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Magnification requirement after photodynamic therapy with verteporfin for subfoveal predominantly classic choroidal neovascularization due to age-related macular degeneration

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PURPOSE. *To prospectively assess the magnification requirement after repeat photodynamic therapy (PDT) with verteporfin in patients with predominantly classic subfoveal choroidal neovascularization (CNV) due to age-related macular degeneration (AMD).*
METHODS. *A total of 103 patients were treated for the first time with PDT between November 1999 and September 2002. These patients were followed up at 3-month intervals for a minimum of 12 months. In addition to the usual investigations undertaken during PDT therapy, the magnification requirement was determined, under standardized conditions, using the SZB test developed by the Swiss Central Association for Blindness.*
RESULTS. *A stable lesion with a stable magnification requirement was achieved in 86 (83.5%) patients; these patients were followed up for 24.8 months (range 12 to 36 months). At the time of the last follow-up examination, the magnification requirement compared with baseline was <3 log units higher in 46 patients (53.5%) and ≥3 log units higher in the remaining 40 patients (46.5%). Seventy-four (86%) of these 86 patients had a magnification requirement of ≤8x. Stability was not achieved in 17 (16.5%) patients; up to the last examination these patients had been followed up for 12 to 30 months (mean 20.8). At the time of the most recent examination, 7 (41.2%) patients had a higher magnification requirement of <3 log units while 10 (58.8%) had changed by ≥3 log units. Sixteen patients (94%) had a magnification requirement of ≤8x.*
CONCLUSIONS. *PDT with verteporfin helps achieve stability without severe impairment in reading ability in most patients with predominantly classic subfoveal CNV due to AMD. (Eur J Ophthalmol 2005; 15: 768-73)*

KEY WORDS. *Age-related macular degeneration, Magnification requirement, Near vision, Photodynamic therapy, Verteporfin*

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INTRODUCTION

Age-related macular degeneration (ARMD) leads to an irreversible loss of vision in up to 28% of individuals over 75 years of age (1). Reading is still possible, despite considerable visual impairment, provided that patients have the appropriate vision aids. Depending on the magnification requirement, however, reading becomes increasingly more difficult and is often limited. Several authors have pointed out that even limited vision may contribute to the

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quality of life and independence of ARMD patients (2, 3). Since the introduction of photodynamic therapy (PDT) with verteporfin for choroidal neovascularization (CNV) in ARMD, there have been several reports of sustained positive results in terms of visual acuity and contrast sensitivity (4-7). We prospectively assessed the change in the magnification requirement as an indirect evaluation of near vision, and thus visual impairment when reading, after repeat PDT for predominantly classic subfoveal CNV in ARMD.

PATIENTS AND METHODS

A total of 138 patients with predominantly classic subfoveal CNV due to ARMD were treated with repeat PDT using verteporfin between November 1999 and September 2002 and prospectively followed up every 3 months. The diagnosis and indications for further therapy were based on clinical examination and stereofluorescence angiography. Patients with previous radiotherapy or laser therapy were excluded from this analysis from the outset. The data of 122 patients with at least 12 months follow-up and unilateral therapy were available for assessment. Of these, 7 patients who died prematurely and 6 who did not attend for follow-up because of health or geographical reasons (living abroad) were not included, as well as 4 patients who discontinued the treatment prematurely. The data of a further two patients who, at the time of the data assessment, were to undergo a cataract operation because of increasing lens opacity were also excluded. A definitive assessment was thus undertaken in 103 patients.

Visual acuity at baseline, determined with logarithmically subdivided Snellen charts at a distance of 5 m, had to be between 20/200 and 20/30. At the time of each examination, the magnification requirement was determined using the SZB test (developed by the Swiss Central Association for Blindness), which is comparable to the well known Sloan test charts and Zeiss reading charts (8). The magnification requirement indicates by how much newspaper text in print of the usual size (8 point size) has to be magnified in order to be read at a distance of 25 cm. The individual sections of the SZB charts, each with four lines of text, were given to the patient to read at a distance of 25 cm, while the patient was wearing his or her best possible correction of near vision. Care was taken to ensure maximum lighting of the charts with a standardized source of light. Each section of text is 1.2589 times larger in size with respect to the previous one, with 16 gradations between 0.6x to 20x. The smallest gradations, 0.6x and 0.8x, are termed the magnification reserve. The patient ideally begins to read the largest writing and continues to read progressively smaller sizes until reaching a size of writing where hesitation starts. On return to the section of text with the next largest magnification, the reading should again be fluent. For each section, the number of diopters (D) of the necessary addition for reading at 25 cm is indicated. As an example, a magnification requirement of 8x means that 32 D are needed in order to be able to read the standard newspaper text at 25 cm.

