

Bupivacaine Injection to Lateral Rectus in Abducens Nerve Palsy

Sungeun Kyung, Jihoon Jeon

Department of Ophthalmology, Dankook University College of Medicine, Cheonan, Korea

A 49-year-old female presented with bilateral abducens nerve palsies. She had 75 prism diopter esotropia. The extraocular movement of the lateral rectus was -1 limitation for the right eye and -4 limitations for the left. After performing orbital magnetic resonance imaging (MRI), 2 mL of bupivacain (5 mg/mL) was injected into the left lateral rectus (LR). One month after injection, a further orbital MRI was performed. Subsequently, recession of both medial rectus (6 mm) and resection of the left LR (9 mm) were performed. After one month, bupivacaine had no hypertrophic effects. There was little change in angle of deviation. The orbital MRI scan showed a 1.91% increase in volume compared to the muscle prior to the injection. Histological findings showed no muscle fibers of the left LR muscle, only the fiber nucleus and the collagen that replaced the fibers. We report on the changes in stiffness and muscle volume and on the histology of the muscle one month after injecting bupivacaine into the paralyzed left LR muscle combined with standard surgical treatment.

Key Words: Abducens nerve diseases, Bupivacaine, Magnetic resonance imaging

Bupivacaine (BUP) injection into the muscles of laboratory animals has been reported to produce myotoxicity, leaving the basal lamina, nerves, and satellite cells intact [1-3]. The damaged tissue releases growth factors, causing satellite cells to proliferate as new muscle fibers. Subsequent satellite cell proliferation repairs the damage and stimulates muscle hypertrophy [3,4]. Strabismus after retrobulbar anesthesia for cataract surgery with BUP injection has been reported, showing enlarged muscles [4]. There is the possibility that the myotoxic effect of BUP may have effects on muscle strength. Improved eye alignment and increased muscle size after bupivacain injection to the lateral rectus (LR) in strabismic patients have been reported [5]. Standard muscle resection and recession techniques are effective for incomplete paralytic patients. However, muscle transposition procedures are indicated for complete paralysis of

an extraocular muscle. We treated a patient with paralytic strabismus by injecting BUP into the left complete paralytic LR muscle to determine whether BUP can stimulate paralyzed muscle hypertrophy and then performed standard surgical treatment in the left complete paralytic eye one month later. We report on the changes in stiffness and muscle volume and on the histology of the paralytic muscle one month after treatment.

Case Report

A 49-year-old female presented with esodeviation, which occurred one year after a traffic accident. Snellen visual acuity was 20 / 20 in both eyes. Bilateral abducens nerve palsies were diagnosed on neurological examination. The primary position deviation was 75 prism diopter (PD) esotropia on the alternate cover test (Fig. 1). The extraocular movement of the LR was -1 limitation for the right eye and -4 limitations for the left. No evidence of neurological impairment was present, and magnetic resonance imaging (MRI) of the brain was normal. After performing orbital MRI and discussing its experimental nature with the subject, informed consent was obtained for a BUP injection. A flaccid LR of the left eye was confirmed by exposing the muscle through a swan incision 8 mm from the limbus. Using a 30-gauge needle, 2 mL of BUP (5 mg/mL) was

Received: June 13, 2011 *Accepted:* October 21, 2011

Corresponding Author: Sungeun Kyung, MD, PhD. Department of Ophthalmology, Dankook University Hospital, #201 Manghyang-ro, Dongnam-gu, Cheonan 330-180, Korea. Tel: 82-41-550-6497, Fax: 82-41-561-0137, E-mail: Kseeye@hanmail.net

This study was presented at 102th Korean Academy of Ophthalmology Annual Meeting in November 6, 2009 (Goyang, Korea).

