The use of systemic steroids and photodynamic treatment for choroidal neovascularisation in young patients

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Advantages of adjunctive corticosteroid treatment in combination with photodynamic treatment (PDT) as against PDT alone in eyes with subfoveal idiopathic choroidal neovascularisation

Idiopathic choroidal neovascularisation (ICNV) is a relatively rare cause of vision loss due to choroidal neovascularisation (CNV). However, it affects young patients (aged <50 years) and thus may have a significant impact on lifestyle and visual acuity over the patient's lifetime. To date, the only randomised clinical trial specifically and prospectively to evaluate treatment for ICNV was the Macular Photocoagulation Study (MPS).¹ In this trial, patients with extrafoveally located ICNV were randomised to either no treatment or standard argon blue-green laser photocoagulation. The sample size (67 eyes) in the idiopathic portion of the MPS was too small to yield definitive conclusions; however, the pattern of response was towards stabilisation and/or improvement in visual acuity with laser treatment. These results were similar to the results of the MPS 1 and 2 studies (for age-related macular degeneration (ARMD) and presumed ocular histoplasmosis syndrome (POHS), respectively). Thus, the MPS group concluded that eyes with ICNV would also benefit from laser treatment.¹⁻³ Since the MPS study, there have been no randomised, controlled clinical trials to evaluate other treatment options for ICNV, primarily due to the small number of eyes with this condition.

Photodynamic treatment (PDT) using verteporfin (Visudyne, Novartis Ophthalmics, East Hanover, New Jersey, USA) has been proven safe and effective for the treatment of predominantly classic CNV due to ARMD and pathologic myopia (PM); however, it has not been prospectively evaluated in other conditions such as ICNV, again owing to the relatively small numbers of eyes with this condition.⁴⁻⁵ It should be noted, however, that the benefits of verteporfin for the treatment of subfoveal CNV in PM seemed to wane in the second year, as reported in the Visudyne in Photodynamic Therapy (VIP) report number 3. A similar finding

was seen with standard laser treatment for extrafoveal ICNV, where the recurrence rate increased in the years following laser treatment, with a recurrence rate of 34% in the idiopathic group by the fifth year, as seen in the MPS, and a consequent decrease in visual acuity.⁶⁻⁷ This decrease in visual acuity seen in the MPS is primarily due to the extension of the ICNV subfoveally.⁷

Corticosteroids in many forms, including systemic, periocular and intravitreal, have been used in the treatment of CNV, owing to various causes that involve an inflammatory component, such as multifocal choroiditis, punctate inner choroidopathy and POHS.⁸⁻¹⁰ The pathophysiology of ICNV is not known; however, a component of inflammation has been postulated, as seen in ARMD and other inflammatory conditions associated with CNV.⁸⁻¹¹ Indocyanine green angiographic findings associated with ICNV have been described by Giovannini as well as others, and the authors have hypothesised that these findings, which include changes in choroidal permeability with dye leakage and hypofluorescence, are compatible with choroidal inflammation.¹²⁻¹³ There are, however, no histopathological reports on ICNV to verify or refute these assumptions.

The only long-term follow-up reported on untreated eyes with subfoveal ICNV comes from a small study by Ho *et al*¹⁴ published in 1995, which included 23 eyes with subfoveal ICNV and an average follow-up of 87 months. This retrospective review showed that the fellow eyes remained unaffected during follow-up and that no other chorioretinal lesions, such as drusen or peripheral scars, developed in the presenting eye.¹⁴ The authors also report a better long-term visual prognosis in eyes with untreated subfoveal ICNV than in those eyes with subfoveal CNV associated with other causes such as POHS or ARMD. Overall, 21% of eyes with subfoveal ICNV maintained a final visual

acuity of 20/40 or better, whereas 63% maintained a final visual acuity of 20/100 or better, and only 16% had a final visual acuity of 20/200 or worse (profound vision loss).¹⁴ Since the MPS did not specifically evaluate subfoveal ICNV, comparisons between the study by Ho *et al* and the MPS are not optimal. However, it is interesting that the final visual acuities in the MPS ICNV study and the Ho study were very similar (median 20/80 at 5 years in the MPS extrafoveal ICNV group and median 20/70 in the Ho study).⁷⁻¹⁴ In both of these studies, the final conclusions indicate that subfoveal ICNV tends to remain small, stable and unlikely to cause severe visual loss.⁷⁻¹⁴

