

Original Article

The Long-Term Results of One Time Treatment by Continuously Fractionated Transpupillary Thermotherapy for Occult Choroid Neovascularization Membrane of Age-Related Macular Degeneration

Background. This study was to assess the long-term results of a novel continuously fractionated transpupillary thermotherapy (cfTTT) in treating occult choroid neovascularization membrane (CNV) of age-related macular degeneration (ARMD).

Methods. After informed consent was obtained, 19 patients were treated with cfTTT in 21 eyes. The diode laser (810 nm) was applied with 6 continuous 9-second sessions to the neovascular membrane. Each session lasted 9 seconds. Every spot (1 mm on retina) was in close contact with each other to entirely cover the CNV.

Results. The average age was 75.9 years (from 61 to 86 years). The mean follow-up time was 19.6 months (from 15 to 24 months). Five eyes (23.8%) had improved visual acuity by 2 or more lines, 6 eyes (28.5%) by 1 line, and 10 eyes (47.6%) had no change in visual acuity. None had decreased vision. In final fluorescein angiography, all eyes treated revealed decreased fluorescein leakage.

Conclusions. cfTTT shows no deleterious side effects in treating subfoveal or juxtafoveal CNV of ARMD at long-term follow-up and is at least as effective as long-pulse TTT.

Keywords: choroidal neovascularization; continuously fractionated transpupillary thermotherapy; macular degeneration; laser

A
gelated macular degeneration (ARMD) is the leading cause of central vision loss in patients older than 50 years of age in most developed countries. The majority of eyes suffer severe visual loss as a result of choroidal neovascularization (CNV). Studies have shown that 41% to 60% of patients with occult CNV suffered a loss of at least 3 lines or more of vision over a 6-12 month period. CNV is the formation of abnormal new blood vessels either between retinal pigment epithelium and Bruch’s membrane or in the subretinal space. Occult CNV has been defined on an angiographic basis as either fibrovascular retinal pigment epithelial leakage or in the subretinal space. The diode laser (810 nm) is mainly absorbed by the melanin of retinal pigment epithelium and choroid, has many advantages such as minimal nerve fiber layer damage, low absorption by xanthophyll, and enabling effective treatment of choroidal lesions. Complications include retinal pigment epithelial leakage, new onset of classic CNV after TTT, and subretinal choroidal neovascularization.

There has been no universal protocol of TTT yet. Neither was there solid evidence to support the present long-pulse protocol. In order to lower the possible side effects of TTT by prolonging laser exposure, to achieve therapeutic results, we develop a novel way of delivering TTT laser, and to achieve a lower and potentially safer retinal temperature elevation than the
long-pulse TTT.

We aim to assess the long-term efficacy of cfTTT for the treatment of occult CNV of ARMD, whether it is as effective as the long-pulse mode TTT, and to evaluate its side effects.

METHODS

A prospective, consecutive, nonrandomized clinical study was conducted from July 2000 to June 2002. One retinal specialist treated all patients recruited in this study. All the patients were 60 years of age or older and had symptoms of visual loss or metamorphopsia in the past 6 months. The vision criteria for the study were from 6/12 to 1/60, best corrected. All the patients were diagnosed as having ARMD with occult subfoveal or juxtafoveal CNV through slit-lamp biomicroscopy with a precorneal lens, in direct ophthalmoscopy and fluorescein angiography. Patients were excluded if they had prior laser photocoagulation, vitreous operation, or ocular diseases associated with choroidal neovascularization such as high myopia, angiod streaks, intraocular tumors, intraocular inflammation, hereditary maculopathies or trauma history.

The patients underwent a general ophthalmologic examination at the baseline visit and at all the follow-up visits, including measurement of Snellen visual acuity, anterior segment examination, IOP measurement, pupillary dilatation with 1% tropicamide, and evaluation of macula by means of slit-lamp biomicroscopy using a 90-diopter lens (Volk Optical, Mentor, OH, USA), fluorescein angiography (10% sodium fluorescein, 5 mL) and color fundus photography (Topcon, Tokyo, Japan). All the patients were followed at the 4th weeks, the 3rd months and around every 3 months, up to the 24th month after cfTTT.

