
Original Article

COMBINED TREATMENT FOR CHRONIC IRVINE-GASS SYNDROME: VISUAL AND MORPHOLOGICAL OUTCOMES

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Abstract

Aim: To evaluate the visual and morphological outcomes of combined treatment for IGS. **Methods:** A prospective study was conducted on 20 consecutive cases diagnosed as postoperative PCME between January 2022 and September 2023. The included 20 eyes underwent phacoemulsification and were classified into two groups; group (I) "STA group" treated with posterior subtenon triamcinolone acetonide and group (II) "The combined treatment group" treated with intravitreal Ranibizumab and subtenon triamcinolone acetonide in the same setting". Fundus examination, fluorescein fundus angiography and OCT evaluation were done at baseline, 2 and 4-months of follow-up. Central macular thickness (CMT) was compared preoperative and postoperative and the complications were assessed. **Results:** In the combined treatment group, the mean CMT decreased significantly from $331.5 \pm 14.1 \mu\text{m}$ at baseline to $288.1 \pm 13.9 \mu\text{m}$ at 2-months and showed much significant reduction to 246.5 ± 12.7 at 4-months post-treatment ($p < 0.01$) and the same trend of results was shown in the STA group but, the reduction was more significant in the combined treatment group as compared to STA group after 4-months post-treatment. Best-corrected visual acuity was improved to 0.5 or better in all patients of the combined treatment group at the end of the 4th month post-treatment compared to 6 cases only (60%) in the STA group ($p = 0.03$). **Conclusions:** Combined treatment for chronic Irvine-Gass syndrome may achieve better functional and morphological improvement in terms of improved vision and reduction of CMT. This effect reaches its maximum after 4-months and is associated with a decrease in leakage by FFA.

Keywords: *Irvine-Gass syndrome, Combined treatment, Triamcinolone, Bevacizumab***1. Introduction**

Irvine-Gass syndrome (IGS) "also known as Pseudophakic Cystoid Macular Edema" is one of the common complications that occurs following eye surgery and it remains a main cause of impaired vision recovery after cataract surgery. Surgical manipulations lead to the release of some inflammatory mediators such as cytokines, arachidonic acid, and vascular endothelial growth

factor (VEGF) which impair the blood-retinal barrier and promote vascular permeability [1]. There are many risk factors for PCME including; diabetes mellitus, anti-glaucoma medications, uveitis in addition to epiretinal membranes [2]. Irvine-Gass syndrome is diagnosed based on clinical findings of visual impairment and or the occurrence of dye leakage, capillary dila-

tation and retinal telangiectasis by Fundus fluorescein angiography (FFA) [2]. The cystoid changes in the maculae may be present and also the staining of the optic nerve may occur, and it characterizes PCME from other causes of macular edema such as diabetic macular edema (DME) [3]. Several treatment modalities have been used for PCME, including the use of systemic, periocular, intravitreal and topical corticosteroids, oral and topical non-steroidal anti-inflammatory agents (NSAIDs), oral and topical carbonic anhydrase inhibitor, laser photocoagulation, interferon alpha, and pars plana vitrectomy and the aim of all of these treatment options is decreasing macular edema and increasing visual acuity [3]. Triamcinolone acetonide (TA) is a synthetic glucocorticoid that has a strong long-acting anti-inflammatory and anti-VEGF effect. Many studies reported that the intravitreal injection of TA is

2. Patients and Methods

This is a prospective case-series study that included patients diagnosed with PCME. The study was conducted during the period between January 2022 and September 2023 and the procedures were done at Al-Nahar Private Eye center, Assiut City, Egypt. The study included 20 eyes of 20 patients (8 males and 12 females) diagnosed as PCME that lasted more than 2 months with central macular thickness $>250 \mu\text{m}$ by OCT without functional or anatomical improvement. These patients were classified into two groups as follow; group (I) "STA group" which included 10 patients who were treated with posterior