In this issue, Giovannini *et al* (see page 620) discuss the results of a small randomised clinical trial comparing PDT alone with high-dose systemic corticosteroids followed by PDT for the treatment of ICNV.¹⁵ Their series includes 20 eyes of 20 consecutive patients with juxtafoveal or subfoveal ICNV who were prospectively randomised to receive either PDT alone or PDT with systemic corticosteroids, with 10 patients randomised to each group. They evaluated both best-corrected visual acuity and change in CNV size as their final outcome measures. They used a standard definition for ICNV, which included no current signs or history of intraocular inflammation, evidence of retinal scars, pathological myopia, retinal degeneration or signs of ARMD in either eye. They also performed standardised visual acuity measurements using the Early Treatment of Diabetic Retinopathy Study chart for all visual acuity examinations, and defined a change in visual acuity as ≥ 2 lines on the Early Treatment of Diabetic Retinopathy Study chart. Their results demonstrate a trend of worsening of visual acuity in the PDT-only group at follow-up, although this was not statistically significant, whereas the PDT and systemic steroid group showed better final visual acuity, which was statistically significant. Also of note is that the lesion size tended to increase in the PDT-only group, whereas the trend was towards decreased size in the PDT and steroid group, although the authors did not provide actual lesion measurements and so statistical significance cannot be assessed. They did find a significant correlation between better final visual acuity and smaller final lesion size as seen in the PDT and steroid group.

There is evidence for the use of systemic corticosteroids to treat CNV associated with inflammatory conditions in healthy young patients with little risk of systemic complications.⁸ However, in the current article, we are not given information on complications related to

steroid use or the lack thereof. We must assume that even with high-dose intravenous steroids for 3 days there were no complications, and that no complications occurred during the steroid taper, about which also we have no information. Oral steroids alone have been shown to reduce vascular leakage and stabilise visual acuity when no other treatment is used. Thus, we can assume that oral steroids would be just as beneficial as intravenous steroids in the current context.⁸ The benefit of the oral route of administration would be lack of hospitalisation for intravenous administration and fewer side effects related to the placement of the intravenous line. It is also possible that treatment with steroids only may have provided the same overall benefit as reported by other authors.^{8–10} Other routes of steroid delivery, such as periocular injection or intravitreal injection, are also possible, and these could very well have the same beneficial outcome reported by the authors (although these routes have their own potential side-effect profiles). Martidis *et al*¹⁰ compared the use of high-dose oral corticosteroids with a single sub-Tenon's steroid injection in POHS and found a similar beneficial effect in subfoveal CNV, with the oral steroid group demonstrating a more rapid vision recovery, which then stabilised with the achievement of similar final visual acuity to the sub-Tenon's steroid group. This study did not have a group of PDT-treated eyes for comparison. There has been one report regarding intravitreal steroids and PDT for subfoveal CNV related to PM. Although this was not a comparative trial, it did demonstrate improved visual acuity in treated eyes within a short follow-up period of up to 6 months.¹⁶ There were a significant number of eyes requiring treatment for increased intraocular pressure, which is usually not the case with systemic corticosteroid administration.¹⁶

PDT is a safe procedure but there is a small risk for sudden vision loss and infusion-related complications, as seen in

the Treatment of Age-related Macular Degeneration with Photodynamic Therapy and VIP trials. Thus, limiting the number of PDT treatments is beneficial.^{4–6} The follow-up in this study by Giovannini *et al*¹⁵ for the PDT-only group was for 22 months and for the PDT and steroid group was for 21 months, with the mean number of PDT treatments reduced in the PDT and steroid group to 1.2 as opposed to 2.3 in the PDT-only group. This is in contrast to the PDT-treated eyes in the PM group in the VIP trial, in which the average number of re-treatments in the PDT-treated group at 2 years was 5.1.⁶

In summary, the clinical results of this small, prospective, randomised clinical trial are in favour of the use of adjunctive corticosteroid treatment combined with PDT in eyes with subfoveal ICNV. It would be beneficial in the future to compare other routes of steroid delivery in these cases to determine whether the results of these other delivery methods compare favourably with the results presented in the present report, as well as with those of a steroid-only treatment arm. This report also does not address the advent of other treatment options for subfoveal CNV, such as antivascular endothelial growth factor agents, which could compare very favourably with PDT treatment with or without corticosteroid treatment.

