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Intra-Vitreal Injection of Triamcinolone Acetonide versus Bevacizumab for Management of Diabetic Macular Edema after Phaco Emulsification

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Abstract

Background: **Several studies were done to assess macular edema after phacoemulsification and after phacoemulsification with intravitreal injection of either triamcinolone acetonide or bevacizumab.** ***Aim:*** **to identify the effect of intravitreal injection of either Triamcinolone acetonide or Bevacizumab for the management of Diabetic macular edema after Phacoemulsification.** ***Patients and Methods:*** **Preoperative BCVA was recorded, Preoperative assessment with Fluorescein Angiography (FFA) and Optical Coherence Topography (OCT) was recorded. Patients were allocated into 3 groups, for all groups phacoemulsification and posterior chamber Intra ocular lens was done then in group A intravitreal injection of triamcinolone acetonide was done, group B intravitreal injection of bevacizumab was done, and group C only phacoemulsification and posterior chamber IOL was done. Postoperatively BCVA for each patient in each group and post operative FFA and assessment of the macular thickness with OCT were taken and recorded.** ***Results:*** **The study was carried on 39 patients, in group A there was an improvement of macular edema and reduction of central macular thickness postoperatively, also best corrected visual acuity was improved. In group B and group C there was deterioration of macular edema and increases in central macular thickness post operatively but best corrected visual acuity improved postoperatively.** ***Conclusion:*** **Intravitreal injection of triamcinolone acetonide is an effective method and more effective than bevacizumab for treatment of diabetic macular edema during phacoemulsification.**

Keywords: Optical Coherence Tomography, Fluorescein Angiography.

Introduction

Diabetic macular edema (DME) is the most common cause of vision loss in diabetic patients[(1-2)]. Although the pathogenesis of DME remains unknown, the Early Treatment Diabetic Retinopathy Study (ETDRS) indicates that focal or grid-laser photocoagulation for clinically significant macular edema efficiently ecreases the risk of progressive visual loss in 50% of diabet-

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ic patients[3-5]. Previously, it was found that both intravitreal concentrations of interleukin-6 (an inflammatory cytokine) and vascular endothelial growth factor (VEGF which is a cytokine related with vascular proliferation and hyper-permeability) were increased in DME[6-7]. Many reports indicate that intravitreal or posterior sub-tenon triamcinolone acetonide injection is effective for reducing macular thickness in DME[8-12]. More recently, an intravitreal injection of bevacizumab**,** a full-length humanized monoclonal anti-VEGF antibody, has been reported to be also effective in reducing DME[13,14]. Cataract is a well-recognized ocular complication of diabetes, and it has been assessed that up to 20% of all cataract surgeries are performed on Diabetics patients[15]. The question of whether cataract surgery causes hastening of diabetic retinopathy or maculopathy has been debated. Squirrellet *et al.*[16] displayed that, uncomplicated phacoemulsification did not cause progression of diabetic retinopathy postoperatively and that any progression observed maybe is the natural history of the disease.

Patients and Methods

This study included 39 patients divided into three groups (13 patients each). Informed consents were taken conformed to local laws and in compliance with the principles of the Declaration of Helsinki. The research protocol was approved by the Faculty of Medicine Ethics Committee, Suez Canal University, Ismailia, Egypt. Patients were divided into 3 groups, for all groups phacoemulsification and posterior chamber Intra ocular lens was done then in group A intravitreal injection of triamcinolone acetonide was done, group B intravitreal injection of bevacizumab was done, and group C only phacoemulsification and posterior chamber IOL was done. All patients with either type I or II diabetes mellitus, and all patients with cataract (allowing doing OCT to assess macular thickness), and all patients with diabetic macular edema were included in this study. A predesigned checklist was used for data collection in conjunction with a designed database computerized program for data entry and analysis. Complete history and thorough ophthalmic examination were done. For all patients preoperative BCVA were recorded, Preoperative assessment with Fluorescein Angiography and Optical Coherence Topography was recorded. A topical antimicrobial drug of gatifloxacin hydrate 0.3% ophthalmic solution was administered 4 times/day in both eyes, at least, two days before starting this study. The procedure of phacoemulsification consisted of, peribulbar anesthesia, Preparation of a 3.2 mm clear corneal incision, Continuous curvilinear capsularhexis, Hydrodissection, phacoemulsification, Removal of cortex material with automated irrigation/ aspiration and Implantation of a foldable acrylic lens with an optic diameter of 6.0mm) in the capsular bag. At the end of cataract surgery, either Triamcinolone acetonide or Bevaci-zumab was injected intravitreal, and the third group was left without injection. Intravitreal In-