We classified the worsening of the magnification requirement as <3 log units or ≥3 log units, as was done in the TAP analyses (4, 5, 7), because of the logarithmic progression of the text sections in the SZB chart. In addition, the magnification requirement was grouped into four theoretical grades in order to illustrate the potential need for an optical vision aid and to take into account the patient's difficulty in reading that accompanies the requirement for increasing magnification: Grade 1, magnification requirement ≤1x, reading with normal reading glasses or more powerful glasses of up to 4 D; Grade 2, magnification requirement 1.25x to 3.2x, magnifying glasses or stronger magnifying spectacles of up to 12 D; Grade 3, magnification requirement 4x to 8x, free-standing/hand-held magnifying glasses of up to 32 D and start of electronic vision aids; Grade 4, magnification requirement >8x, mostly electronic vision aids. Although limited spot reading is still possible with a magnification requirement of 10x and above, especially the elderly with central scotoma and ARMD do not achieve satisfactory reading for a continuous length of time despite greater magnification of visual aids.

PDT with verteporfin was performed in accordance with the guidelines of the TAP and VIP studies (4, 9). Prior to each treatment, fully informed written consent was obtained from the patients. The treatment was considered as complete in the case of documented stability over a period of at least 6 months, that is, the lesion had a flat, scar-like appearance with minimal fluorescein leakage (less than 50% of the area treated at the previous visit could be covered with leakage), no leakage beyond the margins of the treated area, and leakage does not involve the fovea on at least two successive stereofluorescence angiographies. Further, the magnification requirement values had to be stable without any trend towards worsening. Treatment was also stopped if the magnification re-

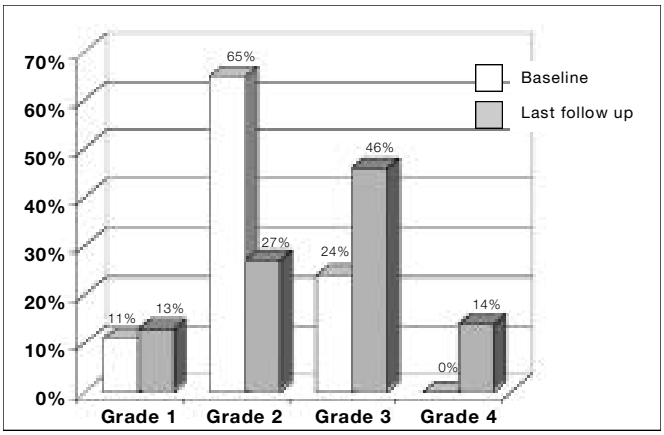

Fig. 1 - *Magnification requirement in patients who have completed treatment (n=86).*

quirement was more than 8x on two successive follow-up examinations and an improvement could not be expected through further PDT.

Changes in the values of the magnification requirement between the baseline (pretreatment) and the different follow-up examinations were evaluated by descriptive statistics and graphic displays of the number (percentage) of patients in the different grades of magnification requirement.

RESULTS

A total of 103 patients, 55 male and 48 female, were followed up consistently for at least 12 months or treated until stability had been achieved. Stability was achieved in 86 patients (83.5%), 44 male and 42 female, after a mean follow-up period of 24.8 months (range 12 to 36 months). The mean age of these patients was 78.3 years, and the mean length of their history until the first PDT was 11.4 weeks. Forty-five individuals (52.3%) had CNV in the first eye and 41 individuals (47.7%) had CNV in the second eye. In the latter patients, in the first eye, active untreatable CNV, subretinal fibrosis, or advanced atrophy were found to have taken their spontaneous course or there was scarring following conventional photocoagulation. Although Snellen visual acuity was assessed during every visit, it was not evaluated in detail, as has already been reported previously, because of a lack of accuracy of these test charts in the critical range below 20/100 (10).