2.1. Procedure

2.1.1. Subtenon triamcinolone

Incision of the bulbar conjunctiva (8 mm from the limbus at the infero-temporal quadrant) was done in addition to dissection of the Tenon's capsule through the wound inferior and posterior to the globe.

economical and effective for treatment of PCME, but it has a side effect raising intraocular pressure [4]. Also, it has been reported that periocular TA "40 mg" is effective for refractory PCME treatment compared to using topical steroids and NSAIDs drops [5]. Intravitreal ranibizumab (Lucentis; Novartis International AG, Basel, Switzerland) has been used successfully to treat diabetic macular edema or the edema that occurs due to retinal vein occlusions as well as other neovascular eye diseases [6,7]. To the best of our knowledge, too little data are available about using the combined treatment "intravitreal Ranibizumab and sub-tenon triamcinolone acetonide" for treatment of IGS. So, the aim of this study is to evaluate the visual and morphological outcomes of using Triamcinolone Acetonide alone or combined with intravitreal Ranibizumab for treatment of chronic Irvine-Gass Syndrome.

sub-tenon triamcinolone acetonide and group (II) "The combined treatment group" which included 10 patients who were treated by the combined treatment "intravitreal Ranibizumab and subtenon triamcinolone acetonide in the same settings". The exclusion criteria were; diabetic and hypertensive patients, patients with media opacity (post-operative vitreous haemorrhage or vitritis) as well as patients with a history of uveitis, glaucoma, retinal atrophy, or epiretinal membranes. An informed consent was taken from each patient included in the study.

Then, injection of 1 ml of triamcinolone acetonide (40 mg/ml) by viscoelastic gauge or blunt 19 gauge infusion cannula. Then, garamycin as well as dexamethasone was injected.

2.1.2. Intravitreal ranibizumab

A dose of 0.1 mL Ranibizumab (Lucentis) solution "0.5 mg" was injected 3:3.5 mm from the limbus into the mid vitreous.

2.2. Postoperative medication, follow-up and outcome measures

All patient received nepafenac eye drops (NSAID), twice daily as a routine postoperative treatment after successful cataract surgery. However there was persistence of postoperative macular edema for 2 months without improvement. All Patients were scheduled for follow-up examinations at

2.3. Statistical analyses

Statistical analyses were performed using SPSS program (version 21) [8]. Categorical data were expressed as frequency and percent while, quantitative data were expressed as mean \pm SD. Kolmogorov-Smirnov test was used for testing the data normality. For quantetative data, independent sample t-test was used to test the

Topical antibacterial and steroid drops are provided postoperatively in both groups.

2nd day of injections to evaluate if there were any serious adverse effects like infection or IOP elevation. Then at 1st week, 2 and 4-months postoperatively. Fundus examination, fluorescein fundus angiography and OCT evaluation were done at baseline follow-ups.

significance between the two groups however, paired sample t-test was used to test the significance among pre-treatment, 2-months and 4-months post-treatment. While, for qualitative data, Chi-square test was used to test the significance between groups. Probability level (P. value) was considered non-significant if ≥ 0.05 .

3. Results

The mean age of the included patients was 56.5 ± 11.7 years (42:67 years). As found by FFA, 12 cases (60%) of the included patients had cystoid leakage while the rest of 8 cases had diffuse one leakage, fig. (1). In the combined treatment group, the mean of CMT decreased significantly from $331.5 \pm 14.1 \mu\text{m}$ at baseline to $288.1 \pm 13.9 \mu\text{m}$ at 2-months and showed much significant reduction to 246.5 ± 12.7 at 4-months post-treatment ($p < 0.01$) and the same trend of results was shown in the STA group (the mean CMT decreased from $330.3 \pm 13.2 \mu\text{m}$ at baseline to $298.3 \pm 10.3 \mu\text{m}$ at 2 months and $269.1 \pm 16.7 \mu\text{m}$ at 4-months post-treatment) but, the reduction was more significant in the combined treatment group as compared to STA group after four months post-treatment,

