

Combined Treatment: PDT, Intravitreal Triamcinolone for Exudative AMD

Cost-effectiveness analyses with regard to PDT have shown differing results.

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The arrival of photodynamic therapy (PDT) to treat exudative age-related macular degeneration (AMD) in 1999 marked the greatest change in the management of this condition.

AMD is the leading cause of legal blindness among patients aged >55 years in developed countries. Below is a discussion of an article we published in *Retina*.¹

Reports from the Treatment of Age-Related Macular Degeneration with Photodynamic Therapy (TAP) and Verteporfin in Photodynamic Therapy (VIP) studies showed that the management of certain choroidal neovascularization (CNV) forms associated with AMD using PDT reduced visual acuity loss when compared with the natural history of the disease. A high number of PDT sessions, however, were usually needed to increase the number of patients who had moderate visual acuity loss (ie, <3 Early Treatment of Diabetic Retinopathy Study [ETDRS] lines). This gave way to the publication of reports proving a low cost-efficacy relationship for the use of PDT.

The cost-effectiveness relationship of the use of PDT in eyes with CNV associated with AMD has been studied on different occasions, with the results being minimally cost-effective, moderately cost effective or very cost-effective.

POOR COST-EFFECTIVENESS

The poor cost-effectiveness relationship is because of the high number of PDT sessions needed to achieve CNV closure due to regrowth/recurrence of CNV following

treatment. Repeated PDT sessions have been shown to induce retinal damage with progressive thinning of neurosensory retina in animal models. Repeated growth of CNV also damages photoreceptors, causing a progressive reduction in visual acuity.

Investigations performed on patients treated with PDT have shown increased local production of vascular endothelial growth factor (VEGF) induced by PDT. This finding suggests that the frequent regrowth/recurrence of CNV after PDT may be caused by one or more of the following reasons: persistence of the original factors that caused CNV; increased local production of VEGF; and inflammation originated by the treatment (the mechanism of action of PDT is mainly inflammatory). Ischemia in the photoreceptors may be an additional local factor, as PDT affects the choriocapillaris increasing VEGF release.

Combining PDT with an angiogenesis suppressor has been proposed on the basis of choroidal hypoperfusion inducing the recurrence of CNV by a reactive angiogenic mechanism. Presently, it is considered necessary to find combined therapies to improve the cost-effective relationship between the high number of retreatments and the progressive loss of BCVA in spite of PDT. The use of triamcinolone acetonide with PDT was established to combine antiinflammatory and antiangiogenic action, as has been demonstrated in animal models.

COMMERCIALIZED AGENT

Another important fact was that the previous status of

triamcinolone as a commercialized drug with a wide experience in intravitreal injection in everyday practice.

The rationale for performing PDT followed by intravitreal triamcinolone has been described previously. In short, the reason is to avoid the opacification of the vitreous body by triamcinolone, which might reduce the efficacy of PDT, and to avoid potential steroid inhibition of free-radical formation, which might interfere with the mechanism of PDT action.

The results of the combination of PDT with intravitreal triamcinolone at low doses (4 mg) and high doses (20 mg to 25 mg) have been previously reported in the literature. Authors of these reports are in substantial agreement that the frequency of PDT sessions is reduced with combined therapy, and visual outcome may be better. Nonrandomized studies performed by Spaide et al^{2,3} have shown that combined PDT and intravitreal triamcinolone (4 mg) significantly improved mean visual acuity by 2.5 lines in treatment-naïve patients at 12-month follow-up. Retreatment rates in this series were 1.24 for the naïve patients and 1.2 for those who had been previously treated by PDT alone over the first year. In a series published by Rechtman et al,⁴ 3 of 14 eyes with combined PDT and triamcinolone (4 mg) needed retreatment, with a favorable visual outcome after 6 to 12 months follow-up.

COMBINATION TREATMENT

Other studies by Nicolo, Augustin and Ruiz-Moreno^{5,6} combining PDT with higher triamcinolone doses are in substantial agreement. Augustin treated 184 eyes with AMD-associated CNV using PDT and 25 mg intravitreal triamcinolone 16 hours later, achieving an average 1.22 Snellen lines improvement after an average 1.21 sessions of PDT for >6 month follow-up in most cases. The authors reported that the response to the combined therapy was good, independent of lesion composition and size. Dr. Augustin treated pure occult lesions using the same combined treatment in 41 eyes, achieving an average BCVA improvement from 20/133 at baseline to 20/81 at 24 months with an average 1.8 PDT sessions.

Dr. Nicolo treated 11 eyes from 10 patients with occult CNV using 25 mg intravitreal triamcinolone followed by PDT 1 month later, improving from an average BCVA 20/160 at baseline to 20/80 at 12 months. Our group achieved an improvement in final BCVA reducing the need for retreatment at 12 months in a comparative study of 30 consecutive eyes in 30 patients with subfoveal AMD-associated CNV treated by PDT followed by 20 mg intravitreal triamcinolone, compared with 15 eyes treated by PDT alone. The mean change in Snellen lines in the control group at month 12 was -2.2 ± 4.0 lines; in the

newly treated group 1 it was 0.7 ± 3.7 lines; and in the previously treated PDT group 2 it was -0.7 ± 1.5 lines.

POSSIBLE COMPLICATIONS

The expected possible complications after the use of intravitreal triamcinolone, such as endophthalmitis, retinal detachment, retinal tears, vitreous hemorrhages and floaters, may be attributed to the procedure. Other complications, such as progressive crystalline lens opacification and increased intraocular pressure (IOP), may be attributed to the pharmacological effects of intravitreal steroids.

Increased IOP has been reported in 22% to 54% of the treated eyes after this therapy. Cataract progression has been reported in 24% to 26% of the cases after the injection of 4 mg triamcinolone and in 42% to 54% after higher doses.

The development of new specific antiangiogenic drugs blocking VEGF and intended for intraocular use and the good results achieved with them will probably reduce the association of intravitreal triamcinolone with PDT because of its frequent adverse events.

The long-term results after cessation of intravitreal antiangiogenic drugs to treat CNV associated with AMD will probably lead to combined therapies of PDT plus antiangiogenic drugs plus intravitreal steroids in an attempt to close CNV, while simultaneously blocking VEGF and the inflammatory mechanisms taking part in the mechanisms of neovascularization. ■

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