Current Role of Photodynamic Therapy in Ophthalmic Practice

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Introduction
Photodynamic therapy (PDT) is a form of light-therapy using light-sensitive compounds that when exposed to light selectively become toxic to targeted cells (phototoxicity).\(^1\) Most PDT applications involve three components: a photosensitizer, a light source and tissue oxygen. The combination of these three components leads to chemical destruction of tissues which have taken-up the photosensitizer and have been locally exposed to light of appropriate wavelength to produce reactive oxygen species (ROS). These ROS are free radicals (Type I PDT) generated through electron abstraction or transfer from a substrate molecule and highly reactive state of oxygen known as singlet oxygen (Type II PDT). It is important to distinguish PDT from other light-based and laser therapies such as laser wound healing and rejuvenation, or intense pulsed light hair removal, which do not require a photosensitizer. PDT is used clinically to treat a wide range of medical conditions.\(^2\) The era of PDT in Ophthalmology was initiated by results of the TAP study.\(^3\) The first indication for which PDT was approved in ophthalmology was choroidal neovascularization (CNV) in patients with age-related macular degeneration (AMD).

The technique of administering PDT requires the combination of laser and photosensitizer Visudyne®. PDT utilizes photosensitizer Visudyne® [liposomal benzoporphyrin derivative monoacid ring A (BPDMA)] given via intravenous infusion at a dose of 6 mg/m\(^2\) of body surface area. Fifteen minutes after the infusion, the ‘standard’ protocol of focal light (light dose of 50 J/cm\(^2\), irradiance of 600 mW/cm\(^2\) of 689 nm light over 83 seconds) is delivered. This treatment is ‘selective’ in that the photosensitizer is selectively taken up by the proliferating endothelial cells of the neovascular tissue thus leading to occlusion and reducing collateral damage. PDT was first recommended for cases of subfoveal classic or occult CNV in AMD.\(^5\)

The approval of intravitreal Ranibizumab for treatment of CNV in AMD has led to decline in the use of PDT. The main advantage of anti-VEGF when compared with PDT is more improvement in BCVA (77% vs 28%) and less reduction in BCVA (21% vs 60%) at 2-year follow-up.\(^6\) PDT is currently recommended for CNV in AMD either refractory to anti-VEGF therapy or as monotherapy in patients with contraindications for anti-VEGF therapy.\(^7\)

The PDT use in myopic CNV was established by the results of the VIP reports 1 and 2 where reduction in BCVA was less with PDT as compared to placebo (36% patients lost at least eight ETDRS letters as compared to 51% with placebo) while more number of patients had improvement in BCVA (improvement in BCVA of at least five ETDRS letters was seen in 40% with PDT as compared to 13% with placebo) at 24-month follow-up.\(^8,9\) Currently, PDT is recommended for use in myopic CNV in cases where anti-VEGF has been ineffective or is contraindicated.\(^10\)

In patients with CNV due to angioid streaks, stability in BCVA is achieved with the use of PDT.\(^11\) However, the success rate achieved with anti-VEGF in angioid streaks by Browning et al. tilted the balance towards anti-VEGF as the preferred modality of treatment.\(^12\) PDT has also been used with some success in cases of inflammatory CNV due to multifocal choroiditis, punctate inner choroidopathy (PIC) and toxoplasmosis.\(^13\)

Polypoidal choroidal vasculopathy (PCV) is a disorder characterized by subretinal polypoidal vascular lesions. PDT was found to be successful in improving BCVA in 56% cases and maintaining vision in 31% cases of PCV.\(^14\) Currently, PDT is recommended for treatment of juxtapfoveal and subfoveal PCV, alone or in combination with intravitreal Ranibizumab (0.5 mg/0.1 ml).\(^15\)

Central serous chorioretinopathy (CSCR) is a disorder characterized by pigmented epithelial detachment with subretinal fluid. The use of PDT is based on the rationale that primary choroidal hyperpermeability is the basic cause of CSCR. Treatment with PDT leads to visual improvement of ≥2 lines in 43% cases while loss of ≥2 lines of BCVA occurs in about 7.5%, cases. RPE atrophy seen in about 4% cases.\(^16\)

Apart from retinal lesions, various ocular tumors have been treated with PDT with variable success rates. PDT is the one of the treatment alternatives in recurrent choroidal melanoma.\(^17\) PDT is also a good option for treatment of symptomatic choroidal nevi, especially in cases with subretinal fluid. However, despite resolution of subretinal fluid, it does not provide good local tumor control.\(^18,19\)

The use of PDT in patients with retinal capillary hemangioblastomas achieves regression of the tumor, resolution of macular edema. However, improvement in BCVA is not always seen (around 50% cases).\(^20,21\) On the contrary, the use of PDT...
in choroidal hemangioma achieves excellent tumor control, resolution of macular edema as well as exudative macular detachment along with improvement in BCVA. This has made PDT as the preferred treatment option for cases of choroidal hemangioma.22,23 There are a number of other ocular tumors such as vasoproliferative tumors of the retina, choroidal osteoma, retinal astrocytoma where PDT has been used with variable success rates.24–26

Ocular surface squamous neoplasia (OSSN) is an ocular condition characterized by growth of neovascular tissue on the surface of the cornea and sclera. PDT was first used for treatment of OSSN by Barbazetto et al. This led to its use for treating OSSN, without extensive invasion, which is its current indication.27,28

With the growing evidence in support of PDT for successful treatment of various retinal neovascular lesions, the use of PDT in corneal neovascularization for prevention of corneal graft rejection was explored. PDT achieves an immediate reduction in corneal neovascularization with decreased neovascularization maintained in 75% and complete vascular occlusion achieved in 50% of treated eyes at 1-year follow-up. Recently, PDT has also been used in combination with subconjunctival Bevacizumab for the treatment of corneal neovascularization. A triple combination of PDT, subconjunctival Bevacizumab and topical cyclosporine has also been tried.29–31

However, with the growing utility of PDT in ocular conditions, its side-effects warrant consideration, too. The most common systemic side-effects encountered are infusion-related back pain and minor allergic reactions at the injection site. Cases of serious allergic reactions are extremely rare though. Sunlight exposure is to be avoided for 3 days following PDT to avoid sunburn. The most important ocular side effects are secondary CNV, persistent choriocapillaris hyperperfusion and pigmentary changes in the RPE in the treated area.32 All these concerns have led to the exploration of reduced fluence PDT (irradiance of 300 mW/cm² instead of 600 mW/cm²) by some authors with success rates similar to those achieved with standard fluence. A novel approach has been reducing the dose of verteporfin from 6 to 3 mg/m². This modification has achieved success rates similar to the standard fluence PDT but with the theoretical advantage of reduced scarring.33–35

In conclusion, indications of PDT extend from ocular surface conditions to intraocular tumors, making it a useful tool in the armamentarium of the ophthalmologist.

References