• Clinical Research •

Intracameral lidocaine as supplement to classic topical anesthesia for relieving ocular pain in cataract surgery

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Abstract

• AIM: To evaluate safety, efficacy, and patient adherence of intracameral lidocaine as supplement of classic topical anesthetic drops in cataract surgery.

• METHODS: A prospective and controlled trial including a large cohort of 1650 individuals suffering with bilateral cataract not complicated, in program by phacoemulsification surgery, were randomly assigned to 2 different groups for the type of anesthesia received, 0.4% oxybuprocaine hydrochloride (INN) drops, and INN drops associated to intracameral 1% lidocaine hydrochloride monohydrate. At the end of surgery, tables were assigned to each patient indicating the degree of pain (0-3) felt during the operation.

• RESULTS: Thirty-two percent of patients in group 1 declared to have not felt any pain against the 77% of patients in group 2. Fifty-nine percent of patients in group 1 complained about only a slight discomfort against 20% of group 2 patients. Only a small percentage of patients in group 1 (5%) admitted severe pain, while no patient in group 2 admitted severe pain. Four patients of group 2 reported an episode of transient amaurosis, lasting several hours after surgery.

• CONCLUSION: Intracameral administration of lidocaine is a simple and secure method able to increase the analgesia during the cataract surgery, eliminating the discomfort and increasing also the cooperation of the patients during the steps of manipulation.

• KEYWORDS: benoxinate; cataract surgery; lidocaine; oxybuprocaine; pain scores; phacoemulsification

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INTRODUCTION

Cataract is the leading cause of preventable visual impairment causing an estimated 43% of all cases of blindness worldwide. Phacoemulsification with intraocular lens (IOL) implantation has become the primary surgery to remove cataracts[1-2]. Recent ophthalmic methods of local anesthesia have been developed to improve preference, comfort, and adherence of treated patients. Some complications associated with retrobulbar or peribulbar anesthesia can be avoided with administration of topical anesthesia in drops. Furthermore, intracameral (IC) anesthesia involves the injection of anesthetics directly into the anterior chamber of the eye at the start of the surgery[1-2]. In fact, lidocaine seems to be a simple and safe method for increasing the topical anesthesia obtained by the use of drops of 0.4% oxybuprocaine hydrochloride (INN) before phacoemulsification of the cataract[3].

INN, is an ester-type local anesthetic, also known as benoxinate hydrochloride, which is used especially in ophthalmology and otolaryngology. INN, when used excessively in the eye and on mucous membranes, can cause irritation, hypersensitivity, anaphylaxis, and irreversible corneal damage, like any other topical anesthetics[1-3].

Lidocaine hydrochloride, also known as xylocaine and lignocaine, is a medication used to cause reversible absence of pain sensation in a specific area, for nerve blocks, and to treat ventricular tachycardia[4-5]. Its acting typically starts within a few minutes and lasts up to several hours. Side effects with intravenous use include sleepiness, muscle twitching, confusion, changes in vision, numbness, tingling, vomiting, low blood pressure, and irregular heart rate[4-5].

Lidocaine was discovered in 1946 and it is on the list of medications proposed by the World Health Organization to meet the most important needs in a basic healthcare system; it can be administered by intravenous, subcutaneous, topical, and oral *via*[6]. More, IC anesthesia is especially useful in the case of handling of tissues, decreasing the discomfort of patient and increasing, therefore, also its cooperation during the surgery[6-11].

Accordingly, the objective of our study was to evaluate patient preference, satisfaction, and acceptability during the cataract surgery, when the patients were treated with supplementation of IC injection of lidocaine. Furthermore, we wanted to determine whether the administration of lidocaine could optimize or not the adherence and clinical outcomes.

SUBJECTS AND METHODS

From January 2014 to December 2016 the eyes of 1650 patients suffering from bilateral cataract and in program to be subjected to surgical intervention, were enrolled in our study from the Ophthalmologic Ambulatory of the Santa Maria Goretti Civil Hospital, Latina, Italy. The study protocol was approved by the Ethics Committees and, in accordance with Helsinki Declaration, written consent was obtained from all the subjects.