© 2013 The Korean Ophthalmological Society

This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

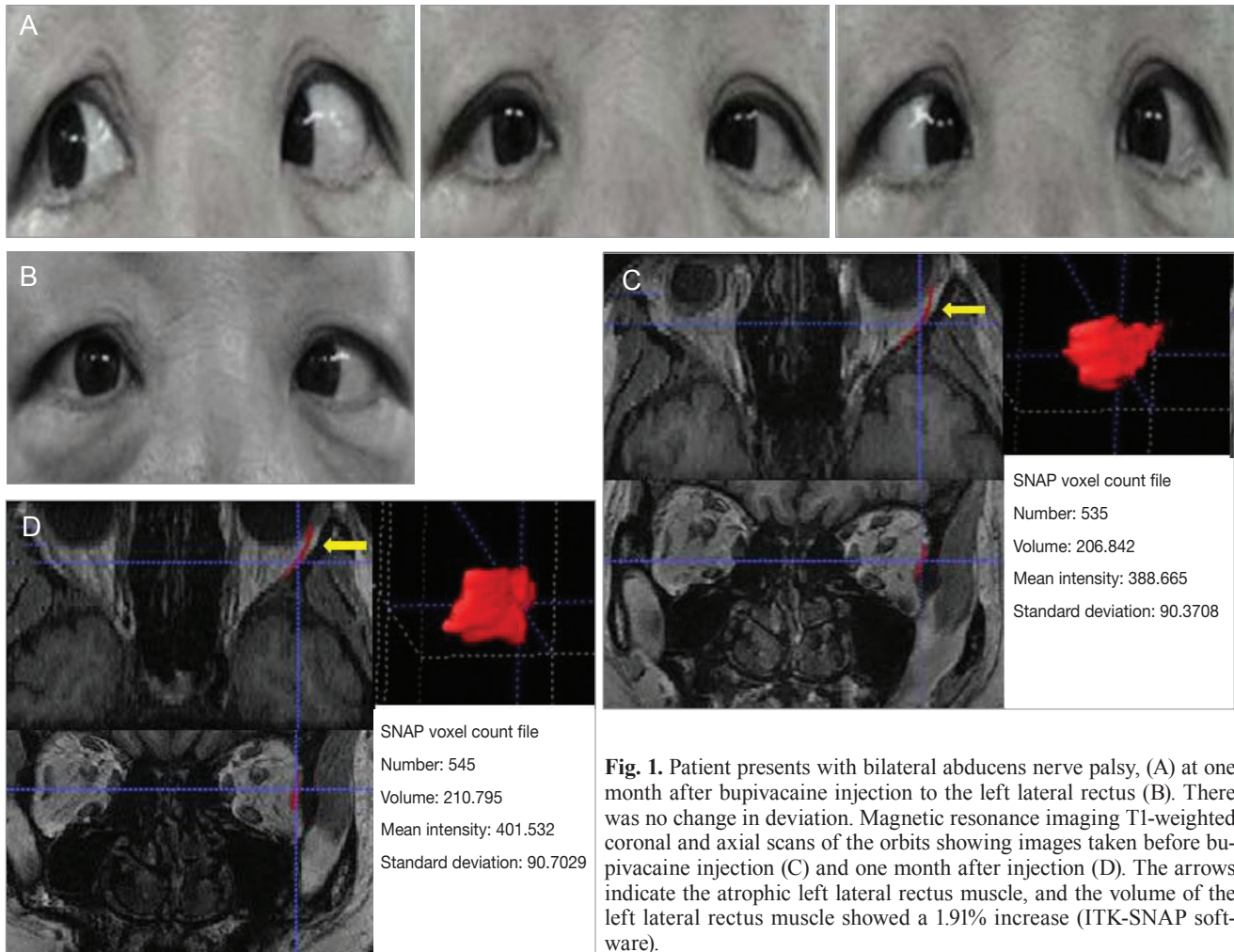


Fig. 1. Patient presents with bilateral abducens nerve palsy, (A) at one month after bupivacaine injection to the left lateral rectus (B). There was no change in deviation. Magnetic resonance imaging T1-weighted coronal and axial scans of the orbits showing images taken before bupivacaine injection (C) and one month after injection (D). The arrows indicate the atrophic left lateral rectus muscle, and the volume of the left lateral rectus muscle showed a 1.91% increase (ITK-SNAP software).

injected into the LR. One month after injection, there was no change in deviation, and a further orbital MRI was performed (Fig. 1). Subsequently, the recession of both medial rectus (6 mm) and resection of the left LR (9 mm) led to orthotropia until 18 months (Fig. 2). At the left LR resection, traction testing demonstrated restriction of the medial gaze compared to before BUP injection. The formerly-injected LR was 'stiff' on surgical observation.

Discussion

BUP selectively damages striated muscle fibers, leaving supporting cellular structures, nerves, and satellite cells intact [1-3]. The damaged tissue releases growth factors, causing satellite cells to proliferate. This process continues, causing hypertrophy. In most cases of complete paralysis, transposition of the rectus muscle is usually considered. However, in this study, recession of both the medial rectus muscle and resection of the paralyzed left lateral rectus muscle one month after BUP injection were performed. After injection of BUP, a hypertrophic effect on the para-

lyzed left LR muscle was expected; however, there was no change in the deviation of esotropia, and stiffness of the flaccid left LR muscle was observed one month after injection. Although it did not increase the effect on the muscle, BUP caused the observed stiffness. The patient maintained orthotropia until 18 months.

