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Effect of prophylactic brimonidine on bleeding complications after cataract surgery

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PURPOSE. *To evaluate the effect of prophylactic brimonidine on bleeding complications after cataract surgery.*

METHODS. *The authors performed a prospective, double-masked, two-surgeon study of 137 patients (137 eyes) who underwent phacoemulsification and intraocular lens implantation with or without prophylactic brimonidine before cataract surgery. The authors also compared the effect of brimonidine among patients with systemic diseases such as diabetes mellitus (types I and II), hypertension, and anticoagulant or antiplatelet treatment.*

RESULTS. *Subconjunctival hemorrhage was observed in 73.70% of the patients not treated with brimonidine before surgery and in only 23.75% of the patients who were given prophylactic brimonidine ($p<0.001$, χ^2). The grade of hemorrhage was also statistically significant ($p<0.001$, Mann-Whitney). No statistically significant difference with regard to the presence of hemorrhage in diabetic patients or in the anticoagulant or antiplatelet treatment group was observed. However, a statistically significant difference ($p<0.027$, χ^2) was found between hypertensive patients treated and not treated with prophylactic brimonidine before cataract surgery.*

CONCLUSIONS: *This study suggests that brimonidine administered before cataract surgery may significantly reduce subconjunctival hemorrhage in the general population. It has been shown to be beneficial in hypertensive patients. A strong statistical trend, but not significance has been found in diabetic patients or in patients treated with antiplatelet or anticoagulant drugs, but further studies are needed to reach conclusive results. (Eur J Ophthalmol 2005; 15: 228-32)*

KEY WORDS. *Brimonidine, Bleeding complications, Cataract surgery*

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INTRODUCTION

Brimonidine tartrate 0.2% (Alphagan, Allergan, Irvine, CA), a relatively selective alpha-2 adrenergic agonist, is indicated for lowering intraocular pressure in open-angle glaucoma or ocular hypertension. Some studies suggest that it has a neuroprotective effect in animals (1). Alpha-2 adrenergic agonist drugs, as a class, are also considered to have a strong effect as vasoconstrictors (2), but some studies report that topical brimonidine has no effect on posterior pole hemodynamics (3, 4). Some authors have studied the use of topical brimonidine before laser in situ keratomileusis (LASIK). Walter and Gilbert (5) reported adverse effects of brimonidine on flap adherence in LASIK patients and Norden (6) concluded that brimonidine administered before LASIK may significantly reduce the amount of hyperemia and improve the postoperative appearance without inducing flap slippage. Nowadays many refractive surgeons administer it prophylactically to reduce postoperative subconjunctival hemorrhage or hyperemia and improve aesthetic appearance.

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In a literature review, we found no previous report assessing the prophylactic effect of brimonidine in preventing bleeding in cataract surgery. Many patients undergoing cataract surgery have systemic illnesses such as diabetes mellitus (DM) and hypertension or need antiplatelet or anticoagulant treatment. Because these patients have increased risk of bleeding complications due to microvascular abnormalities, these variables were included in our study.

PATIENTS AND METHODS

A total of 137 patients with cataracts were studied according to the correlative order from the cataract waiting list of La Fe University Hospital. We excluded patients in whom extracapsular surgery was indicated, those who were candidates for topical anesthesia, and oncologic, immunosuppressed, or immunocompromised patients.

Patients received mydriatic drops (tropicamide 0.5%, atropine, and cyclopentolate hydrochloride 1 %, Alcon Laboratories, UK) and diclofenac 0.1% preservative free (Voltaren, CIBA Vision Ophthalmics, Atlanta, GA) every 15 minutes starting 1 hour before surgery, and phenylephrine 10% only twice, until the anesthesia was performed in the preanesthesia room, in the operating theater. We randomly selected patients who would receive brimonidine treatment in the preanesthesia room. The ophthalmic technician nurse in the theater applied brimonidine, one drop 15 minutes before surgery plus an additional drop 5 minutes before the procedure, as Norden's brimonidine dosage protocol (6). Patients and surgeons (A.N., E.F.) were masked to brimonidine administration.

The cataract surgery was done under peribulbar anesthesia in all patients. We prepared a solution with 5 cc of mepivacaine hydrochloride 2%, 5 cc of bupivacaine hydrochloride 0.75%, without vasoconstrictors, and 75 UI hyaluronidase. We injected 4 cc in the inferotemporal quadrant and 4 cc in the superior-nasal quadrant of the orbit, through the skin, with a 25 G needle.

