Original Article
Yonsei Med J 2023 Sep;64(9):581-585
https://doi.org/10.3349/ymj.2023.0111
Yonsei Medical Journal
YMJ
pISSN: 0513-5796 · eISSN: 1976-2437

Intramuscular Neural Distribution of Adductor Pollicis Muscle Spasticity in Cadaver Model Regarding Botulinum Neurotoxin Treatment

Kyu-Ho Yi[1,2*], Kang-Woo Lee[1*], Yousun Hwang[3], Min Ho An[4], Hyo-Sang Ahn[1], Hyewon Hu[1], Ji-Hyun Lee[5], and Hyung-Jin Lee[6]

[1]Division in Anatomy and Developmental Biology, Department of Oral Biology, Human Identification Research Institute, BK21 FOUR Project, Yonsei University College of Dentistry, Seoul;
[2]Maylin Clinic (Apgujeong), Seoul;
[3]Haedrin Clinic, Seoul;
[4]Department of Biomedical Informatics, Ajou University School of Medicine, Suwon;
[5]Department of Anatomy and Acupoint, College of Korean Medicine, Gachon University, Seongnam;
[6]Department of Anatomy, Catholic Institute for Applied Anatomy, College of Medicine, The Catholic University of Korea, Seoul, Korea.

Purpose: The adductor pollicis muscle is frequently targeted for botulinum neurotoxin injective treatment for spasticity. However, there are no injective guidelines for delivering injection to the muscle.
Materials and Methods: A method known as the modified Sihler's method was used to stain the adductor pollicis muscle in 16 specimens to reveal intramuscular neural distribution of the muscle.
Results: The most intramuscular neural distribution was located on 1/5 to 3/5 of the muscle regarding midline of 3rd metacarpal bone (0) to the base of the 1st proximal phalanx (5/5). The nerve entry point was mostly located on 0 to 1/5 of the muscle.
Conclusion: The result suggests that botulinum neurotoxin should be delivered at the middle of second metacarpal bone via deep injection.

Key Words: Adductor pollicis muscle, Sihler's method, botulinum neurotoxin, spasticity, injection, intramuscular neural distribution

INTRODUCTION

Botulinum neurotoxin (BoNT) is a toxin produced by the gram-positive anaerobic bacterium called clostridium botulinum. Upon injection into the muscle, BoNT is taken up by endocytosis from the presynaptic nerve terminal at the neuromuscular junction and inhibits acetylcholine release by affecting fusion proteins. As a result, the toxin causes flaccid paralysis by blocking acetylcholine secretion and leads to muscle relaxation, which starts at 5–7 days post-injection and lasts for 12–16 weeks. This relaxation may be followed by longitudinal muscle growth, with the effects potentially lasting up to 6 months.[1]

In recent decades, the treatment applications of BoNT in clinical medicine have increased, particularly in movement disorders, such as dystonia, tremors, and cerebral palsy, as well as autonomic dysfunctions, including excessive sweating and neurogenic bladder. It is also used for treating spasticities caused by conditions, such as multiple sclerosis, spinal trauma, hereditary spastic paraplegia, and pain treatments, such as chronic migraine, that are resistant to medical treatment.

Received: April 26, 2023 **Revised:** June 1, 2023
Accepted: June 19, 2023 **Published online:** August 18, 2023
Co-corresponding authors: Ji-Hyun Lee, PhD, Department of Anatomy and Acupoint, College of Korean Medicine, Gachon University, 1342 Seongnam-daero, Seongnam 13120, Korea.
E-mail: anatomy@gachon.ac.kr and
Hyung-Jin Lee, PhD, Department of Anatomy, Catholic Institute for Applied Anatomy, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seoul 06591, Korea.
E-mail: leehj221@catholic.ac.kr

*Kyu-Ho Yi and Kang-Woo Lee contributed equally to this work.
•The authors have no potential conflicts of interest to disclose.