In all 103 patients, the magnification requirement was <8x at baseline. The mean baseline magnification requirement was 2.5x (0.8x to 8x) in the 86 patients who had achieved stability. At the last follow-up examination, 46 patients (53.5%) showed worsening of the magnification requirement of <3 log units; 20 (23%) of these patients had an improvement of 1 or more log units. The other 40 (46.5%) patients had worsening of ≥3 log units (Tab. I); 20 (23%) of these patients had a deterioration of 6 or more log units. At baseline (pretreatment), 65 (76%) of the patients had a magnification requirement of ≤3.2x (Grades 1 and 2) compared with 34 (40%) at the time of the last follow-up examination (Fig. 1). At the last follow-up, 12 (14%) patients had passed into a profound low vision range with a magnification requirement of >8x (Grade 4, Fig. 1) while the other 74 (86%) had a magnification requirement of ≤8x (Grades 1, 2, 3; Fig. 1). The mean baseline size of the CNV (>50% classic with/without an occult portion) was 2778 µm (range 769 µm to 5420 µm); this had increased by a mean of 990 µm at the completion of treatment. A mean of 5 (range 1 to 11) PDT sessions were performed. Seventeen (16.5%) of our 103 patients failed to achieve stability during their still ongoing follow-up lasting an average of 20.8 months (range 12 to 30 months). These patients had a mean age of 72 years at the start of treatment and the mean length of their history up to the first PDT was 11.4 weeks. Twelve (70.6%) of these patients had CNV requiring treatment in the first eye and 5 (29.4%) patients had it in the second eye. The mean baseline magnification requirement was 1.6x (range 0.8x to 3.2x). Up to the most recent assessment, 7 patients (41.2%) had a worsening in the magnification requirement of <3 log units while the other 10 patients (58.8%) had a worsening of ≥3 log units; 5 (29.4%) patients in the latter group had a worsening of ≥6 log units. None of these 17 patients had so far shown an improvement in the magnification requirement (Tab. I).

At baseline, all 17 patients had a magnification requirement of ≤3.2x compared with 8 (47%) at the completion of treatment. One patient (6%) passed into a profound low vision range with a magnification requirement of >8x while the other 16 (94%) had a magnification requirement of ≤8x (Grade 4) (Fig. 2). The mean baseline size of the CNV was 2263 µm (range 1153 to 3100 µm); this had increased by a mean of 1208 µm up to the most recent follow-up assessment. A mean of six PDT sessions were necessary (range 2 to 10).

The magnification requirement in all 13 patients who died prematurely or no longer attended follow-up appointments had changed by <3 log units. In the other 4 pa-

tients, who had discontinued treatment, the magnification requirement worsened by >3 log units; one of these had a magnification requirement of >8x.

DISCUSSION

In this prospective and uncontrolled series, we chose the assessment of the magnification requirement as the basis for evaluating the efficacy of repeat PDT with verteporfin in the treatment of predominantly classic subfoveal CNV due to ARMD.

The idea of assessing the magnification requirement as an indicator of reading vision in patients with markedly subnormal vision is not new (11). Further, as we did not assess visual acuity using ETDRS charts but with Snellen charts at a distance of 5 meters, there is a great danger of underestimating visual acuity in the region below 20/100 (12).

Quantification of reading speed is not part of the assessment of the magnification requirement. The examiner can, however, qualitatively assess the reading speed because the patient has to fluently read aloud the relevant text. It is thus comparable to the reading index used by McLure et al to evaluate the daily living tasks dependent on vision in patients with ARMD (2).

We reported in a previous study (10) that magnification requirement was stable in patients with predominantly classic CNV secondary to ARMD who were treated with PDT and followed up for 12 months.

In general, our results for the change in the magnification requirement are comparable to those of the change in visual acuity in the TAP study where patients with predominantly classic subfoveal CNV in ARMD had lost, on average, 2.4 lines after 24 months (5).

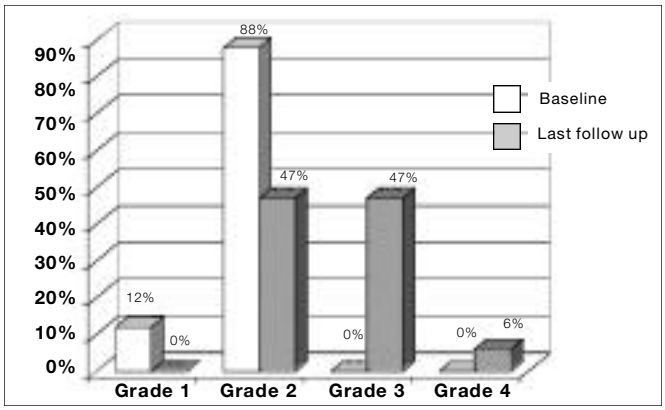

Fig. 2 - *Magnification requirement in the patients who are yet to complete treatment (n=17).*

For comparison, we observed a worsening in the magnification requirement of a mean of 2.2 log units over a mean observation period of 24.8 months in patients in whom PDT was completed (Tab. I). In the TAP study, contrast sensitivity remained stable in the verteporfin group while it decreased by a mean of 2 lines in the placebo group (5, 6).

