

# **An Unrecognized Cause of Post-blepharoplasty Lagophthalmos: Local Anesthetic Orbicularis Myotoxicity**

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**Precis:**

Myotoxic effects of local anesthetics can be responsible for localized postoperative orbicularis oculi dysfunction.

**Abstract:**

**Purpose:** To report postoperative localized and occasionally persistent orbicularis oculi weakness presumably attributable to local anesthetic myotoxicity.

**Methods:** Nonrandomized retrospective clinical case series identified 32 patients seen in a tertiary care referral oculoplastic practice over a seven-year period. Follow-up ranged from 0.5 to 7 years with an average of 1.3 years.

**Results:** Patients demonstrated varying degrees and duration of orbicularis oculi dysfunction manifest primarily as lagophthalmos. Although most patients improved with observation alone, 6 of 32 patients did not.

**Conclusion:** Orbicularis oculi dysfunction may result from local anesthetic injections. In most cases, this complication is transient, yet permanent dysfunction can occur. To minimize the risk of developing this complication, local anesthetics should be judiciously administered in low volume and concentration away from the critical pretarsal orbicularis at the eyelid margins. Additionally, patients should be counseled preoperatively about the potential risks of local anesthetic use.

Injection of local anesthetics into the upper and lower eyelids is routinely performed during a variety of common surgical procedures, including cosmetic and functional blepharoplasties. A myotoxic effect of local anesthetics (such as lidocaine, bupivacaine, and mepivacaine) on skeletal and extraocular muscle has been well documented in the laboratory, where profound, almost complete degeneration of injured muscle has been seen.<sup>1-3</sup> Clinically significant myotoxicity of extraocular muscles and levator palpebrae superioris, though a rare and uncommon side effect of local anesthetics, has been reported to result in both permanent and temporary diplopia and ptosis with the use of periocular anesthesia.<sup>4,5</sup>

Although skeletal muscle injury is a very well documented side effect of virtually all local anesthetics, there are few reported cases of orbicularis myotoxicity despite its common exposure to periocular injections. The relative immunity of the orbicularis to local anesthetic myotoxicity has been studied in the past with observed injury but not destruction of the myofibers after repeated injections of high concentrations of local anesthetics like bupivacaine, and it has been hypothesized that the tight fasciculation of the myofibers prevent infiltration of the local anesthetic to the individual fibers.<sup>2</sup> Hence, it has hitherto been assumed that the orbicularis is relatively safe from local anesthetic myotoxicity. However, our experiences lead us to believe otherwise and, herein, we report the first cases, to our knowledge, of persistent orbicularis oculi weakness resulting in post-operative lagophthalmos, secondary to presumed local anesthetic myotoxicity and suggest strategies to minimize this problem.

## Case Series

A 72-year-old woman was brought to the operating room for right lower eyelid reconstruction. In anticipation of harvesting a full-thickness skin graft, the left upper eyelid was injected at the start of the case with 1.5cc of 1% lidocaine and 0.25% bupivacaine with 1:200,000 epinephrine. The right lower eyelid defect, however, was closed with adjacent tissue advancement, and no incision was made in the left upper eyelid. Post-operatively, the patient demonstrated left upper eyelid orbicularis dysfunction with lagophthalmos lasting at least four years. As no intervention other than local anesthetic infiltration was performed on this eye, and a comprehensive neurologic evaluation was otherwise negative, the lagophthalmos was presumed to be secondary to local anesthetic induced orbicularis oculi myotoxicity.

Over 7 years (1995-2002), two of our authors (CNSS and JRP) recognized three additional patients from their practice and 28 more upon referral (total = 32 patients, 43 eyelids) with orbicularis oculi dysfunction characterized by lagophthalmos following local anesthetic injection for blepharoplasty or blepharoptosis repair (Figure 1, Table 1). None of the patients showed clinically detectable evidence of internal eyelid scarring (excluded by easy movement of affected eyelids with the examiner's finger) or pre-existing facial nerve weakness to account for the lagophthalmos. Six of 32 patients (19%) showed no clinically significant improvement over an average follow up of 47 months (range 17 to 86 months) for permanently paretic eyelids and an average follow up of 4 months (range 2 to 9 months) for temporarily paretic eyelids.

## Discussion

Transient lagophthalmos is not uncommon following blepharoplasty or blepharoptosis repair. In the first few days after surgery, dysfunctional eyelid closure is often ascribed to “eyelid edema”. More persistent problems, however, can be perplexing. Excessive skin resection, middle lamellar cicatrix, and tarsal tethering to the orbital septum are all well-known causes of postoperative lagophthalmos; yet some patients without these problems still have difficulty closing their eyes. It is unlikely that removal of the preseptal orbicularis is responsible for the observed lagophthalmos, as eyelid kinematic studies show no change in blink main sequence after blepharoplasty.<sup>6</sup> Furthermore, many patients maintain essentially normal eyelid closure after aggressive orbicularis myectomy for intractable blepharospasm where only 2-3 mm of pretarsal orbicularis is left behind.