There are several concerns when it comes to improving the outcomes of BoNT injections into the upper limb muscles, which include: 1) identifying the target muscles, 2) accurately locating the target muscles, and 3) determining the optimal dose. It is quite important to give injection in the right location with minimal doses. The effectiveness of BoNT injection is dependent on the dose and location of the injection. To be most effective, the BoNT must be injected near the neural arborized region, which is the area where there are many neuromuscular junctions. Studies have shown that intramuscular distribution-based injections are more effective in reducing the muscle volume compared to the control groups.[2,3] However, identifying the exact location of small nerves is difficult when using the naked eye. A method called Sihler staining can be used to solve this problem, as it makes the muscle fibers transparent and only stains the nerves.[4] This study aimed to use Sihler staining to understand intramuscular nerve distribution in the adductor pollicis muscle.

MATERIALS AND METHODS

This study was conducted in compliance with the Act on Dissection and Preservation of Corpses of the Republic of Korea (Act number: 14885), and approval was granted by the Institutional Cadaver Research Committee of the College of Medicine at the Catholic University of Korea (MC23EISE0022). This study was conducted in compliance with the principles set forth in the Declaration of Helsinki. Consent was received from the families of the deceased patients before beginning the dissections.

This study used the modified Sihler's method to reveal the intramuscular nerve patterns in the adductor pollicis muscle using eight cadavers. The cadavers used were of Korean origin, with four males and four females, and had a mean age at death of 73.1 years. The 16 adductor pollicis muscles were anatomically aligned, dissected (Fig. 1), harvested (Fig. 2A and B), and stained (Fig. 2C and D) to detect intramuscular neural distribution.

The adductor pollicis muscle was harvested from the 3rd metacarpal bone (0) to base of the 1st proximal phalanx (5/5). The arborization patterns in the muscles were elucidated (Fig. 3) with respect to the vertical length of the muscle with five divisions.

Modified Sihler's staining

The modified Sihler's staining technique was used to study

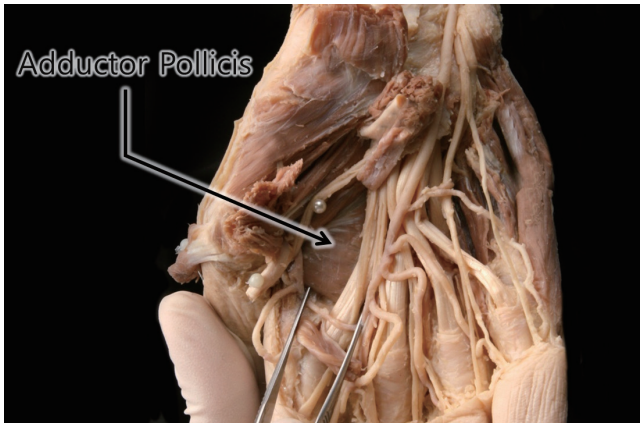

Fig. 1. The adductor pollicis muscle was revealed with delicate dissections. The muscle was located deeply above the 2nd metacarpal bone.

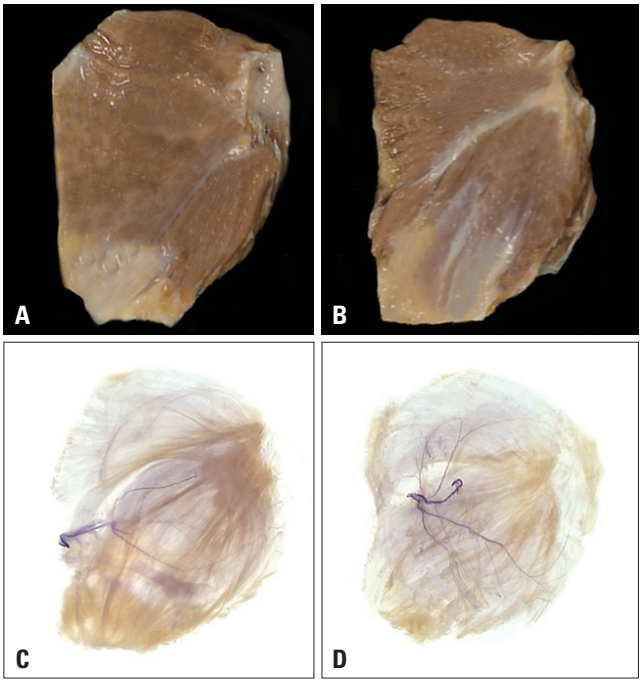

Fig. 2. The harvested specimen of the adductor pollicis muscle was harvested from the midline of 3rd metacarpal bone (0) to base of the 1st proximal phalanx (5/5). The adductor pollicis muscle was harvested (A, deep and B, superficial) and stained (C, deep and D, superficial).