tab. (1) & fig. (2). Best-corrected visual acuity was improved to 0.5 or better in all patients of the combined treatment group at the end of the fourth month post-treatment, while 6 cases only (60%) in the STA group were improved to 0.5 and the rest of 4 cases did not improved more than 0.2 and this difference between groups was significant ($p = 0.03$), tab. (2) & fig. (3). Regarding complications, no rise of IOP, glaucoma or infection occurred in any case of both groups. All cases in the combined group did not need to repeat ranibizumab injection. Figures (4, 5, 6 & 7) shows macular edema changes by flurescien angiography and OCT before and after treatment

Figure 1: The percentage of fluorescein leakage.

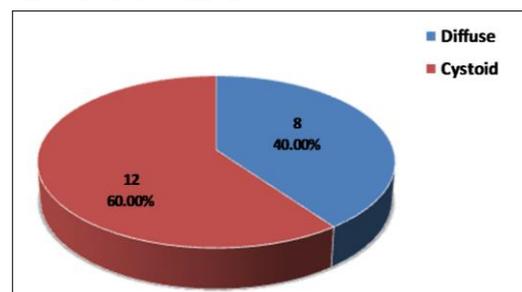


Table 1: The mean CMT (μm) during follow-up periods.

Group	Pre-treatment	2-months postoperative	4-months postoperative	p. value (Sig.) (2)
STA group (n=10)	330.3 ^a \pm 13.2	298.3 ^b \pm 10.3	269.1 ^c \pm 16.7	<0.01**
Combined treatment group (n=10)	331.5 ^a \pm 14.1	288.1 ^b \pm 13.9	246.5 ^c \pm 12.7	<0.01**
p. value (1) (Sig.)	0.85 ^{NS}	0.08 ^{NS}	<0.01**	

STA group (Subtenon Triamcinolone Acetonide); P. value (1) for the significance between groups; P. value (2) for the significance between follow-up periods; ^{a, b, c} Means in the same row with different superscript are significantly different (Paired sample t-test).

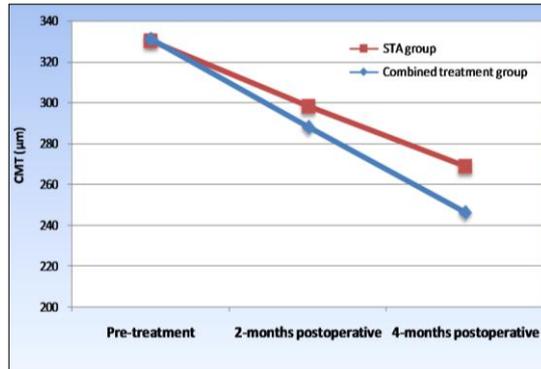


Figure 2: Changes in CMT at 2 and 4-months postoperative by OCT.

Table (2): Best-corrected visual acuity between groups after 4-months post-treatment.

Variable	STA group (n=10)	Combined treatment group (n=10)	p. value (Sig.)
Improved to 0.5	6 (60%)	10 (100%)	0.03*
Improved \leq 0.2	4 (40%)	0	

Chi-square test was used for the significance between groups; ** highly significant ($p < 0.01$)

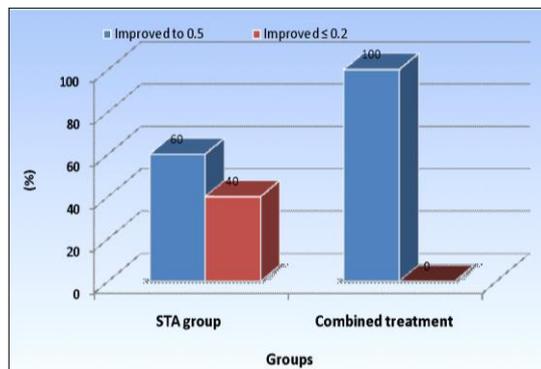


Figure 3: Best-corrected visual acuity between groups after 4-months post-treatment.

