

USE OF TRIAMCINOLONE AND BEVACIZUMAB IN 25G PHACO-VITRECTOMY SURGERY FOR THE TREATMENT OF CATARACT AND DIABETIC MACULAR EDEMA

USO DE TRIAMCINOLONA Y BEVACIZUMAB EN CIRUGÍA DE FACO-VITRECTOMÍA 25G PARA EL TRATAMIENTO DE CATARATA Y EDEMA MACULAR DIABÉTICO

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ABSTRACT

Objective: To evaluate the safety and efficacy of combined phacoemulsification and triamcinolone-assisted vitrectomy with intravitreal injection of bevacizumab in patients with cataract and diffuse diabetic macular edema.

Methods: In this prospective, non randomized, interventional case series we included 13 eyes of 13 patients with posterior subcapsular cataracts and diffuse macular edema who underwent phacoemulsification, 25G triamcinolone-assisted vitrectomy, endophotocoagulation and had a bevacizumab injection at the end of the procedure. The follow-up consisted of basal best corrected visual acuity, fluorescein angiography, and optical coherent tomography performed at 2 weeks, one, three and six months post-operatively.

Results: An improvement in the best corrected visual acuity of at least two lines was seen in 10 of the 13 patients. The basal average central macular thickness initially was 358.23 μ (SD 50 μ) while at the end of follow-up was 216.6 μ (SD 23.2 μ).

RESUMEN

Objetivo: Evaluar la seguridad y eficacia de la cirugía combinada de facoemulsificación y vitrectomía asistida con triamcinolona y aplicación de bevacizumab intravítreo en pacientes con catarata y edema macular diabético difuso.

Pacientes y métodos: Estudio prospectivo, longitudinal, no aleatorizado, ensayo clínico no controlado. Se incluyeron trece pacientes en forma consecutiva que presentaron esencialmente catarata subcapsular posterior y edema macular difuso, a los que se les realizó cirugía de facoemulsificación, vitrectomía a tres puertos 25G asistida con triamcinolona, endofotocoagulación y aplicación de bevacizumab intravítreo. Se realizó seguimiento con medición de agudeza visual, fluorangiografía retiniana y tomografía óptica coherente (OCT) basal, a las 2 semanas, en el primer, tercero y sexto meses.

Resultados: Se encontró una mejoría visual de al menos 2 líneas de visión al final del seguimiento en diez de los pacientes. En cuanto al grosor central

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Conclusion: This combined surgical and pharmacological treatment resulted in an improvement of central macular thickness and non-progression of diabetic retinopathy in the six month follow-up period. Larger comparative studies are necessary to establish the real impact of this therapeutic approach (*Arch Soc Esp Oftalmol* 2008; 83: 293-300).

Key words: Cataract, phacoemulsification, vitrectomy, triamcinolone, bevacizumab.

macular, el promedio fue de 358,23 μ (DS 56,0 μ) preoperatoriamente, mientras que al final del seguimiento fue de 216,6 μ (DS 23,2 μ).

Conclusiones: El tratamiento quirúrgico y farmacológico combinado aquí expuesto en el periodo de seguimiento de seis meses, mostró una reducción significativa en el grosor macular así como mejoría de agudeza visual en la mayoría de los pacientes. Estudios comparativos con series mas grandes serán necesarios para establecer la eficacia real del procedimiento a largo plazo.

Palabras clave: Catarata, facoemulsificación, vitrectomía, triamcinolona, bevacizumab.

INTRODUCTION

Diabetes mellitus involves a number of late complications such as diabetic retinopathy and the formation of cataracts which has been defined as metabolic. The duration of the disease and an inadequate control of glycemia, among others, are factors which accelerate the appearance of these conditions (1-3)

Cataract surgery is worthy of note because diabetes mellitus patients submitted to this procedure show a progression of the diabetic retinopathy and frequently exhibit the appearance of macular edema or worsening thereof if it already exists (4-6). The established procedure in many of these cases is the application of photocoagulation in the macula before surgery when the opacity of the lens allows it or immediately after (7-9). However, in many cases, it is not possible to control or diminish the macular thickening and the visual results are rather poor in the long run (10). Other treatments used in recent years have been: intravitreal steroids such as triamcinolone (11-23), antiangiogenic drugs (bevacizumab) (24-25) and surgery resources (vitrectomy) (26-28). All these, used in isolation have their advantages but also certain risks and temporary effects as in the case of intravitreal drugs. (29-32)

The goal of this study is to describe a technique concurrently combining the options of a minimally invasive surgery and pharmacological treatment, without the effect of laser thermal energy in the macular area, as well as evaluating its efficiency, security and results in a sample series of thirteen patients during six months.