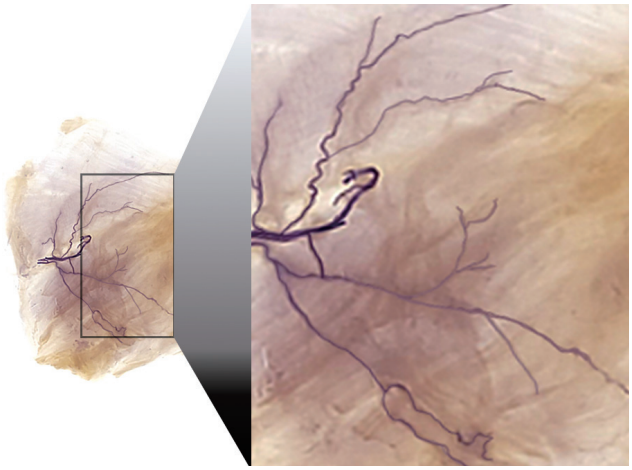

Fig. 3. The intramuscular neural distribution of the adductor pollicis muscles was observed. The enlarged panel demonstrates neural arborization of the adductor pollicis muscle.

https://doi.org/10.3349/ymj.2023.0111

the intramuscular neural arborization pattern of the adductor pollicis muscles. The muscle specimens were first fixed in non-neutralized formalin for a month. They were then soaked for three weeks in a solution comprised of 3% potassium hydroxide, to which a single drop of 30% hydrogen peroxide per liter was added, in order to make them transparent. They were then decalcified for a week in a solution composed of 10% glycerin and 7% glacial acetic acid. After that, the muscles were stained for three days in a solution of 10% Ehrlich's hematoxylin and glycerin. The nerves were made visible by resoaking in the decalcification solution. Finally, the muscles were displayed by soaking them in increasing concentrations of glycerin solution (40%, 60%, 80%, and 100%).

RESULTS

Locations of nerve entry points

Fifteen of the 16 specimens had a nerve entry point located between 0 to 1/5, while the one specimen had a nerve entry point between 1/5 to 2/5 of the muscle (Fig. 4).

Intramuscular arborization patterns

Thirteen out of the 16 adductor pollicis muscles had the largest arborization patterns, located on 1/5 to 3/5 of the muscle (Fig. 4). Three adductor pollicis muscle had the largest arborization patterns in the 2/5 to 3/5 part of the muscle. A schematic image of the injection point of the adductor pollicis muscle is shown in Fig. 5. Injection should be placed above the middle of the 2nd metacarpal bone.

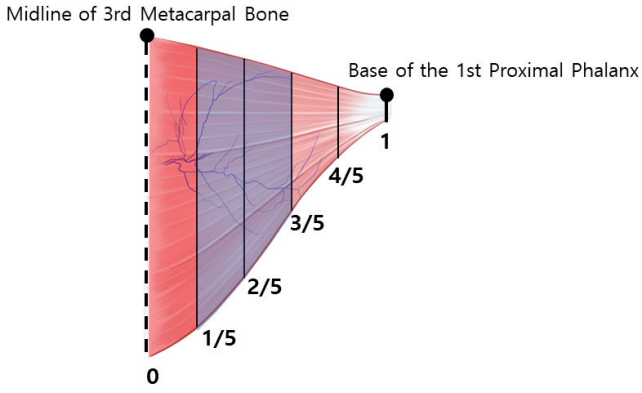

Fig. 4. The adductor pollicis muscles had the largest arborization patterns, located on 1/5 to 3/5 (blue shaded) of the muscle from the midline of 3rd metacarpal bone (0) to the base of the 1st proximal phalanx (5/5). The nerve entry point was mostly located on 0 to 1/5 (red shaded) of the muscle, an area which should be avoided to prevent nerve trunk damage.