The inclusion criteria for all patients enrolled were: participants of Caucasian race classified as well-nourished with measurable visual acuity, normal intraocular pressure (IOP), not complicated bilateral cataract, macular areas and retinal nerve fibre layers with normal values by spectral domain-optical coherence tomography.

The exclusion criteria from the study were: patients with hypermature cataract, signs of exudative or atrophic age-related macular degeneration, or other ocular disorders associated, such as macular pucker, neovascular membranes, chorioretinal disease, glaucoma, optic neuritis, ocular trauma, *etc*. Individuals affected from systemic diseases, like: mutiple sclerosis, Parkinson disease, dementia, diabetes mellitus, vasculitis, renal and hepatic diseases, cancer, *etc*. Patients with problems that would make it more difficult to fixate the microscope light, like: movement disorders, nystagmus, hearing problems, high degree of anxiety, *etc*.

The individuals were randomly divided into 2 groups according to the type of anesthesia to which the eye being examined was subjected. The first eye of 1650 patients with less visual acuity was enrolled in the first study group. These eyes were anesthetized using 4 drops of INN (sold by Novartis Pharma SpA Schweizerhalle AG-Rothausweg, CH-4133 Pratteln Switzerland under the brand names of Novesin). The second group was composed of the contralateral eye of the same patients who underwent surgery 1 or 2mo before. These eyes were anesthetized using 4 drops of INN and a supplementation of IC preservative-free 1% lidocaine hydrochloride monohydrate (sold by Fisiopharma S.r.l. Palomonte, Salerno-Italy under the brand names of Lidocaina Cloridrato Fisiopharma) introduced in the anterior chamber immediately after the corneal incisions and before the capsulorhexis. During the surgery a clear corneal incision was made with a keratome. Immediately prior to capsulorrhexis the contents of the syringe (0.2 mL) was injected by irrigation into the anterior chamber only in the patients of the group 2. The solution of 1% lidocaine hydrochloride was then left in the eye for two minutes. After this, viscoelastic was injected to fill the anterior chamber and the surgeon proceeded with the remainder of the surgery: capsulorrhexis, hydrodissection, phacoemulsification, aspiration of cortical material and insertion of an IOL. The wounds were not sutured at the end of the surgery.

Table 1 Pain scores reported by patients after surgery; percentage breakdown of the pain level intraoperative of 3300 eyes in 1650 patients

Pain score	Group 1 pain level	Group 2 pain level
0	32%	77%
1	59%	20%
2	4%	3%
3	5%	0
Mean±SD	0.82±0.73	0.26±0.50

SD: Standard deviation; 0: No pain; 1: Low pain; 2: Mild pain; 3: Severe pain. Statistically significant with $P<0.05$.

Immediately after the surgery, each patient was asked to fill a numeric table descriptive from 0 to 3, which would indicate the pain experienced during surgery suffered. Zero indicated complete absence of pain, 1-mild discomfort, 2-pain tolerable, and 3-pain very strong. The patient was asked, "Did you experience any pain during the surgery? Would you make a mark on the line to show us how much pain you experienced?" From 2014 to date, the following steps were taken. First the patients were followed up weekly and then every two months. This was to ensure that the lidocaine did not cause any toxic effect, especially on corneal epithelium, by an ocular examination consisting of: measurement of unaided and best corrected visual acuity, evaluation of the anterior segment using the slit-lamp biomicroscopy, IOP check using the Goldmann's applanation tonometer, and eye fundus examination.

Statistical Analysis Gender distribution was compared by Chi-square test (χ^2). The scores corresponding to pain assessment were compared by means of the Chi-square test. The variation in the percentage of patients who reported not to feel pain between the immediate postoperative period and six hours after surgery was assessed by the Fisher exact test. Statistical analysis was performed using the STATA 14.0 (Collage Station, Texas, USA), and the null hypothesis was rejected if $P<0.05$.

