

Indocyanine Green (ICG) enhanced trans pupillary thermo therapy (TTT) as a preferred choice to standard TTT.

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Purpose: To compare the efficacy of Indocyanine Green (ICG) enhanced trans pupillary thermo therapy (TTT) to standard TTT for sub foveal Choroidal neovascular membrane (Ocult and Classic).

Methods: A prospective randomized controlled study (54 eyes) with sub foveal choroidal neovascular membrane underwent 810nm diode laser TTT. Group A (25 eyes) with ICG enhancement and Group B (29 eyes) without enhancement. Visual acuity, FFA and OCT were evaluated preoperatively and followed post operatively over 9 months.

Results: Visual acuity improved by 84 % in Group A and 34.48% in Group B. Lesion regressed in 92% (Group A), 65.51% in Group B.

Characteristic features of age related macular degeneration (AMD) include visual acuity loss due to atrophy or exudation, haemorrhage caused by choroidal neovascularisation

(CNV), and subretinal fibrous tissue formation. Although considerable and reliable information exists on the efficacy of subfoveal CNV photocoagulation, ophthalmologists

have abandoned such treatment for subfoveal lesions because it damages viable photoreceptors overlying the treated lesion; instead, they utilise other alternatives that tend to spare the retina, such as photodynamic therapy (PDT) with verteporfin, a treatment that involves intravenous injection of a photosensitiser that accumulates in neovascular tissue. This photosensitised tissue is then irradiated by light at the absorption maximum of the dye leading to cytotoxicity and selective effects on the choroid and neovascular tissues. Unfortunately, verteporfin PDT is not affordable for many

patients with a potential indication. For this reason, new equally effective and less expensive photosensitisers for CNV management in patients with AMD are under investigation. Indocyanine green (ICG), an anionic tricarboyanine, is a relatively large, protein bound, photosensitive molecule

with selective intravascular retention that is characterised by low skin phototoxicity, high tissue targetability, rapid biodistribution and clearance, as well as easy administration and

monitoring. Its peak absorption (805 nm) is close to peak emission (810 nm) of the conventional diode laser typically used in commercial near infrared wavelength photocoagulators. It thus offers the advantage of deeper tissue penetration. In TTT (Trans Pupillary Thermo therapy) the 810 nm Diode laser is used to destroy the CNVM, but the collateral surrounding tissue damage is very significant. We report the use of this ICG enhanced TTT (Group -1), where the energy required is significantly lower to standard TTT (Group -2).

PATIENTS AND METHODS

This was a prospective, comparative interventional case series. 54 eyes aged between 36 and 87 years with central vision loss resulting from subfoveal CNV (Classical or Occult) due to AMD, high myopia or idiopathic were enrolled in the study. 25 eyes (Group -1) underwent ICG enhanced TTT, while 29 eyes underwent standard TTT. Before treatment, patients were informed about the possible side effects and written informed consent was obtained. Patients underwent complete ocular examinations including medical histories, visual acuity testing, color fundus photography, fluorescein as well as

optical coherence tomography (OCT). Fundus camera (/IMAGEnet, Topcon, Tokyo, Japan). The angiographic studies were performed with sodium fluorescein 20% in 3.0 ml.

Pretreatment examinations, considered as baseline for those included in the study, were completed within 7 days before treatment. The fluorescein angiography inclusion criteria was subfoveal predominantly classic CNV or Occult as defined in the TAP study. Follow up examinations included the same evaluations as baseline and were scheduled 1 week after the initial treatment session as well as at 12 week intervals up to completion of a 9 months follow up period. For this study purposes, outcomes measurements—that is, visual acuity and morphological changes from baseline, were performed at

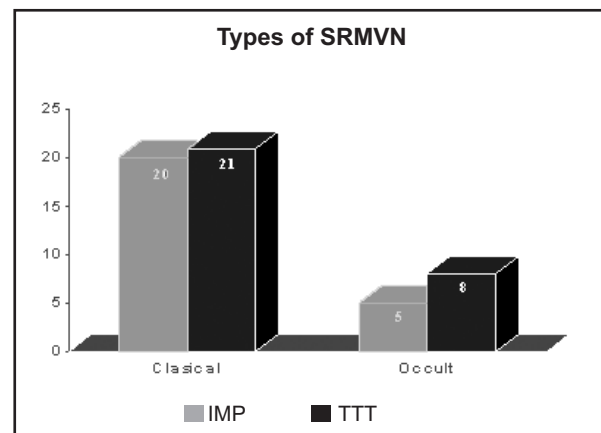
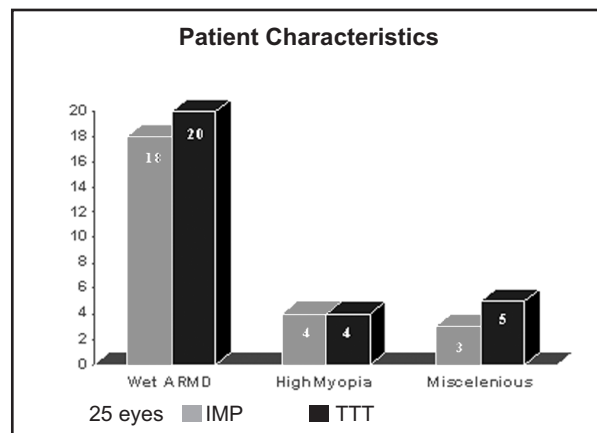
1 week, 12 (2) weeks and 36 weeks after treatment. For the procedure, ICG dye in dehydrated powder form was reconstituted into solution form using sterile distilled