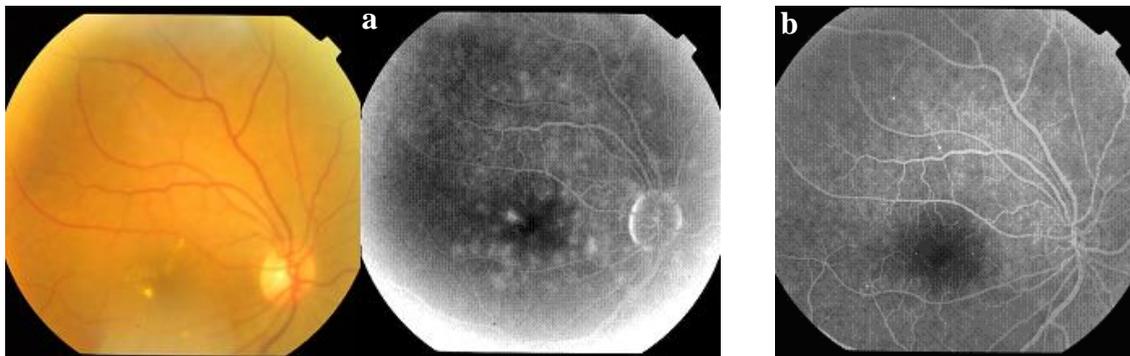


Figure 4: **a.** FFA of pseudophakic cystoid macular edema case received STA (CMT was about 340 micron), **b.** FFA after 4 month (CMT was about 255 micron).



Figure 5: FFA of pseudophakic cystoid macular edema case received combined treatment (CMT was about 320 micron).



Figure 6: Relief of cystoid macular leakage 4-months post-treatment.

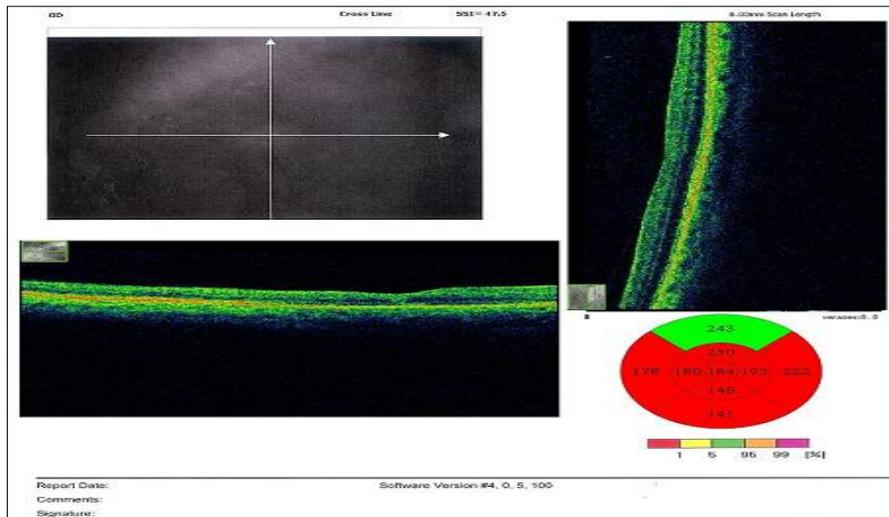


Figure 7: An OCT (4-months post-treatment) for a cases received combined treatment showing decrease macular edema, CMT of about 200 micron.