After povidone-iodine 10% preparation, surgery drapes and speculum were placed, the phacoemulsification was performed through a tunnelized clear cornea incision, and a foldable intraocular lens was introduced in the capsular bag. No posterior capsule tear or any other surgical complication occurred in any case. All corneal incisions were sutureless. No subconjunctival antibiotics or steroids were injected. The operating surgeon performed the postoperative examinations under the theater microscope, and recorded the presence or absence of subconjunctival hemorrhage, which was graded according to the number of involved quadrants (1 through 4). Figures 1 and 2 show different grades of subconjunctival hemorrhage. The type of hemorrhage within the quadrant (blob, splinter) was not graded. We used dexamethasone 0.05% and chloramphenicol ointment 1% (Deicol Oilment, Alcon Laboratories, UK) after surgery and occluded the eye until the following day. Slit-lamp microscopy was performed again 24 hours postoperatively. We recorded the grade of hemorrhage and paid attention to the

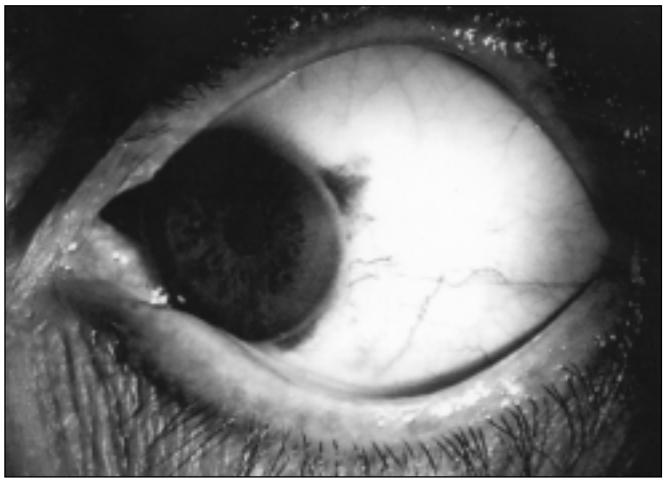

Fig. 1 - *Grade 2 of subconjunctival hemorrhage.*

Fig. 2 - *Grade 4 of subconjunctival hemorrhage.*

presence or absence of corneal incision leaking (Seidel). The postoperative medication regime consisted of tobramycin 0.3% and dexamethasone 0.1% drops (Tobradex, Alcon Laboratories, UK) three times a day and diclofenac preservative free three times a day (Voltaren, CIBA Vision Ophthalmics, Atlanta, GA) for a month, and tropicamide drops noote (Alcon Laboratories, UK) for 3 days, to induce a soft mydriasis and avoid an inflammatory reaction after surgery.

A professional statistician used the suitable statistical significance tests to compare the presence or absence of subconjunctival hemorrhage (Fisher exact test, χ^2 of Pearson) and the rates between the treated and untreated groups (Mann-Whitney U test). The statistical significance level used was 5% (a=0.05) in all cases.

RESULTS

Phacoemulsification and intraocular lens implantation were performed in 137 patients for cataract surgery, with peribulbar anesthesia. Ninety-four (68.6%) patients were men and 43 (41.4%) women. Mean age was 71.4 years (range 32–92). Eighty patients (58.4%) received brimonidine.

Subconjunctival hemorrhage was observed in 61 of 137 eyes (44.5%). Nineteen of the 80 eyes (23.7%) received brimonidine and 42 of the 57 (73.7%) did not receive brimonidine ($p<0.001$ χ^2). The grade of hemorrhage in both groups of eyes is shown in Figure 3 ($p<0.001$, Mann-Whitney).

No significant difference with respect to the presence or absence of hemorrhage or in its grade was found when assessed immediately after surgery and in the following 24-hour examination. No defect in the corneal incision healing was observed in the follow-up of the patients (negative Seidel).

