Photodynamic Therapy: A Novel Approach to the Treatment of AMD

1. Barbazetto, Ursula Schmidt-Erfurth

10.1 Photodynamic Therapy: Historical Background – 145
10.2 The Principle of Photodynamic Vascular Occlusion – 145
10.3 Photosensitizer – 147
10.4 Current Status of Photodynamic Therapy – 148
10.5 Indications for Different Forms of Laser Therapy – 148
10.5.1 Clinical and Angiographic Characteristics – 149
10.6 Study Results – 152
10.6.1 The TAP Study – 152
10.6.2 The VIP Study – 152
10.7 Safety Issues – 154
10.8 Guidelines for Photodynamic Therapy – 154
10.8.1 Angiographic Criteria – 154
10.8.2 Whom Not to Treat – 155
10.9 Future Indications – 155
10.10 Perspectives – 155

References – 155
Age-related macular degeneration (AMD) is a degenerative eye disease that can cause severe and irreversible loss of central vision. While most patients with AMD experience only a slow, moderate decrease of visual acuity as a result of atrophic changes of the retina, 10% of patients suffer from a severe and rapidly developing visual loss. According to literature and clinical experience, up to 90% of this significantly affected group present with the neovascular form of AMD (Bressler et al. 1982; Guyer et al. 1986; Bressler et al. 1988). This form is characterized by the development of abnormal blood vessels under the retina, which leak fluid, lipids and blood. Over time the leakage leads to fibrosis of the central retina with loss of photoreceptors and concomitant vision decline (Bressler et al. 1982). In North America and Europe this is the leading cause of legal blindness in people over 65 years of age (Leibowitz et al. 1980).

Age-related macular degeneration presents with numerous phenotypes and the etiology has been poorly understood. Therefore any potential treatment will be limited to the prevention of visual loss, as long as the mechanisms leading to the development of choroidal neovascularization (CNV) and the underlying role of changes in the retinal pigment epithelium (RPE), Bruch’s membrane and photoreceptors remain unclear.

However, the pathological correlate for a poor prognosis can be clearly identified: it is CNV (Guyer et al. 1986). Targeting this structure and thereby treating the severest form of AMD should have highest priority in our therapeutic considerations.

For many years conventional laser photocoagulation was the only approved treatment based on the criteria established by the Macular Photocoagulation Study (MPS) Group (1991). Thermal laser photocoagulation leads to a non-selective necrosis of the CNV and all adjacent outer retinal and inner choroidal structures. Many patients with subfoveal lesions experience immediate additional visual loss as a result of this destructive treatment (MPS Group 1994). Recurrence after therapy is not uncommon and is seen in up to 50% of patients within 2 years.

In addition, the majority of patients with neovascular AMD do not meet the criteria for laser treatment because the lesion is too large or not well defined on angiography (MPS Group 1986).

Other treatments such as radiation (Berking et al. 1998; Holz et al. 1999; Spaide et al. 1998) and interferon therapy (Pharmacological Therapy for Macular Degeneration Study Group 1997) have been investigated and not shown to be beneficial. The role of transpupillary thermal therapy still needs to be proven in AMD treatment with supporting study data from clinical controlled trials (Reichel et al. 1999; Mainster and Reichel 2000).

Surgical approaches such as submacular surgery, macular rotation and translocation are highly invasive and therefore may be unsuitable for many patients of this age group. Also these techniques have to be investigated in larger clinical trials to evaluate their true potential (Machemer and Steinhorst 1993; Bressler 1986; Eckardt et al. 1999).

Photodynamic therapy is a novel therapeutic approach, which has been approved recently by health authorities in various countries for the treatment of predominantly classic CNV secondary to AMD. The therapy combines the potential of non-thermal laser light to induce localized chemotoxic reactions by activating a photosensitizer (light-activable compound) in neovascular tissue (Schmidt-Erfurth et al. 1998). It allows a more selective treatment of the CNV as a result of preferential concentration of the photosensitizer in the target tissue and the possibility in ophthalmology to direct the light irradiation to the specific target area by using a laser light source (Schmidt-Erfurth and Hasan 2000). The induced photochemical reaction differs substantially from other treatments, as it does not involve any thermal or mechanical damage. Two major clinical trials have demonstrated that photodynamic therapy safely reduces the risk of vision loss in patients with subfoveal CNV (Treatment of Age-related Macular Degeneration with Photodynamic Therapy (TAP) Study Group 1999, 2001; VIP Report 2003). The therapy is currently recommended for patients with predominantly classic CNV in AMD or CNV secondary to pathologic myopia.