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REFERENCES

- 1 **Macular Photocoagulation Study Group.** Argon laser photocoagulation for idiopathic neovascularization: results of a randomized clinical trial. *Arch Ophthalmol* 1983;**101**:1358–61.
- 2 **Macular Photocoagulation Study Group.** Argon laser photocoagulation for age-related macular

degeneration: results of a randomized clinical trial. *Arch Ophthalmol* 1982;**100**:912–18.

- 3 **Macular Photocoagulation Study Group.** Argon laser photocoagulation for ocular histoplasmosis syndrome: results of a randomized clinical trial. *Arch Ophthalmol* 1983;**101**:1347–57.
- 4 **Verteporfin in Photodynamic Therapy (VIP) Study Group.** Photodynamic therapy of subfoveal choroidal neovascularization in pathologic myopia with verteporfin: 1-year results of a randomized clinical trial—VIP report no. 1. *Ophthalmology* 2001;**108**:841–52.
- 5 **Treatment of Age-related Macular Degeneration with Photodynamic Therapy (TAP) Study Group.** Photodynamic therapy of subfoveal choroidal neovascularization in age-related macular degeneration with verteporfin: two-year results of 2 randomized clinical trials—TAP report 2. *Arch Ophthalmol* 2002;**119**:198–207.
- 6 **Verteporfin in Photodynamic Therapy (VIP) Study Group.** Verteporfin therapy of subfoveal choroidal neovascularization in pathologic myopia: 2-year results of a randomized clinical trial—VIP report no. 3. *Ophthalmology* 2003;**110**:667–73.
- 7 **Macular Photocoagulation Study Group.** Argon laser photocoagulation for neovascular maculopathy after five years: results from randomized clinical trials. *Arch Ophthalmol* 1991;**109**:1109–14.
- 8 **Flaxel CJ, Owens SL, Mulholland B, et al.** The use of corticosteroids for choroidal neovascularisation in young patients. *Eye* 1998;**12**:266–72.
- 9 **Rechtman E, Allen, VD, Danis RP, et al.** Intravitreal triamcinolone for choroidal neovascularization in ocular histoplasmosis syndrome. *Am J Ophthalmol* 2003;**136**:739–41.
- 10 **Martidis A, Miller DG, Ciulla TA, et al.** Corticosteroids as an antiangiogenic agent for histoplasmosis-related subfoveal choroidal neovascularization. *J Ocul Pharmacol Ther* 1999;**15**:425–8.
- 11 **Reddy VM, Zamora RL, Kaplan HJ.** Distribution of growth factors in subfoveal neovascular membranes in age-related macular degeneration and presumed ocular histoplasmosis syndrome. *Am J Ophthalmol* 1995;**120**:291–301.
- 12 **Giovannini A, Scassellati-Sforzolini B, Mariotti C, et al.** Indocyanine green angiography findings in idiopathic choroidal neovascularization. *Int Ophthalmol* 1996;**20**:171–9.
- 13 **Gharbiya M, Pantaleoni FB, Grandinetti F, et al.** Indocyanine green angiographic findings in idiopathic choroidal neovascularization. *Eye* 1999;**13**:621–8.
- 14 **Ho AC, Yannuzzi LA, Pisicano K, et al.** The natural history of idiopathic choroidal neovascularization. *Ophthalmology* 1995;**102**:782–9.
- 15 **Giovannini A, Neri P, Mercanti L, et al.** Photodynamic treatment versus photodynamic treatment associated with systemic steroids for idiopathic choroidal neovascularization. *Br J Ophthalmol* 2007;**91**:620–3.
- 16 **Marticorena J, Gomez-Ulla F, Fernandez M, et al.** Combined photodynamic therapy and intravitreal triamcinolone acetate for the treatment of myopic subfoveal choroidal neovascularization. *Am J Ophthalmol* 2006;**142**:335–7.