SUBJECTS, MATERIAL AND METHODS

Informed consent was asked of each patient included in the study. The criteria for inclusion were: patients with non-proliferative diabetic retinopathy and diffuse macular edema according to the established criteria by the ETDRS (Early Treatment Diabetic Retinopathy Study), posterior subcapsular cataract, degree II according to the LOCS classification (Lens Opacities Classification System) P1 to P2, adequate metabolic control for at least three months before the procedure, considered as having glycosylated hemoglobin (Hb1aC) with figures below 7. Arterial blood pressure control was also required, defined as below 140/190 mmHg during at least 3 months before the operation. The criteria for exclusion were: patients with inadequate metabolic control, kidney failure, uncontrolled arterial high pressure, proliferative diabetic retinopathy, and opacity of the lens which was not classified according to the LOCS classification mentioned above.

A base corrected visual acuity test was done to all patients with a decimal scale, anterior and posterior segment biomicroscopy with Goldman's three mirror lenses, intraocular pressure (IOP), eye fundus test, fluorangiography and optical coherence tomography using the basal «fast macular» strategy, the second day after surgery, after two weeks, 1, 3 and 6 months after the procedure, thus completing the follow-up.

The surgery technique consisted firstly in phacoemulsification with the "stop and chop" technique

(fig. 1) in the first stage, insertion of an Acrysoft acrylic single block intraocular lens (Alcon laboratories, Inc. Huntington West, Virginia, USA), leaving the viscoelastic material in anterior chamber, and subsequently performing a three-port central vitrectomy 25Ga with the Accurus equipment (ALCON, Fort Worth, Tx, USA), endoillumination with xenon light, BIOM panoramic visualization system (Insight Instruments, Sanford, FL) (fig. 2).

A vitrectomy was done at 1,500 cuts per minute and 200 mmHg aspiration, with prior application of preservative-free triamcinolone 1 mg in 0.1 ml (ATLC, Labs Grin, Mexico, DF, Mexico) to impregnate the central vitreous and posterior hyaloids (fig.3). A central vitrectomy was carried out first and subsequently the posterior hyaloids was separated by simple aspiration with the vitrector head, increasing aspiration up to 350 mmHg. After that, a disperse endophotocoagulation was performed with a laser diode outside the macular area with an average of 800 shots of about 500 μ diameter (IRIS medical, Stanford, California, U.S.A.). The entrance ports were withdrawn and 0.05 ml (1.25 mg) of Bevacizumab were injected intravitreous (Avastin, Labs Roche, Mexico, D.F., Mexico) (fig. 4) in the superior temporal quadrant at 3 mm of the sclerocorneal limbus. Then, the viscoelastic material was extracted by aspiration with the irrigation-aspiration probe. A combination of tobramycin and dexametasone in suspension was utilized in the postsurgery follow-up for topical application for 3 weeks, 4 times a day.

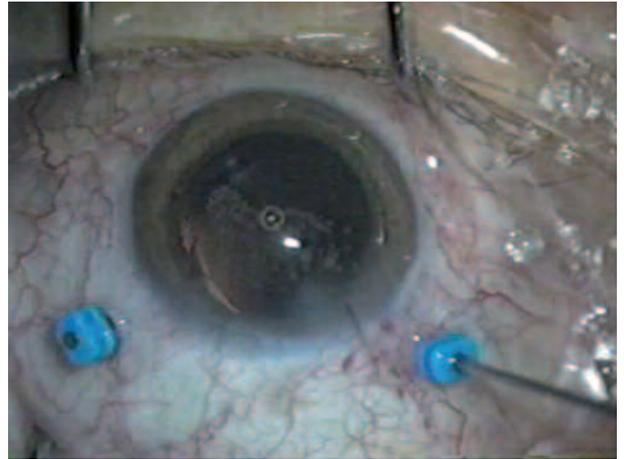


Fig. 2: Vitrectomy gauge 25.



Fig. 3: Triamcinolone intravitreous injection.