Orbital MRI images were used to measure muscle size with 3 mm slices from the orbital apex to the equator of the eye, coronally and axially. ITK-SNAP software (Penn Image Computing and Science Laboratory; University of Pennsylvania, Philadelphia, PA, USA) was used to evaluate any changes in MRI and to estimate muscle volume. Using the coronal plane, the incised surface of the left LR muscle was measured from the orbital apex to the junction of the extraocular muscle, and the volume calculated. The incised surface of the muscle was measured twice by different observers to reduce bias. The volume of the left LR muscle showed a 1.91% increase in volume compared to the muscle prior to the injection (Fig. 2). It was difficult to compare the changes in muscle volume due to the severity of the atrophy in the rectus muscle prior to the injection. Scott

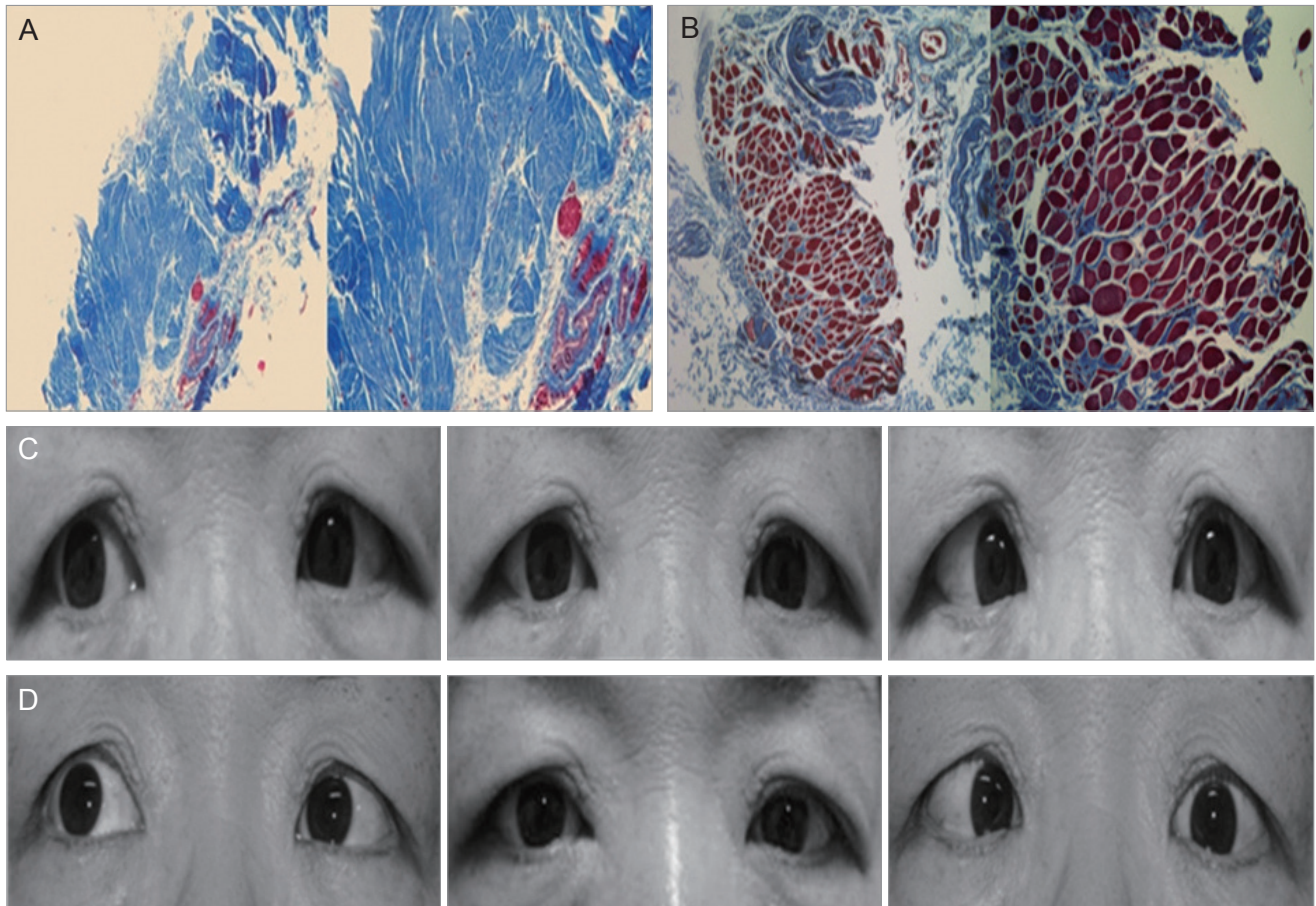


Fig. 2. Photomicrographs of left resected lateral rectus after bupivacaine injection ($\times 10$, $\times 20$). The nuclei of the muscle fibers and the collagen that replaced the fibers were observed (A), control (intermittent exotropia, 43-year-old woman, $\times 10$, $\times 20$) (B), Masson's trichrome staining. Patient six months (C) and 18 months (D) after standard treatment (recession of both medial rectus muscles and resection of the left lateral rectus). Orthotropia is maintained, and adduction of the left eye is limited compared to that at six months due to stiffness of the injected left lateral rectus at 18 months.

et al. [5] reported a 6.2% increase in volume of the rectus muscle and changes of 6 PD when BUP was injected into the rectus muscle of an esotropic patient. Denervated muscle hypertrophy also occurs after bupivacaine injection in animals, arguing for therapeutic trial in parietic strabismus [6]. However, in our subject, there were subtle increases in volume.