A myotoxic effect of local anesthetics (Figure 2) has been described since the 1950's.<sup>7-8</sup> Subsequent studies have confirmed that all local anesthetics in clinical concentrations have potentially severe injurious effects, with procaine and tetracaine producing the least and bupivacaine and chlorprocaine the most severe muscle injury. Furthermore, the myotoxic effects are clearly dose dependant and increase with serial administrations of the anesthetics. The histological pattern of injury for all anesthetics is uniform with hypercontracted myofibrils and lytic degeneration followed frequently by vigorous muscle regenerative response by local stem (satellite) cells.<sup>9,10</sup>

The concomitant use of epinephrine with local anesthetics is also believed to potentiate the myotoxicity.<sup>11,12</sup> Epinephrine has been reported to significantly increase lidocaine-induced skeletal muscle necrosis, even in low concentrations that elicit no damage by

themselves.<sup>12</sup> In 1985, Rainin and Carlson suggested local anesthetic myotoxicity as an etiology for post-operative blepharoptosis and strabismus following cataract surgery.<sup>4</sup> McLoon and Wirtschafter have since eloquently demonstrated the toxic effects and regenerative process following injection of local anesthetics in rabbit orbicularis oculi.<sup>2,13</sup>

Most recently, the mechanism of bupivacaine-induced myotoxicity has been carefully described as a concentration-dependant mitochondrial depolarization leading to opening of a cyclosporine-A sensitive permeability transition pore. Intracellular free calcium rises, cellular ATP falls, and apoptosis factors such as cytochrome C, endonuclease G, and SMac-Diablo are released causing cell death.<sup>14,15</sup> Following myocyte degeneration, macrophage-mediated phagocytosis of damaged muscle fibers occurs, leaving behind an intact basal lamina and a population of myogenic stem cells. Activation of these myogenic stem cells, satellite cells, via a complex sequence of events leads to division into myoblasts that coalesce to regenerate the muscle fiber.

Myocyte cell death and subsequent phagocytosis begins within minutes of exposure to local anesthetics and peaks around 2-3 days. Satellite cell activation also peaks around 2-3 days post injury, but regeneration has been shown to extend at least 30 days.<sup>2,13</sup> Even though laboratory studies suggest a rapid and complete regeneration of chemically injured muscle with attainment of normal myofiber diameter, normal physiologic function may not be regained, and permanent muscle dysfunction has been described.<sup>10-</sup>

In light of the well-established toxicity of local anesthetics and the high frequency of temporary lagophthalmos after eyelid surgery, we postulate that post-operative difficulties in eyelid closure may frequently be caused by local anesthetic orbicularis myotoxicity, a phenomenon that is typically transient, but may result in permanent eyelid dysfunction.

In the clinical series presented herein, a high percentage of patients (19 %) demonstrated long-term (perhaps permanent) orbicularis dysfunction for at least a year. Likely, this strikingly high morbidity reflects the tertiary nature of care of the practice studied. Why some people develop permanent eyelid muscle dysfunction and others do not remains speculative. Further study is needed to understand the age, environmental, hormonal, nutritional, and inherited influences that possibly define the interpersonal variability inherent in the complex cascade required for functional muscle repair. Also the concomitant use of other myotoxic or myotoxicity potentiating agents like epinephrine cannot be ignored. Until specific risk factors are defined, since we believe that some degree of post-operative eyelid myotoxicity is common, the following steps should be considered to minimize orbicularis damage from local anesthetics during all eyelid surgery:

1. Place injections high in the upper eyelid and low in the lower eyelid to avoid damaging the pretarsal orbicularis that lies within 5 millimeters of the eyelid margins and is critical for normal blinking and eyelid closure.
2. Minimize the volume and concentration of local anesthetic used.

Finally, although anesthetic-related orbicularis dysfunction probably resolves spontaneously in the vast majority of cases, weakness may be permanent, and the clinical implications and patient morbidity from this condition can be profound. Therefore, it seems prudent to inform patients of the potential risk pre-operatively.

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**Legend: Table 1**

“Eyelids Injected” = number of eyelids injected during surgery, “Eyelids Involved” = number of eyelids with post-operative orbicularis oculi dysfunction, “Problem Duration” = time in months (rounded to the nearest month) until dysfunction resolved from all eyelids, “Injection Volume” = total amount of local anesthetic used in milliliters. M = male, F = female, Bleph = blepharoplasty, Ptosis = blepharoptosis repair, CA = cancer reconstruction, UL = upper eyelid(s), LL = lower eyelid(s), \* = at last contact with patient dysfunction still present, Li = lidocaine, BU = bupivacaine, Me = Mepivacaine, E = epinephrine, H = hyaluronidase, empty space = data not available. Concentrations of local anesthetics used ranged from 0.5 – 2% lidocaine and 0.25 - .75% bupivacaine. Mepivacaine concentration used was not available.

**Legend: Figure 1**

(A) Patient # 11 with relaxed lid closure showing bilateral upper eyelid orbicularis weakness and lagophthalmos following blepharoplasty.

(B-E) Patient # 21 after four eyelid blepharoplasty shows lagophthalmos on the right (B) that drifts down to full closure (C), but demonstrates clear orbicularis dysfunction with forced closure (D). Above lighting casts greater shadows (E) and suggests that the myotoxicity may have involved the lower eyelid and glabellar muscles as well.