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Laser photocoagulation

Author:

Rufino Silva, MD, PhD
Coimbra University Hospital. Faculty of Medicine. Coimbra. Portugal

Introduction

Currently, three types of therapy are approved for the treatment of exudative age-related macular degeneration (AMD): laser photocoagulation, photodynamic therapy with Verteporfin and intravitreal injections of antiangiogenic agents (Ranibizumab and Pegaptanib).

Other treatments revealed to be ineffective or even more aggressive than natural disease progression. Examples of these later are radiotherapy, surgical removal of the subfoveal membranes, alpha 2 Interferon, transpupillary thermal therapy and anecortave acetate injections.

Laser photocoagulation in exudative AMD

The Macular Photocoagulation Study Group (MPS, 1982-1997)[(1-16)] has performed several randomized, double-blind, placebo-controlled studies in patients with exudative AMD.

These studies showed that laser photocoagulation might be effective in reducing loss of vision in cases of well defined exudative AMD lesions.

The importance of well-defined limits resulted from the absolute need to treat the entire lesion in order to maximally reduce recurrence and persistence rates, generally associated to greater loss of vision.

For extrafoveal and juxtafoveal lesions, results were evaluated for well-defined lesions before any differentiation based on angiographic patterns (occult or classic) was made.

In the subfoveal lesion study, results were evaluated for well-defined lesions with a classic component.

In addition to defining which cases to treat and the benefits expected from laser photocoagulation, the MPS defined the angiographic characteristics of neovascular lesions and guidelines for treating each type of membrane (extra, juxta or subfoveal), including preparation for treatment, treatment techniques, the wavelength to be selected, post-treatment care, special circumstances and expected complications.

Other studies of extra, juxta and subfoveal lesions with less impact on everyday clinical practice were performed by various authors using the same treatment technique studied by the MPS (for extra and juxtafoveal lesions) or macular grid photocoagulation (subfoveal lesions)[(17,18,9)].

Macular Photocoagulation Study Group (MPSG): extrafoveal lesions.

The first study was performed by the MPSG in patients with well-defined extrafoveal neovascular lesions (located 200 to 2500 µm from the foveal centre), with drusen, age ≥ 50 years and VA ≥ 20/100.

No differentiation was made between classic and occult membranes in this study.

Choroidal neovascularization was angiographically defined as the presence of leakage in the external retina.

Patients were enrolled in the study between 1979 and 1982 and treated with blue-green Argon laser.

The first results were published in the latter year (MPS, 1982)[(1,2)].

The MPS concluded that laser photocoagulation with blue-green or green Argon laser of sufficient intensity to produce nearly white lesions in the retina and cover the entire neovascular lesion, as well as adjoining blood, reduces the risk of additional and severe loss of vision, when compared to natural progression of the disease.

The benefits of laser were greater during the first year following treatment, having persisted after 5 years[(5)].

The probability of stabilizing or increasing VA doubled for treated eyes; a 58% reduction in the risk of severe loss of vision (6 lines in the ETDRS scale) was also observed.

After 5 years, 48% of treated eyes and 62% of non-treated eyes had lost ≥ 6 lines.

These results show reduced efficacy when evaluated in terms of the number needed to treat[(20)].

It was necessary to treat 7 patients for one patient to benefit from the treatment.

Average VA after 5 years was 20/125 in the treated group and 20/200 in the non-treated group (MPS, 1982, 1986).

After 5 years, 54% of treated eyes had shown recurrence with severe loss of vision most of them occurring in the first 2 years after treatment, they have been responsible for the majority of cases of severe loss of vision in the treated group.

Smokers had a greater risk of recurrence (recurrence was observed in 85% of patients smoking more than 10 cigarettes per day, compared to 51% of non-smokers).

Similar results were obtained in two other studies performed in the United Kingdom[(17)] and France[(19)].

Macular Photocoagulation Study Group (MPSG): juxtafoveal neovascular lesions

A second study was performed with juxtafoveal membranes and using a Krypton laser [(11)].

Inclusion criteria allowed treatment of well-defined choroidal neovascular lesions located 1 to 199 µ from the foveal centre, or 200 to 2500 µm from the foveal centre but showing blood or pigmentation less than 200 microns from the foveal centre (resulting in a barrier effect in fluorescence).

As opposed to the study with Argon laser in extrafoveal membranes, this trial did not require treatment of the entire area where bleeding occurred. Under no circumstances should treatment reach the foveal centre.

After 3 years, severe loss of vision (≥6 lines) had occurred in 49% of treated eyes and 58% of non-treated eyes[(14)].

The efficacy of this treatment in terms of the number needed to treat(20) was very low: 11.1.

This treatment reduced the risk of severe loss of vision by 10%.

However, this benefit was not observed in patients with hypertension or taking antihypertensive medication.

Nevertheless, the MPS maintained the indication to treat for these non-normotensive patients due to the absence of similar findings in other MPS studies.