4. Discussion

Pseudophakic cystoid macular edema is the commonest cause of visual loss after cataract surgery and its occurrence was obviously declined by the advances in cataract surgery as well as the introduction of phacoemulsification, but it still remains a common morbidity [9]. Although many treatment modalities have been reported in the last 3 decades, there is still a lack of clinical trials focusing this issue. Invasive procedures including intravitreal corticosteroids, periocular steroids, and anti-VEGF are usually used and achieved significant favorable outcome. This study attempts to evaluate the visual and morphological outcomes of using Triamcinolone Acetonide alone or combined with intravitreal Ranibizumab for treatment of chronic PCME. To the best of our knowledge, too little data are available about using the combined treatment for treatment of PCME as well as the comparison between the combined treatment and mono-therapy. The present results demonstrated that there was a significant reduction in CMT in the combined treatment group from $331.5 \pm 14.1 \mu\text{m}$ at baseline to $288.1 \pm 13.9 \mu\text{m}$ at 2-months and showed much significant reduction to 246.5 ± 12.7 at 4-months post-treatment ($p < 0.01$) and the same trend of results was shown in the STA group but, the reduction was more significant in the combined treatment group as compared to STA group after 4-months post-treatment and this means that all cases showed resolution of macular edema by the end of the study, this was associated with improvement of BCVA in all patients of this combined group for 0.5 by decimal or better. Similar findings were reported in a retrospective study by Kueley, et al. who found a significant improvement of macular morphology and visual acuity after sub-tenon injection of triamcinolone acetonide in PCME cases. In addition, they did not find a significant difference between sub-tenon (40 mg) and intravitreal (2 mg) triamcinolone acetonide in

the morphological and functional efficacy. Also, they found that 7% of the intravitreal grouped were complicated by ocular hypertension and they were managed medically by topical anti-glucoma [3]. Also, a study included 36 eyes with chronic IGS refractory to topical NSAIDs found that eyes were improved by a combination of periocular TA and intravitreal injection with promising anatomical and visual outcomes [10]. Benhamou *et al.* found that the achieved improvement of macular edema by the combination of intravitreal anti-VEGF and subtenon steroid in patients with chronic IGS was higher in management of chronic cases compared to the intravitreal injection alone as done in our study [11]. Several studies in the last decade on the use of intravitreal steroid focused on alternative use of an intravitreal dexamethasone implant (IVD) (700 micrograms, named commercially OZURDEX), most of the patients treated with IVD demonstrated significant better functional and anatomical results than using intravitreal steroid without serious adverse effects [12-14]. In a previous study by Warren, et al., they found that the combination of anti-VEGF and steroids achieved obvious improvement in treatment of PCME and using NSAID therapy could potentiate this improvement [15]. In a retrospective study, Erden, et al. found that sub-tenon injection of 40 mg of TA resulted in a significant improvement of mean BCVA and significant decrease in CMT [5]. Also, Tsai, et al., found similar results to the Erden's study with insignificant elevation of (IOP < 21 mmHg) in the subtenon group [12]. In addition, Singal, et al. confirmed the successful efficacy of combined topical corticosteroids and NSAID topical drops for treatment of IGS in 10 cases [13]. Furthermore, a significant improvements in visual acuity and CMT were observed in eyes treated with subtenon TA for cystoid macular edema unresponsive to carbonic anhydrase inhibitors [16]. A

study compared subtenon and intravitreal TA for the treatment of PCME and both achieved significant improvement in vision and CMT with no significant differences between interventions at 3 and 6-months follow-ups [3]. On the other hand, Spitzer reported that the refractory Pseudophakic

macular edema was not significantly improved by intravitreal anti-VEGF, however there was mild reduction of retinal thickness [14]. Finally, this study had some limitations. Of these, the lack of long-term follow-up and the relatively not-large sample size.

5. Conclusion

The combined treatment for chronic Irvine-gass syndrome "intravitreal Ranibizumab and subtenon triamcinolone acetonide" may achieve better functional and morphological improvement of the macula than the use of subtenon triamcinolone acetonide alone. This improvement reaches its maximum after 4 months. The combination of intravitreal anti-VEGF and subtenon steroid may be a better choice in management of chronic cases as the improvement of macular edema after intravitreal injection alone in patients with chronic IGS is transient. Larger comparative studies are needed to confirm the results of this study.

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