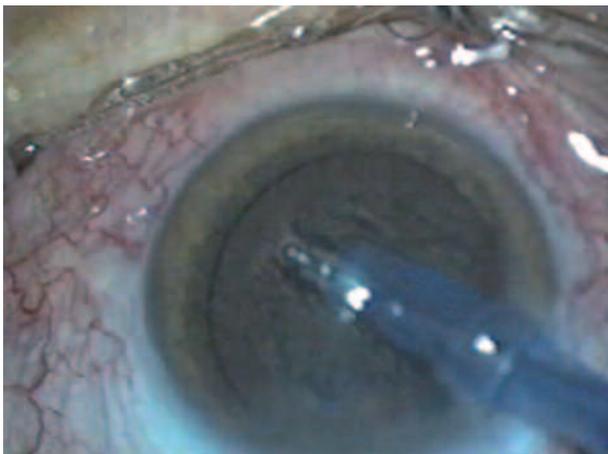


Fig. 1: Phacoemulsification with «stop and chop» technique.



Fig. 4: Intravitreous bevacizumab injection (AVASTIN).

RESULTS

Thirteen eyes from 13 patients were included in this study. The age of the patients ranged between 40 and 78 with an average of 58 . Five patients were male. The presurgery visual acuity changed from HM (hand movements) to 20/70. The presurgery intraocular pressure ranged between 12 and 20 mmHg. An increased IOP, above 20 mmHg was observed in six patients on day 1 post-op. In all cases, the IOP was controlled with a combination of timolol maleate and dorzolamide. In the second week of follow-up, three patients exhibited IOP values above 20 mmHg. After one month, none of the patients showed high IOP figures, thus the anti-glaucomatous medication was discontinued.

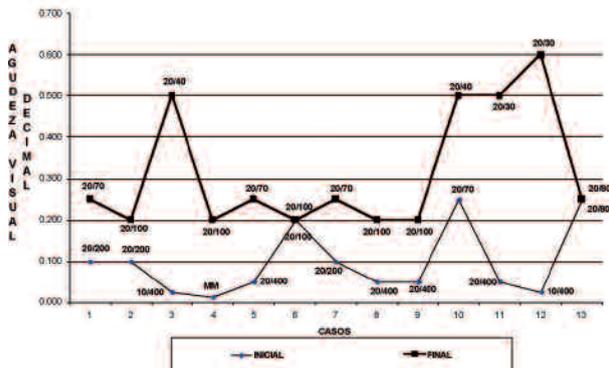
Graph 1 shows the basal visual acuities and after six months after the procedure.

The mean central foveal thickness was 358,23 μ with a range of 285 to 503 μ in the second day post-op. At the end of the follow-up (six months), the mean foveal thickness was of 215,6 μ with a range of 198 to 280 μ (graph 2).

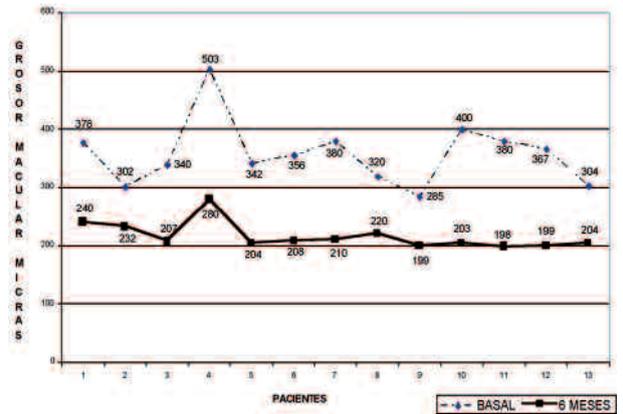
During the follow-up, none of the patients exhibited retina detachment, vitreous hemorrhage, iris neovascularization and/or angle.

DISCUSSION

The results obtained in our publication show a significant decrease of the central macular thickness, documented by the OCT, which was maintained throughout the follow-up of the patients. In what concerns visual acuity, an improvement was achieved in 11 of the 13 patients studied, and in ten



Graph 1: Initial and final visual acuity comparison.



Gráf. 2: Comparison of the basal OCT and after six months.

an improvement of at least two lines was documented at the end of the follow-up. Compared to publications such as Oshima's et al (28), the improvement was lower in ours, although Oshima only included patients without macular pathology. On the other hand, the article by La Heij describes visual improvements in the range of 0.25 to 0.5 , while in our study the improvement was marginally better (0.25 to 0.6).