Of our 86 patients who had achieved stability, at the time of the final follow-up examination, 46 (53.5%) patients were found to have a worsening in the magnification requirement of <3 log units compared with 7 (41.2%) of the 17 patients who had still not achieved stability during the observation period.

Although the follow-up period of 20.8 months in the latter group was 4 months shorter than in the group with stability, on average, this group had one more PDT session (six versus five). In this still unstable group, the pa-

TABLE I - CHANGES IN MAGNIFICATION REQUIREMENT (MR) IN THE COMPLETED AND YET TO BE COMPLETED PATIENTS

Change in MR	**PDT completed n = 86**	**Under PDT n = 17**
≥ 6-log levels increase	4 (4.6%)	0
≥ 3 to < 6-log levels increase	2 (2.3%)	0
≥ 1 to < 3-log levels increase	14 (16.3%)	0
No change	7 (8.1%)	2 (11.8 %)
≥ 1 to < 3-log levels decrease	19 (22.1%)	5 (29.4 %)
≥ 3 to < 6-log levels decrease	20 (23.2%)	5 (29.4 %)
≥ 6-log levels decrease	20 (23.2%)	5 (29.4 %)
Mean loss	-2.2 log levels	-3.6 log

PDT = Photodynamic therapy

tients were on average 6 years younger, their magnification requirement was 2 log units better at the beginning, and they had a CNV lesion size that was on average 515 µm smaller than patients with stability. However, due to the nature of our analyses, it is not clear how these clinical features contributed to the observed differences between the two groups in their response to PDT with verteporfin.

Similar results were also seen in the TAP study; patients with better initial vision experienced a more marked decline in vision (5). However, Axer-Siegel et al (13) recently reported the opposite results: smaller membrane sizes and a better initial vision led to better vision results after PDT with verteporfin and vice versa.

Overall, a simple grading of the magnification requirement into a change of 3 or 6 log units tells us little about what this actually means for the patient since reading becomes more difficult with each subsequent higher magnification. Occasional reading of bank statements, price tags, et cetera is possible with a magnification requirement of 6x using simple vision aids. However, longer periods of reading become more difficult with higher magnification requirements such as >8x because of increasing instability of the image and smaller reading distance.

Although simple systems such as magnifying glasses can be used, electronic vision devices with a higher linear magnification are often required to achieve the best results (7, 14-18).

These considerations led us to group magnification requirements into the four grades described in Patients and Methods where we assessed a magnification requirement of >8x as considerable impairment since reading with the appropriate magnification in this group is so slow that many patients prefer to use audio books.

Twelve (14%) patients who completed treatment belonged to this group (Fig. 1) compared with one patient (6%) in the not yet stable group (Fig. 2).

Thirty-six (88%) out of a total of 41 patients with CNV in the second eye and no useful vision (magnification requirement higher than 16 to 20x) in the first eye because of macular scarring (due to CNV progression or conventional laser therapy) used this second, PDT-treated eye for reading.

Overall, our results are in contrast to a recently published study, according to which PDT in the second eye is not cost-effective when baseline visual acuity is 20/200 and moderately cost-effective when baseline visual acuity is better than 20/200 (19). The authors reached this conclusion using a theoretical calculation that took into account the treatment effect in the TAP study and its benefit in terms of quality-adjusted life-years (QALYs) for patients who could potentially be treated. We believe that a patient's quality of life cannot be analyzed simply on the basis of theoretical numerical calculations.

We can be criticized for not taking into account reading speed as a study parameter. This factor is important because of the possibility of quantifying it, especially in controlled studies comparing the effect of different therapeutic measures (20-22). However, this method is too time-consuming for routine use in busy eye clinics and, in any case, the SZB test gives a qualitative assessment of the reading speed. It has been reported that reading performance is strongly associated with subjective quality of life and that central visual field loss adversely affects reading (23). Thus, central visual fields may be a more sensitive measurement of visual function than visual acuity; verteporfin PDT has been shown to have a significant beneficial effect for the preservation of central visual field in patients with ARMD (24).

CONCLUSIONS

In our analyses of patients with predominantly classic subfoveal CNV due to ARMD, the magnification requirement increased over an observation period of 12 to 36 months following repeat PDT with verteporfin. However, the magnification requirement remained ≤8x in most patients; this allows, with appropriate vision aids, reading for relatively long periods of time and is of great importance for coping with everyday life. Along with PDT that has to be consistently repeated until the lesions are stable, appropriate low vision training is essential in order to derive maximal benefit from this therapy (25).

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