RESULTS

A cohort of 1650 patients suffering from bilateral cataract to be subjected to surgical intervention was enrolled in our study. Once the study started, no patient was excluded and 3300 eyes were operated. The mean age of the 1650 individuals included was 71.2±5.4y (range 59-85); 42% were male and 58% were female. All subjects had day-case surgery. None of our patients had intraoperative complications related to the administration of IC lidocaine (ICL), that would interfere with the continuation of the intervention and no one needed peribulbar or retrobulbar anesthesia or sedation with intravenous benzodiazepines. The pain scores reported by patients after surgery are shown in the Table 1 and Figure 1. Thirty-two percent of patients in group 1 reported no pain (score=0) against the 77% of the group 2. Fifty-nine percent of patients in group 1 complained of mild discomfort (score=1) against the 20% of the group 2. Only 4%

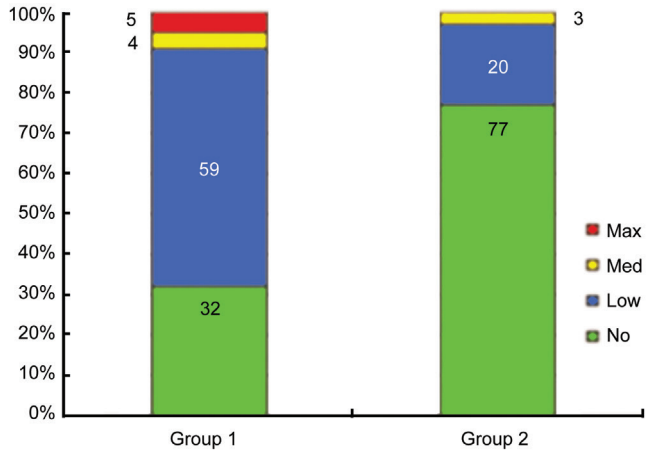

Figure 1 Comparison of the percentage of pain levels in the two study groups (3300 eyes of 1650 patients).

of the patients in group 1 complained of pain (score=2) and 5% of severe pain (score=3) during surgery, while 3% of the patients belonging to the second group claimed to feel pain and none of severe pain during the same procedures (Table 1). At time 6h after surgery, 98.1% of the participants reported no pain, and 1.9% reported mild discomfort (score: 0/1). During the months of follow up, the patients showed no evidence of corneal damage related to IC injection of lidocaine.

Surgical complications included only one case of small posterior capsule rupture and vitreous loss in a patient belonging to the group 2. However, this patient was able to tolerate a mechanical anterior vitrectomy without supplemental retrobulbar anesthesia. Right after a foldable IOL was implanted into the capsular bag in the eye without difficulty.

Adverse events after surgery occurred in four of the patients treated with lidocaine who developed transient amaurosis. Two of them were highly myopic. In a word, the posterior capsule was not intact, while the fourth subject had undergone a vitrectomy 25y earlier. All patients in the span of a few hours regained their sight without other side effects or permanent deficit.

DISCUSSION

The objective of our research consisted of evaluating the compliance and adherence of the patients during cataract surgery using combined IC injection of lidocaine as supplement to classic topical anesthesia for the treatment of ocular pain in cataract surgery. Moreover, we wanted to determine whether or not the administration of lidocaine could optimize the safety and efficacy of the clinical outcomes in a large group of monitored eyes.

It is also clear that the percentage of patients experiencing pain decreases considerably from the first to the second group, with the addition of ICL, the perception of pain disappears or at least it is widely reduced. In fact, 59% of the patients of the group 1 declared discomfort during several times of the surgery: manipulation of iris, sudden distension of the anterior chamber by irrigating fluid, after introduction of the phacoemulsification tip, or hydrodissection, or rotation of the nucleus. The most afflicting pain happened during the use of spatula to reposition a prolapsed iris. A smaller proportion of patients in group 2 (20%) reported ocular discomfort during such manipulations, although most described a sensation of ocular soreness when the lidocaine was injected in anterior chamber. Generally, such discomfort lasted for only few seconds and some words of comfort and encouragement were sufficient to ward off the patient's anxiety. Despite the fact that majority of the patients did not suffer intraoperative uneasiness, the difference in mean pain scores for the two groups was statistically significant. Similar findings have been recorded by other authors[2,11].