The objective of our paper was to carry out a procedure in patients with cataract and diabetic macular edema, combining options avoiding the application of laser to the macular area with the aim of determining the evolution of this series of patients in a six-month period. Even though some authors such as Padel and co. (26), did not observe differences between laser therapy and pars plana vitrectomy for treating macular edema, we considered that the addition of triamcinolone and bevacizumab together with the vitrectomy could yield better functional results which could be maintained in the long term.

The use of triamcinolone was an important topic in several publications (11-23) where a tangible benefit was seen in macular thickness reduction and, in some cases, improvement of the visual acuity, mainly in the initial studies (11-14). In said studies, this treatment was used for macular edema refractory to laser therapy. However, the effect of the drug is still temporary (20) and reinjections are needed in many occasions, with the risk this involves (high IOP, retina detachment, vitreous hemorrhage, sterile and infectious endophthalmitis (29-32).

In other cases, triamcinolone was used as adjuvant in the vitreoretinal surgery for enhancing the view of the posterior hyaloids for a more effective extraction (33, 34). In our study we decided to use a dose below 2 mg with the hypothesis of diminishing the prevalence of high IOP but keeping its effect to impregnate the posterior hyaloids and thus remove it with greater ease as well as reducing the macular thickness. However, high IOP appeared, albeit temporarily (1 month), in six of our patients.

Another alternative to photocoagulation already mentioned in patients having concurrent cataract and diabetic macular edema is vitrectomy. With the advent of optical coherence tomography, in many macular edema cases the vitreoretinal traction syndrome involved in such edema has been documented. While performing the vitrectomy, mainly with the extraction of the posterior hyaloid (which sometimes cannot be done due to it being outside the field of vision) the edema remits and the macular thickness and visual acuity can improve (23, 24). There are papers in which, even without evidence of vitreomacular traction syndrome, a vitrectomy can produce an improvement in the edema and the macular function (27), probably due to removal of proangiogenic factors such as the vascular endothelial growth factor (VEGF) and cytokines involved in the breaking of the hematorretinal barrier, as well as the increase of oxygen levels in the vitreous cavity (35). Such factor is involved in the rupture of the blood-retinal barrier and the subsequent maintenance and/or worsening of the edema in the macular area.

In itself, vitrectomy has some complications such as retinal detachment mainly when performed with gauge 20 tools (a lower prevalence of retina detachment with gauge 25 tools has been reported) (28), iris and angle neovascularization, with the usual neovascular glaucoma that frequently leaves patients blind, although the introduction of endophotocoagulation systems have decreased said prevalence rates. Rubeosis can be partially due to the persistence of significantly high levels of VEGF after the surgical procedure (36).

In our publication these complications were not observed during the entire follow-up due to the use of a small gauge which reduces the possibility of the vitreous herniation by the entrance ports and therefore also reducing the risk of retina detachment as well as a reduced inflammatory reaction (28,33). However, the sample of our article is pro-

bably not representative to support such statement, due to it being a pilot study. The other factor we believe may reduce the risk of developing rubeosis is the concomitant application of bevacizumab, the antiangiogenic drug.

In this regard, bevacizumab has been reported as producing an improvement in macular edema (24,25). However, the intravitreal application of this drug must also be repeated due to its temporary effect which (as well as the triamcinolone injection) involves risks such as retina detachment, vitreous haemorrhage and endophthalmitis (25). In our series we used bevacizumab with a double goal: to reduce the prevalence of neovascular glaucoma due to it blocking the action of the VEGF levels in the vitreous cavity after the procedure, and because it hypothetically has an additive action both in effect and duration together with vitrectomy and triamcinolone to reduce the central macular thickness.

The use of this combined surgical-pharmacological therapy has demonstrated its safety in our group of patients, effective in the reduction of the central macular thickness and also in improving visual acuity in most cases and maintaining it stable during a six-month period. In conclusion, we have endeavored to communicate an alternative to the current modes of treatment avoiding repeated intravitreal injections for longer periods (with the known adverse effects of retina detachment, endophthalmitis, vitreous hemorrhage, etc.) macular thermal laser burns and the reduction of risks inherent to vitrectomy (such as retina detachment) using small gauge tools (25 G). However, comparative studies with larger series will be necessary to establish the feasibility of this technique for treating patients with cataracts and diabetic macular edema.

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