrhage or even RPE rips, with or without treatment. We propose that steroids probably help reduce the chances of such an occurrence by hastening its resolution. Additionally, steroids may help quell increased inflammation secondary to therapy such as laser photocoagulation or photodynamic therapy, as is seen in Figs. 1–3. Thus steroids probably help accelerate the resolution process that has been initiated by laser photocoagulation or photodynamic therapy and prevent an inflammatory increase in fluid.

The use of oral steroids did not seem to influence recurrence in our study.

A look at available literature suggests that combination therapy is superior to anti-VEGF monotherapy for management of polypoidal vasculopathy. The EVEREST study looked at the role of combination therapy with verteporfin based photodynamic treatment with or without intravitreal ranibizumab vs monotherapy with intravitreal ranibizumab. The authors concluded that PDT, either alone or in combination with intravitreal ranibizumab was superior to ranibizumab monotherapy in achieving complete polyp regression. Additionally, aflibercept has been shown to be beneficial in patients with refractory poloidal vasculopathy who demonstrate tachyphylaxis to ranibizumab, as well as in patients with treatment naïve PCV. The authors suggest that aflibercept may halt exudation and thus expedite PED resolution.

This article has the usual limitations of a retrospective study. Additionally, there was no standardized treatment protocol in terms of the exact PED size beyond which steroids would be advisable. Also, there may be hesitation in prescribing oral steroids to patients in the age bracket described, given that steroids carry with them well known adverse effects. Despite these limitations, however, this study presents certain features of interest: This study is the largest in terms of patients who received anti-inflammatory therapy to supplement local treatment in patients with IPCV. In addition to recurrence rates and visual benefit, we also look at PED resolution between the two arms, as tense PEDs are likely to give way and create further problems. Steroids appeared to aid as well as hasten the PED resolution as per our findings. The role of steroids in PCV is thus not clear, and future prospective trials are warranted.

To conclude, oral steroids appear to improve visual outcomes and aid PED resolution in patients with IPCV when prescribed as an adjunct to treatment. A randomized trial will help ascertain conclusively the role of steroids as an aid to IPCV management.

Conflict of Interest

The authors declared that there is no conflict of interest.

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