After 5 years, the number of eyes with final VA ≥ 20/40 was double for treated eyes[(14)].

Persistence (incomplete treatment) and recurrence (neovascularization later than six weeks after treatment) were responsible for the majority of loss of vision in the treated group.

The MPS reclassified membranes as 100% classic, classic with an occult component and 100% occult.

Results were better in classic membranes: 54% of treated eyes and 72% of non-treated eyes lost 6 or more VA lines.

No statistically significant differences were observed between the treated and non-treated groups in cases of mixed membranes (only the classic component was treated) and 100% occult membranes.

Therefore, treatment of occult membranes and the classic component of mixed membranes was not effective in reducing loss of vision[(14,16)].

In conclusion, the MPS showed that laser photocoagulation of well-defined extrafoveal choroidal membranes and classic extra and juxtafoveal membranes secondary to AMD may prevent of delay loss of vision in patients fulfilling the inclusion criteria.

Macular Photocoagulation Study Group (MPSG): subfoveal neovascular lesions

In 1986, the MPS started two studies[(12,13)] to determine the efficacy of laser photocoagulation in subfoveal choroidal neovascularization.

In the first study, the effect of laser photocoagulation (Argon or Krypton) was evaluated in eyes with subfoveal exudative AMD not previously treated; in the second study, the efficacy of laser treatment in subfoveal recurrence in eyes with extra or juxtafoveal membranes was evaluated.

The results of this study and treatment recommendations generated a great deal of controversy.

In fact, treated eyes displayed a very marked loss of vision immediately after treatment.

After 4 years, 30% of treated eyes and 60% of non-treated eyes displayed VA ≤ 20/400, whereas 45% of non-treated eyes and 23% of treated eyes has suffered severe loss of

vision.

The efficacy of this treatment in terms of the number needed to treat was 4.5[(20)].

A large percentage of ophthalmologists did not agree with the MPS recommendations for treating subfoveal lesions.

In fact, patients were losing 3 lines immediately after treatment.

The MPS re-evaluated treatment efficacy in terms of lesion size and difference from baseline VA, having established treatment groups and criteria according to these two variables[(13)].

Ophthalmologists could advise their patients and help them choose whether or not to undergo treatment according to lesion size and baseline VA.

With the emergence of photodynamic therapy with Verteporfin, laser photocoagulation for subfoveal lesion became obsolete.

It remains indicated only for extrafoveal lesions and the angiographic control should be performed 15 days after treatment.

Treatment

Preparation for treatment

Regarding preparation for treatment, the MPS recommended that patients should be informed that photocoagulation causes permanent paracentral scotoma in cases of juxta and extrafoveal choroidal membranes.

Patients should also be informed that they may continue to lose vision, even under the best treatment conditions, and that treatment does not cure AMD but it is only a means of reducing the risk of marked loss of visual acuity.

A fluorescein angiography (FA) should be performed 72 to 96 hours before photocoagulation in order to select treatable cases and to guide the ophthalmologist during treatment.

Patients should undergo treatment as quickly as possible, since neovascular lesions may grow 10 to 18µ per day[(21)].

Most neovascular lesions are extra or juxtafoveal at the onset, becoming subfoveal with rapid growth towards the fovea.

Treatment technique

The MPS recommends that treatment should be performed so that a white lesion in the retina is obtained.

The neovascular lesion should be surrounded by laser marks with a diameter of 200µ and duration of 0.2 to 0.5 seconds.

After surrounding the perimeter of the neovascular lesion, its central part is covered with 200µ burns; the remaining lesion is covered with 200 to 500µ burns, with duration of 0.5 to 1.0 seconds.

In cases of juxtafoveal lesions, the foveal centre should be preserved, although it should be ensured that the entire lesion is treated.

If bleeding extends to the area under the fovea, treatment should include the entire neovascularization area and stop at the limit of the fovea.

Since the emergence of new treatments, namely intravitreal antiangiogenic treatments, laser photocoagulation of juxtafoveal lesions has become controversial.

The MPS demonstrated that the wavelength selected does not affect laser results.

Laser treatment should avoid retinal blood vessels and the optic nerve (treatment should start 10-200 µm from the optic nerve), as well as preserve at least 1.5 hours of the papillomacular bundle (no peripapillary treatment).

Treatment of serous pigment epithelial detachment (PED) could be indicated when photocoagulation is used to treat subfoveal lesions including serous PED as a component (1,3,8,10,11).

Post-treatment follow-up

Follow-up of treated patients was also recommended and defined by the MPS.

In addition to self-evaluation, it is necessary to perform medical examinations and control FA 2 to 3 weeks, 4 to 6 weeks, 3 to 4 months and 6, 8, 9 and 12 months after treatment.

Recurrence is rare after 2 years.

The greater risks exist 6 weeks to 12 months after treatment. Detection through biomicroscopy without FA is sometimes difficult.