water

10 minutes before laser application. Light protected status was maintained at all times during the procedure to prevent inadvertent dye activation. The laser delivery system consisted of a modified infrared diode laser and a slit lamp biomicroscope. A diode laser

(Trimode-L, Opto, Saˆo Carlos, Brazil)10 tuned to 810 nm, near the maximum absorption peak of ICG, was fitted with an adjustable beam width (settings at 0.8, 1.0, 1.2, 1.5, 2.5, and 4.3 mm) and coupled to a slit lamp biomicroscope. Before any light application, a fundus contact lens of 1.56 magnification (Mainster widefield, Ocular Instruments, Bellevue, USA) was placed on the cornea. All patients were submitted to one sessions of

i-MP. The patients underwent treatment with a total dose of 2 mg/kg of ICG solution. For the procedure, a loading dose of a highly concentrated solution of ICG (25 mg/ml (approximately 1 mg/kg body weight)) was administered as an intravenous bolus, followed immediately by a 5.0 ml



RESULTS

In all cases (Group -1 & 2), there was no apparent colour change in the treated area during or immediately after treatment, suggesting that there was no clinically significant thermally induced alteration. The mean energy required in Group 1 was 355 mw while it was 512 mw in Group 2, which was significantly higher in the latter group. The pretreatment best corrected visual acuity scores ranged from 6/60 to 6/18. At 9 months of follow up, 19.5% of the patients treated with ICG enhanced TTT (Group -1) showed stabilisation of visual acuity, while 56.6% showed improvement of vision. At 9 months of follow up, 72.3% of the patients treated with standard TTT (Group -2) showed stabilisation of visual acuity while only 12.2% showed improvement of vision (VA change less than two lines). No eyes had moderate

visual acuity loss (three lines). FFA stabilization was obtained in 92% of patients in Group 1, while it was 65.5% in Group 2 at 9 months post treatment. Morphological changes by OCT at last follow up visit showed significant reduction in macular thickness at 9 months follow up. Adverse events such as visual disturbances, retinal vascular occlusion, photosensitivity reactions, injection site events, and deaths were neither observed nor reported in any patients.

DISCUSSION

This study shows that i-MP using small volume infusions of high concentrated ICG solution and low irradiance, large spot 810 nm diode laser delivered by slit lamp may have a positive influence in the outcome of CNV due to AMD myopia or idiopathic. Although most patients experienced stabilisation or some improvement in visual

acuity, it was observed that that visual improvement was significantly higher in Group 1 the ICG enhanced TTT, probably as a result of lesser energy used with respect to the standard TTT, resulting in lesser collateral surrounding tissue damage. In our initial report about the use of i-MP for CNV management in AMD, a

lower-intensity light to direct laser energy continuously after IV ICG infusion is a safe and cost effective technique for rapid induction of CNV hypoperfusion and is associated with considerable improvement in visual acuity and partial restoration of the retinal architecture

Study	Type of LASER	Nos. of eyes	Stable/ Improvement in BCVA
Gustavsson etal	TTT	28	38%
Newson etal	TTT	36	70%
Rodin etal	PDT	28	85.71%
Verma etal	TTT	50	72% (3 Months)
Costa etal	iMP	5	100%
Costa etal	iMP	9	88%
	iMP	25	84%
Our Study	TTT	29	34.48%

Conclusion

Photothrombosis of the CNV ingrowth site by using

Abbreviations:

AMD : age related macular degeneration;

CNVM :choroidal neovascularisation

ICG : indocyanine green;

iMP : ICG mediated photothrombosis;

OCT : optical coherence tomography

PDT : photodynamic therapy

TTT : Trans Pupillar Thermotherapy

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