The paralyzed left LR muscle tissue, excised during surgery, was fixed in 10% neutral buffered formalin for 24 hours and fixed in paraffin blocks. The longitudinal axis of the muscle was sliced 10 μ m thick and stained using Masson's trichrome for histological examination. The normal LR muscle has two histologically significant layers. The global layer consists of larger fibers compared to the orbital layer and stains bright red with Masson's trichrome solution. The orbital layer muscle fibers have smaller diameters and stain dark red with Masson's trichrome solution [7-9]. In the abducens paralytic strabismus case presented, it was difficult to divide the two layers, and nuclei of muscle

fibers and collagen that replaced the fibers were observed (Fig. 2). In addition, muscle biopsy did not document hypertrophy in this material.

LR paresis after injection of BUP and botulinum toxin into agonist and antagonist muscles have been reported [10]. One patient without LR atrophy was changed by 55 PD, and the other patient with LR atrophy was corrected only 4 PD after injection of BUP and botulinum toxin [10]. A large correction can be obtained in an incomplete paralyzed muscle so long as it is not atrophic. Muscle shortening and stiffening in BUP-injected LR were also demonstrated. We treated a patient with bilateral abducens nerve palsies, injecting with BUP to the complete paralyzed left LR along with standard surgery. The patient showed no muscle hypertrophy on MRI or deviation changes but did show muscle stiffness in the BUP-injected LR. Orthotropia was maintained, and adduction of the left eye was limited compared to that at six months due to stiffness of the injected left LR at 18 months.

The influence of BUP on atrophic extraocular muscle shows little benefit or change in muscle volume. The releasing growth factors causing satellite cells to proliferate might not be possible with severely atrophic muscle tissue. BUP injection to the atrophic muscle in this case was not useful for increasing muscle volume in a complete paralytic strabismus patient. However, the BUP-injected LR did exhibit muscle stiffening. It is possible that BUP injection to the complete paralyzed muscle has the effect of maintaining eye alignment after standard surgery even though there was no effect on muscle hypertrophy or deviation. BUP-injected atrophic muscle acts as a bridge for the complete paralytic strabismus patient with severe eye-movement limitation needing muscle transposition when combined with standard surgery. We will continue our efforts toward BUP injection to atrophic muscles in order to compare the effects of alignment between incomplete and complete paralytic patients combined with standard strabismus surgery.

Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Acknowledgements

This research was conducted by the research fund of Dankook University in 2010.

References

1. Benoit PW, Belt WD. Destruction and regeneration of skeletal muscle after treatment with a local anaesthetic, bupivacaine (Marcaine). *J Anat* 1970;107(Pt 3):547-56.
2. Bradley WG. Muscle fiber splitting. In: Mauro A, editor. *Muscle regeneration*. New York: Raven Press; 1979. p. 215-32.
3. Hall-Craggs EC. Survival of satellite cells following exposure to the local anesthetic bupivacaine (Marcaine). *Cell Tissue Res* 1980;209:131-5.
4. Capo H, Roth E, Johnson T, et al. Vertical strabismus after cataract surgery. *Ophthalmology* 1996;103:918-21.
5. Scott AB, Miller JM, Shieh KR. Bupivacaine injection of the lateral rectus muscle to treat esotropia. *J AAPOS* 2009;13:119-22.
6. Billington L, Carlson BM. The recovery of long-term denervated rat muscles after Marcaine treatment and grafting. *J Neurol Sci* 1996;144:147-55.
7. Durston JH. Histochemistry of primate extraocular muscles and the changes of denervation. *Br J Ophthalmol* 1974;58:193-216.
8. Spencer RF, Porter JD. Structural organization of the extraocular muscles. *Rev Oculomot Res* 1988;2:33-79.
9. Oh SY, Poukens V, Cohen MS, Demer JL. Structure-function correlation of laminar vascularity in human rectus extraocular muscles. *Invest Ophthalmol Vis Sci* 2001;42:17-22.
10. Scott AB, Miller JM, Shieh KR. Treating strabismus by injecting the agonist muscle with bupivacaine and the antagonist with botulinum toxin. *Trans Am Ophthalmol Soc* 2009;107:104-9.