Topical 0.5% proparacaine was applied before placement of a contact lens (SuperQuad, Volk, USA, magnification 0.5x). cfTTT was delivered through a slit-lamp using an infrared diode laser at 810 nm (Iris Medical Oculight SLx, Iridex Corporation, Mountain View, CA, USA). The application of cfTTT was done within one week of fluorescein angiography. All the patients received cfTTT once in the whole course. The shot of cfTTT was delivered in a novel way having 6 continuous sessions. With each session lasting 9 seconds, totaling 54 seconds of laser was applied. The lesion was treated with multiple laser spots. Laser beam diameter on the retina was 1.0 mm. Ev ery effort was made to place every laser spot in close contact with each other with minimal overlap to ensure cover the CNV. The laser power was set at 250 mW in the beginning and was adjusted stepwise up or down in 60 mW increments, according to the results of test shot in the mid-peripheral area, creating no visible change or a barely detectable light gray appearance in the irradiated area. Continuous observation through slit-lamp ensured fixation. Generally, the treatment area was confined to the observed limits of the hyperfluorescent lesion on the angiography. There was no extension of the laser exposure out of the CNV lesion. The fluorescein angiograms before and after cfTTT were digitized and the fluorescein leakage areas were counted accordingly.

RESULTS

There were 21 eyes of 19 patients enrolled in the study, including 17 men and 2 women. The average age was 75.9 ± 5.6 years (from 61 to 86 years). The initial best-corrected Snellen visual acuity ranged between 6/12 and 1/60. Of these occult CNV membranes, 3 eyes were juxtafoveal, and 18 eyes were subfoveal. The average size of the occult membranes was 3.06 disc area (DA; from 0.124 DA to 6.36 DA). The average laser power used was 270 ± 62 mW (from 190 to 430 mW). The average number of the spot applied was 4.2 spots. The average follow-up period was 19.6 ± 1.7 months (from 15 to 24 months).

At the end of the study, 5 eyes (23.8%) experienced visual acuity improvement by 2 lines or more, 6 eyes (28.5%) by 1 line, and 10 eyes (47.6%) had no change in visual acuity. None developed visual worsening (Table 1). The pre-treatment logMAR value was 1.1 (logMAR = log 1/VA); the post-treatment logMAR value was 0.8. (paired t-test, p = 0.014).

In final FAG, all eyes revealed decreased fluorescein leak age. (Fig. 1) The average age per cent age of the final decrease of fluorescein leak age was 58.1%.
DISCUSSION

Bressler et al.\(^4\) and Stevens et al.\(^5\) demonstrated that 60% of patients with occult CNV suffered a loss of three or more lines of vision over a 6-month period. The macular photocoagulation study established that 41% of eyes with occult CNV had a decrease in visual acuity of 6 or more lines within 12 months of follow-up.\(^6\) It is thus beneficial to intervene the natural course of occult CNV.