When we reviewed the number of diabetic patients included in the study, we found 11 patients with DM type 1 and 15 with type 2. In type 1 DM subconjunctival hemorrhage occurred in 5 of the 11 patients; 3 of them had not received brimonidine. In type 2 DM we found subconjunctival hemorrhage in 6 of the 15 patients; 3 of them had not been given brimonidine. The specific findings for these patients are shown in Figures 4 and 5. Although the statistical tests showed no significant results because of the small number of

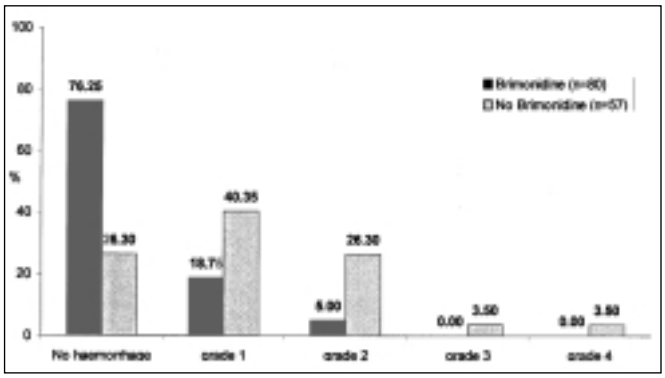

Fig. 3 - *Grade of subconjunctival hemorrhage in eyes after cataract surgery with and without prophylactic brimonidine.*

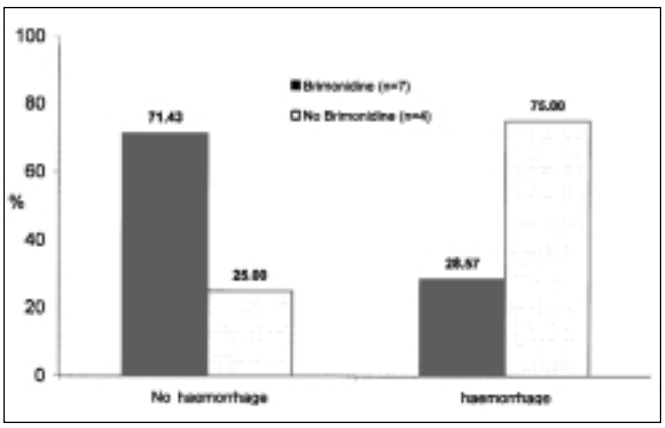

Fig. 4 - *Subconjunctival hemorrhage in eyes after cataract surgery with and without prophylactic brimonidine in type 1 diabetes mellitus patients.*

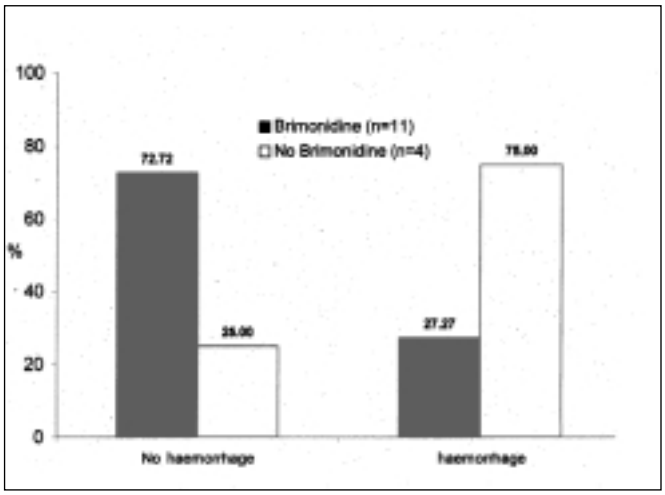

Fig. 5 - *Subconjunctival hemorrhage in eyes after cataract surgery with and without prophylactic brimonidine in type 2 diabetes mellitus patients.*

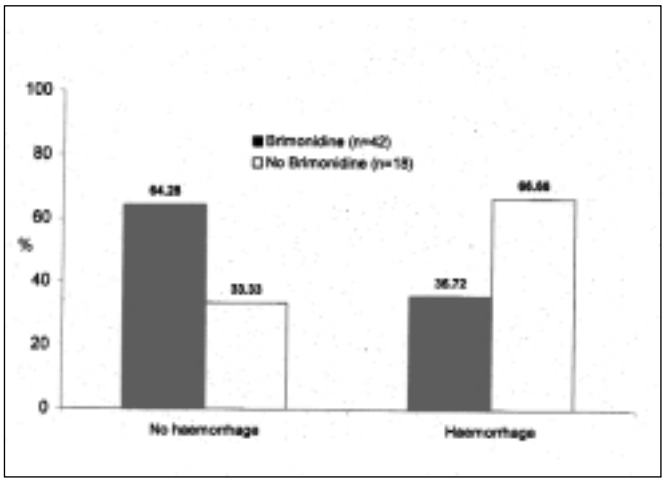

Fig. 6 - *Subconjunctival hemorrhage in eyes after cataract surgery with and without prophylactic brimonidine in hypertensive patients*