So, while some researchers declare that ICL seems to be safe for cornea, anterior chamber, retina, and no relevant systemic levels of lidocaine have been reported[11-13]. We reported 4 events of amaurosis fugax similar to other authors[7-8,14-15]. In addition, Macky *et al*[16] have carried out some investigation on the toxicity of a solution that combines sodium hyaluronate 1.5% with lidocaine (0.5%, 1.0%, and 1.65%) to intraocular tissues during phacoemulsification in both eyes of 29 rabbits. The results showed no evidence of an inflammatory reaction, cell necrosis, or cell degeneration was observed in the histological sections in intraocular structures such as the iris, lens capsular bag, ciliary body and retina. The researchers have concluded that the use of 3 lidocaine concentrations during phacoemulsification of the lens appeared to be safe, with no tissue histopathological abnormalities observed in multiple sections of eyes from iris, ciliary body, lens, and retina[16].

We know that the lidocaine alters the signal conduction in sensory neurons as well as in muscle cells by blocking fast sodium channels and increasing the depolarization threshold[17-18]. The adverse drug reactions are rare when lidocaine is used as a local anesthetic and is administered correctly. In the eyes it can cause: local burning, conjunctival hyperemia, corneal ulceration, diplopia, and visual changes. While, cardiovascular adverse effects can be: hypotension, bradycardia, arrhythmias, venous insufficiency, increased defibrillator threshold, edema, and cardiac arrest[17-19]. However, these were not seen in our study intra- and postoperatively.

On the other hand, in amaurosis fugax, also known as transitory monocular blindness, the sight in one eye is temporarily lost. To the best of our knowledge, we have found in the literature a few similar events of transient amaurosis after cataract surgery with IC anesthetic of lidocaine. These adverse events are, perhaps, linked to the large number of patients we have treated and carefully monitored to assert the safety of the lidocaine. Accidentally, also other authors reported cases of transient visual loss after use of ICL with or without posterior capsule rupture[14-15,20]. Although in a Lincoff *et al*[7] research only one subject developed a permanent visual field defect and the other patients showed improvement in retinal function up to 16h.

Researchers stated that lidocaine temporarily paralyzed the pupil in mydriasis and temporarily extinguished the b-wave of the electroretinogram for decrease in amplitude and increase in implicit time. Nevertheless, electroretinogram responses recovered within 24h[7,14-15]. Eshraghi *et al*[20] concluded that to reduce retinal toxicity risks, ICL should not be repeated during the surgery.

Probably, the temporary visual loss in our patients could be caused by action of topical anesthetic agent on the retinal vessels, we also remember vasodilatation effect of the lidocaine[17-18], through a retinal ischemia or directly on the retinal nerve fiber layer, in turn, because of lack of barrier effect of posterior capsule, zonules, and vitreous humor. However, the retina and optic nerve head of our 4 patients appeared normal. Therefore, the retina could be resistant to the toxic effects of ICL only to lower concentrations of the anesthetic. In a recent study, it was confirmed *in vitro* the toxic effect of lidocaine on ganglion cells by molecular degenerative damage and also observed that lidocaine 0.25% decreases cell viability and causes DNA degradation in murine fibroblasts 3T6[8].

In conclusion, based on the results obtained, we believe that the combined topical IC approach will probably become the standard ophthalmic anesthetic technique in phacoemulsification for the majority of our patients undergoing cataract surgery. However, it is very important to note the need for the moderate use of the anesthetic agent's concentration and quantity, particularly in case of rupture of capsule bag.

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