TTT differs from traditional retinal photocoagulation...
be cause it uses lengthy ex po sures and large ret i nal spot size to produce lower ther apeu tic ret inal ir radia nce.2,3
TTT uses in fra red ra di a tion that has deeper chorioret i nal tis sue penetration than vis i ble light, and has the ad vantages such as decreased photoreceptor pig ment bleach ing, less potent ial Henle fiber optic transmission, and less neg li gi ble risk of ret i nal phototoxicity than blue or green la ser sources.7
TTT has been ex per i men tally em ployed for the treat ment of chori oreti nal mel a no mas,7 but it is not well known how the di ode la ser pro du ces a closer sure of CNV. It has been pro posed that the clo sure is a con se quence of the in flam ma to r y pro cess sub se quent to the ener gy ab sorp tion by melanin and con nective tis sues present in the mem brane,2 throm bosis of ves sels, CNV apo to sis or de creased an giogenic fac tor from pro lif er a tion cells af ter TTT.15-13
Cain et al.14 re por ted that chorioret i nal tem per a ture in duced by la ser was as cen to or de scend from the peak with in a few ten ths of a sec ond when a la ser pulse is turned on or turned off re spectively.3,14,15 When ap ply ing cfTTT, we shot suc cess i ve la ser ses sions with instant in terrup tion by trea dle; so it still takes several ten ths of a sec ond to ig nite suc cess i ve la ser shot. Such a short break may prob a bly re sult in a lower, flat ter and possibly safer re tinal tem pera ture ele va tion than the long-pulse TTT.
In Isola et al.16 study of di ode la ser re tin op e xy treat ment of chorioretinal le sions pro du ces a closer sure in eyes with dark brown irises and more pig ment en ded fundi to yield a suit able burn was 325 mW; in eyes with blue-green irises and slight ly pig ment en ded fundi, the ses ions were in duced by higher power (mean 471 mW). The ob servation ex plains the dif fer ence in the lower power set ting in the Ori ental. Since the Ori ental has denser ret i nal pig men ta tion, the la ser power set ting can not be de ter mined by the for mul a only. The pre tests on the mid-periph eral re tina be fore ap ply ing la ser onto fovea pro vide in va lue able in for ma tion in the power set ting.
Max i mal chorioret i nal tem per a ture rises in TTT oc curs on the in ner sur face of the RPE and in the cen ter of the la ser spot. Less in ten se pe riph eral la ser power may re veal lower nor mal tis sue dam age in the choroidal level. Larger di a meter of the ir ra di a tion beam may in crease the pen etration of heat into the tar get tis sue and de crease the dis si pation of heat to the sur round ing tis sues. Dis si pation of heat by con duct ion to the sur round ing tis sues occurs more effec tively in beams with a relatively smaller diam et er.14-19
Com pared with the long-pulse TTT, in which 2 mm or 3 mm spot is usu ally ap plied, we in stead used smaller spots (1 mm on ret ina) not ex tend ing out of the CNV le sion. It has the ad va n tage of bet ter con trol to the of ten ir regu lar con tour of patho logical choroidal neovas cu lar lesion and de stroy ing less the adja cent nor mal cho rioretina.7 Mean while, a smaller spot bears the ad va n tage of faster heat dis si pa tion than larger ones.2,14-19
In the ex per i men tal study of large spot, long-pulse method to treat oc cult CNV of ARMD, Reichel et al.4 fol lowed 16 eyes of 15 patients for 13 months to find that 3 eyes (19%) ex per i en ced a more than 2 lines im provement, nine eyes (56%) had sta bil i za tion of vi sion (± 1 line), and 4 eyes (25%) showed a sig nif i cant de crease (> 2 lines). Newsom et al.3 showed sim i lar re sults in treat ing oc cult CNV. Four of 32 eyes (12.5%) had a more than 2 lines im provement, 19 eyes (59.4%) had sta bil i za tion of vi sion (± 1 line), and 9 eyes (28.5%) showed a sig nif i cant de crease (> 2 lines) in 7.2 months of fol low-up.
Our find ings showed that 23.8% ex per i en ced a more than 2 lines im provement, 76.2% had sta bil i za tion of vi sion (in crea sing 1 line or no change), and none of them showed a loss more than 1 line.
As for exudates of occult CNV, Reichel et al.4 re ported 15 of 16 eyes (94%) with de creased exu da tes. Newsom et al.3 re vealed 25 of 32 eyes (78%) with de creased exud a tes, 4 eyes (12.5%) in per sist ent state, and 1 eye (5.1%) was re cur rent in 7.2 months of fol low-up. In our study, all eyes (100%) showed de creased leak age in the fi nal FAG.
Com pli ca tions re ported in the treat ment of chori oret i nal neovas cu larization af ter TTT in clude ret i nal pig men t ep i the li um tear, new on set of clas sic CNV, and sub retinal chori oret i nal neovas cu larization.8,10
In our study, we did not ex per i ence any of the above com pli ca tions af ter treat ment of CNV. One eye re vealed re tinal hy perpig me tation over la ser area in 2 months,
but visual acuity was not affected.

The eTNTT shows no deleterious adverse effects in treating occult choroidal neovascularization of ARMD in the long-term follow-up. The result is better than the natural course of ocular CNV, and is at least as effective as the long-pulse TT.

REFERENCES