jection Technique consists of a needle inserted in the inferotemporal quadrant of the globe (the stab is given 3 to 3.5 mm apart from the limbus); group A: 4 mg of triamcinolone acetonide (Kenacort 1 ml) was injected into the vitreous body of the eye. Group B: 1.25 mg of bevacizumab (Avastin 1 ml) was njected into the vitreous cavity of the eye. Group C: No intravitreal injection is given after cataract surgery; needle removed, cotton-tipped applicator applied over the site of the entry to avoid regurgitation of the injected material[17-20]. Postoperatively, 1% prednisolone acetate eye drops, 5% Ofloxacin eye drops 4/day for 1week, then decreasing down weekly over a 3-week period. At baseline examination, each patient was examined with recording BCVA assessment by a Snellen's chart, IOP, and OCT on macular thickness at the 6th week after surgery.

Results

The relation between pre operative and post operative VA is shown in table (1). The mean pre operative VA in group A was 0.9±0.1, and was improved to 0.5±0.2 post operatively (p=0.006), in group B, it was 1.5±0.3 and was improved to 0.7±0.1 post operatively (p=0.002), while in group C, the difference was not significant (p=0.08).

Table 1: Pre and Postoperative mean visual acuity

	VA pre operative	VA post operative	χ	P
Group A (n=13)	0.98 ± 0.11	0.53 ±0.2	46.222	0.006*
Group B (n=13)	1.5±0.34	0.7 ±0.1	13.000	0.002*
Group C (n=13)	1.08± 0.29	0.54 ±0.36	4.952	0.084

Data are presented as mean± SD; *= Significant level ≤0.05; VA: Visual acuity, Group A: Phaco-emulsification and posterior chamber IOL implantation was done followed by Intra vitreal injection of Tri amcinolone acetonide; Group B: Phaco-emulsification and posterior chamber IOL implantation was done followed by Intra vitreal injection of Bevacizumab; Group C: Phaco-emulsification and posterior chamber IOL implantation was done only.

Table 2: Pre and Postoperative mean Central macular thickness

	Macular thickness pre-operative	Macular thickness post-operative	χ	P
Group A (n=13)	383.31 ± 51.14	326.69 ± 20.64	65.000	0.001*
Group B (n=13)	406.7 ± 72.54	430.08 ± 78.6	39.000	0.001*
Group C (n=13)	295 ± 21.44	354.85 ± 64.71	39.000	0.001*

Data are presented as mean± SD; *= Significant level ≤0.05; VA: Visual acuity, Group A: Phaco-emulsification and posterior chamber IOL implantation was done followed by Intra vitreal injection of Tri amcinolone acetonide; Group B: Phaco-emulsification and posterior chamber IOL implantation was done followed by Intra vitreal injection of Bevacizumab; Group C: Phaco-emulsification and posterior chamber IOL implantation was done only.

The relation between the pre and post operative macular thickness assessed by OCT is shown in table (2). The mean pre-operative central macular thickness in group A was 383.3±51.1, and was improved to 326.6±20.6 post operatively (p= 0.001), in group B, it was 406.7±72.5 and was increased to 430±78.6 post operatively (p= 0.001), while in group C, it was 295±21.4 and was increased to 354.8±64.7 post operatively (p= 0.001).