Angiography allows detection of approximately 12% of the cases that go unnoticed in medical examinations.

Recurrence and persistence rates are much greater in cases of choroidal neovascular or disciform lesions caused by AMD in the non-treated eye.

Other factors that appear to increase recurrence rates include smoking, hypertension and choroidal neovascularization with reduced pigmentation(1,2,8,11).

Treatment complications

Laser photocoagulation treatment may also lead to complications, including choroidal haemorrhage (rarer if spots ≥ 200 microns and time intervals ≥ 0.2 seconds are used), premacular fibrogliosis, accidental treatment of the fovea in extrafoveal or juxtafoveal lesions (minimised by retrobulbar anaesthesia, drawing of lesion limits and correct identification of the fovea), rupture of the pigment epithelium (more frequent in cases of PED) and atrophy of the RPE in the area adjoining the laser scar (immediately after treatment or years later)(2,3,7,8).

Treatment of occult membranes

The MPS also defined guidelines regarding occult membranes.

When extrafoveal and juxtafoveal neovascular lesions caused by AMD started to be studied no distinction was made between classic and occult membranes.

Subsequent analysis of all angiography results obtained during study of juxtafoveal lesions revealed that treatment was effective for classic neovascular lesions with no occult component.

In cases where an occult component (not treated) coexisted with a classic component no benefits were gained from treatment(15).

Photocoagulation may be reasonably considered in cases of well-defined, symptomatic, occult neovascular lesions with no classic component, in order to reduce the risk of membrane growth towards the fovea.

However, little knowledge exists of the natural progression of these occult membranes and it would not be wrong to delay treatment while examining patients at regular intervals (of months, albeit varying according to the type of membrane), in order to wait for the appearance of a classic membrane that would benefit from laser photocoagulation treatment.

Only 25% of occult choroidal membranes maintained baseline VA values after 3 years and approximately 50% suffer severe loss of vision within the same time period[(13)].

Other laser photocoagulation studies

In a retrospective study, Soubrane et al.[(18)] demonstrated the absence of benefits for the treatment of extrafoveal and juxtafoveal occult neovascular lesions.

Scatter or grid photocoagulation revealed to be ineffective in ill-defined neovascular lesions[(18)].

In an attempt to preserve the foveal centre, Coscas et al[(19)] described a form of ring treatment for subfoveal membranes.

This randomized, placebo-controlled study included eyes with VA 20/200–20/1000.

Treatment surrounded the 400 central µ of the central avascular area.

After one year, baseline VA has been maintained or increased in 41% of treated eyes and only 20% of non-treated eyes.

This technique was not well received. Several groups determined the efficacy of laser photocoagulation in eyes with AMD and PED.

In MPS studies, cases with PED were excluded. The Moorfields Macular Study Group(17) showed that grid laser photocoagulation of “pure” PED (with no clinical or angiographic signs of choroidal membrane) had worsened prognosis in terms of VA.

With the advent of indocyanine green (ICG) angiography, enhanced imaging of occult CNV allowed a characterization of at least 2 forms of occult CNV: a plaque of late staining and a focal area of active vessel proliferation or a so-called “hot spot”[(22,23)].

ICG-laser photocoagulation was used in several centers[(23-28)], in uncontrolled studies, to treat these hot spots with apparently relative success.

Polypoidal choroidal vasculopathy (PCV) and retinal angiomatous proliferation (RAP), two AMD sub-types, represented the great majority of these treated cases.

Laser photocoagulation in RAP lesions have shown very poor results with a high rate of persistence and recurrences[(29-30)].

Better results may be obtained in early lesions with extrafoveal hot spot resulting in stabilization of the pathology and visual acuity.

However, an accurate follow-up is mandatory after the treatment due to the high rate of recurrences.

Direct laser photocoagulation of polypoidal lesions has shown controversial results[31-34]
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Treatment of leaking polyps has proven short-term safety and efficacy for extrafoveal lesions[31-32].

Yuzawa et al[33] reported good efficacy of laser photocoagulation in near 90% of the eyes if all the polyps and abnormal vascular network were treated.

If the treatment involved only the polyps more than half of the eyes suffered VA decrease related with exudation, recurrences, or foveal scars.

Considering the possibility of using other treatment modalities, laser photocoagulation should be reserved for well defined extrafoveal active polyps.

Conclusion

Laser photocoagulation remains currently indicated for the treatment of well-defined extrafoveal choroidal membranes.

For classic juxtafoveal membranes, laser photocoagulation could theoretically be considered as an option for cases in which the entire neovascular lesion can be treated without damaging the fovea.

However, considering the great incidence of persistence and recurrences, intravitreal antiangiogenic agents are the first treatment option.

Photodynamic therapy with verteporfin and antiangiogenic agents eliminated all indications for the treatment of subfoveal neovascular lesions, with laser photocoagulation.

>> References

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