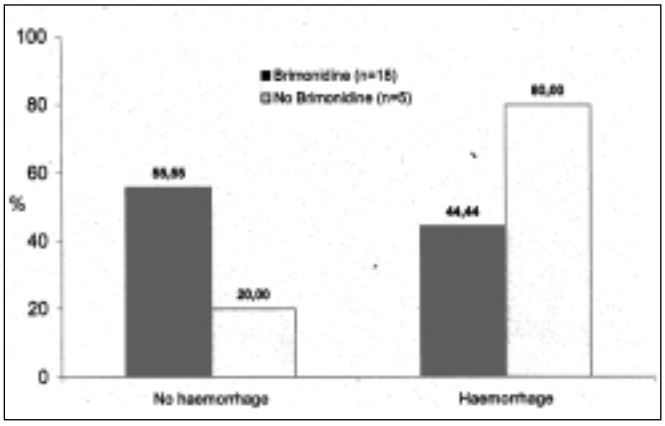

Fig. 7 - *Subconjunctival hemorrhage in eyes after cataract surgery with and without prophylactic brimonidine in patients with antiplatelet or antiaggregant treatment*

the sample, a strong trend could be seen (p=0.242 for type 1 DM and p=0.235 for type 2 DM; Fisher exact test). There was no significant difference between the groups of diabetic patients.

Sixty hypertensive patients were included in the study. Forty-two were treated with brimonidine (27 of the 42 did not present subconjunctival hemorrhage) and 18 were not treated with brimonidine (6 of the 18 did not present hemorrhage). The chi-square test showed statistical significance (p=0.027, χ^2) (Fig. 6).

We reviewed patients with antiaggregant (AA) or antiplatelet (AP) treatment included in the study. There were 23: 5 with AA and 18 with AP treatment. Antiaggregant treatment was stopped 3 days before surgery and replaced by subcutaneous heparin. Antiplatelet treatment was discontinued 1 week before surgery and no replacement treatment was given. Subconjunctival hemorrhage occurred in 12, but only 4 did not receive brimonidine. We did not find any statistical difference with or without brimonidine treatment because of the small number of patients in this group, but a strong tendency was observed in AA or AP patients (p=0.317, Fisher exact test) (Fig. 7).

DISCUSSION

These data demonstrate that brimonidine administered before cataract surgery (phacoemulsification and intraocular lens implant) can significantly reduce subconjunctival hemorrhage. Bleeding can magnify postoperative patient anxiety and can also increase postoperative discomfort, because the conjunctiva has a larger and irregular surface, with tendency to dryness. These results are consistent with Norden's study (6) of prophylactic brimonidine on bleeding in LASIK patients.

When we studied patients with systemic diseases associated with microvascular abnormalities such as DM or hypertension, or patients treated with antiplatelet or antiaggregant treatment, we found a statistically significant correlation between the use of prophylactic brimonidine and the presence of subconjunctival hemorrhage in hypertensive patients. No conclusions can be reached due to the small number of patients in the group of DM and antiaggregant or antiplatelet treatment patients.

There was no evidence of abnormalities in corneal incision healing in eyes treated with brimonidine. This must be taken into account because some authors report flap abnormalities after prophylactic brimonidine treatment in LASIK surgery (5).

This study suggests that brimonidine minimizes subconjunctival hemorrhage in cataract surgery. These findings are conclusive in hypertensive patients but further studies are needed to reach conclusive results in diabetic patients and in patients treated with antiaggregant or antiplatelet drugs.

This finding must be due to the important vasoconstrictor effect of brimonidine. Vasoconstrictors associated with topical anesthetics are commonly used to reduce the

surgical bleeding from capillaries and small arterioles (7). The response of constricted vessels to a trauma injury (mechanical suction or direct trauma) is smaller. There are two reasons to explain this: the diminution of the vessel caliber and the contraction of the smooth muscle fibers in the tunica media vasculosa, which increased the vessel resistance to the traumas. The mechanism of preventing bleeding after cataract surgery seems to be clearly the same as after LASIK surgery: the inhibition of direct trauma due to vasoconstriction.

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