Discussion

Chung *et al.*[21] investigated the effects of phacoemulsification on the diabetic retinopathy in subjects who had the same degree of retinopathy (n=75) in both eyes. They used the non-operated contralateral eye as a control. They stated that diabetic retinopathy progressed significantly especially in the operated eye (23 patients or 30.6%); this agrees with our study results where retinopathy was assessed by OCT, progressed significantly, and diabetic macular edema deteriorated. Patel *et al.*[22] analyzed the aqueous level of VEGF in 7 eyes of 6 patients ranging from severe non-proliferative diabetic retinopathy to early proliferative diabetic retinopathy with uneventful phacoemulsification with IOL. The aqueous concentration of VEGF increased one day after surgery from 68 pg/ml (22-87 pg/ml) up to 723 pg/ml (336-2071 pg/ml), then decreased to 179 pg/ml (range 66-811 pg/ml) one month after the surgery. These changed concentrations of VEGF after Phacoemulsification maybe encourages a subclinical or clinical deterioration of diabetic retinopathy. Therefore, the noticeable increase in aqueous VEGF in eyes with diabetic retinopathy can justify the need for a high concentration of intravitreal bevacizumab as compared to other studies (2.5 mg instead of 1.25 mg). Intravitreal bevacizumab also has a role in the inhibition of associated retinal neovascularization, neovascular glaucoma, rubeosis iridis and controlling macular edema in eyes that need intraoperative or postoperative photocoagulation[23]. Lam *et al.*[24] injected 4 mg of triamcinolone intravitreal during phacoemulsification (19 eyes of 15 diabetic patients with cataract and CSME). They revealed a significant improvement in visual acuity (average 2.4 lines) at the 6-month postoperative. In a parallel prospective study of phacoemulsification in eyes with DME by Habib *et al.*[25], 83% of patients had a dry fovea two weeks after phacoemulsification, and 75% of them had visual improvement at the 2nd month postoperatively. This agrees with our study as there was an improvement in both best BCVA and macular thickness assessed by OCT in the group A. Another study was carried out by Lanzagorta-Aresti *et al.*[26], where the patients were divided into 2 groups. Group I phacoemulsification and intravitreal injection of bevacizumab, group II only phaco-emulsification. Preoperative macular thickness was 282.6 ±57.6 µm in group I and 310.3±82.9 µm in group II respectively. Preoperative BCVA was 0.27±0.17 in group I and 0.24±0.16 in group II, by Snellen chart. At the 3rd

and the 6th months, BCVA improved in group I (0.4±0.28) and (0.4±0.27) more than recorded in the group II (0.21±0.13) and (0.14±0.13). These average macular thickness values differed significantly between the two groups at 3rd months (*P*=0.04) and at 6th months (*P*=0.004). OCT values were also better in group I (292.46± 104.75 µm) at 3rd months and (277.62±92.99 µm) at 6th months. For group II, the results were (367.62± 75.24 µm) at 3rd months and (387.46±74.11 µm) at 6th months. These average macular thickness values differed significantly between groups at 3rd months (*p*=0.046) and 6th months (*p*=0.002). This study concluded that Intravitreal bevacizumab injection directly after phacoemulsification prevents progression of the macular edema seen in several diabetic patients undertaking cataract surgery. Adding, this effect appears to hold in the short term[27]. This study is nearly similar to our study as diabetic macular edema Progressed significantly in the control group but in the other group macular edema also progressed but minimally. A study by Lam *et al.*[24], 17 eyes completed six months of follow-up, 58.8% showed improvement in BCVA of more than2 lines, with statistically significant improvement in mean Snellen BCVA of 2.4 lines at 6th months. BCVA was achieved at 4th months. Central macular thickness improved about 28.5% reduction, achieved at 2nd months, with a statistically significant reduction at all postoperative time intervals until the 6th months. Four eyes (23.5%) developed transiently elevated IOP that normalized by the 6th months in all patients except one. No injection- or surgery-related complications were recorded. This study stated that Phacoemulsification with concurrent 4 mg IVTA injection is a safe option for treating CSMO with cataract. However, large-scale trials are necessary for outlining the relative influences of cataract removal and CMT reduction on vision improvement. Also, the temporary effect on CMT may deserve further studies to determine optimal timing and dosage of further IVTA injections.

Conclusion

The injection of triamcinolone acetonide Intravitreal is an efficient method and more effective than bevacizumab for treatment of diabetic macular edema during phacoemulsification.

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