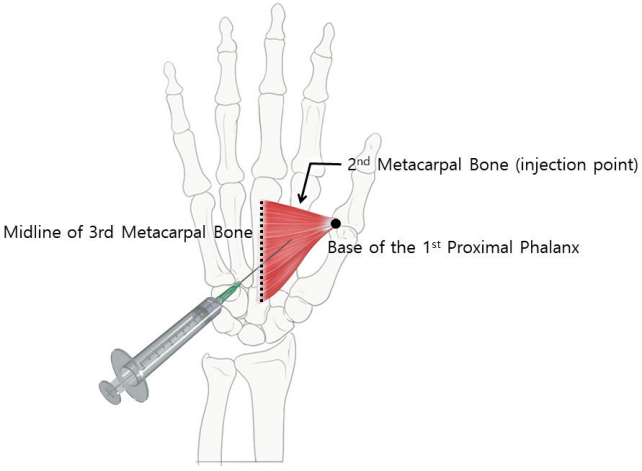

Fig. 5. The schematic image suggests that BoNT should be delivered in the level of second metacarpal bone with deep injection.

DISCUSSION

The evaluation and management of patients presenting with spasticity are challenging due to the deep located nature of the adductor pollicis muscle. Adductor pollicis muscle is located in the hand and is responsible for adducting the thumb. The muscle has two heads, the oblique head and the transverse head, and is innervated by the deep branch of the ulnar nerve. The origin of the transverse head is the front portion of the third metacarpal, while the oblique head originates from the bases of the second and third metacarpals as well as the nearby trapezoid and capitate bones. The insertion point is on the inside of the base of the thumb's proximal phalanx and the ulnar sesamoid. The muscle lies beneath the long flexor tendons and lumbrical muscles in the thenar compartment, and overlies the metacarpal bones and interosseous muscles.[5]

Adduction of the thumb is mainly produced by the adductor pollicis muscle, but it can also be assisted by the flexor pollicis brevis and opponens pollicis muscle. A compromised adductor pollicis can be tested using Froment's sign, and its strength can be measured in neuromuscular monitoring by stimulating the ulnar nerve.[6] Wall, et al.[7] presented a therapeutic option for the treatment of thumb-in-palm deformity in cerebral palsied children using BoNT of the adductor pollicis muscle. The study assessed the early results of a clinical trial in five hemiparetic cerebral palsy children using a prospective non-trialist-biased study design based on an independent panel assessment of pre- and post-intervention photographic and videotaped records of hand function and appearance, grip dynamometry, and goniometry. The results showed that all cases improved in terms of both function and appearance, with statistical significance. Ever since the study by Wall, et al.[7] first presented the effectiveness of BoNT injection at adductor pollicis, many articles have been published.

Study by Autti Rämö, et al.[8] discussed the lack of universal guidelines for the optimal dosing of BoNT in the upper extremity. The study suggested that clinical improvement did not directly correlate with the level of denervation, indicating that the doses should be calculated individually based on the

treatment aims. The study adopted a semiquantitative clinical assessment scale, the upper limb physician's rating scale, to assess the efficacy of BoNT treatment. They emphasized the importance of appropriate dosing, especially in the muscles involved in finger movements, to prevent impairments in grip strength and the development of swan neck deformity in children with dystonic involvement.[8] They assumed that the appropriate dosing of BoNT for the thumb muscles, including adductor pollicis. The study suggested that smaller doses are required for the muscles, and that it may be preferable to treat only one of these muscles if the thumb is involved in grasping. The recommended dosing paradigm is 5 U BoNT if the thumb actively participates in grasping, 7.5 U BoNT if the thumb has some active abduction but tends to go into the palm in function, and 10 U BoNT if the thumb is not involved in grasping and has no active abduction. Fehlings, et al.[9] used the amount of BoNT based on the weight of the patient, with 1 Unit/kg. Fehlings, et al.[9] emphasized that in their experience, there was no need to increase the dose beyond 10 U BoNT, which is far less than the upper limit suggested by Russman, et al.[10]

Children with cerebral palsy can experience more upper limb problems than lower limb problems, including higher rates of dystonia, weakness, sensory impairment, and selective motor control problems. These issues can decrease the effectiveness of BoNT-therapy, and lead to limited and shorter-lasting results. The best candidates for BoNT therapy should be able to actively move their fingers and activate and strengthen their antagonist muscles to take advantage of the temporary BoNT induced muscle weakness. Good grip strength is also important, as BoNT injections may reduce the grip strength. It is also crucial to carefully analyze family-identified limitations, problems, and goals. It is recommended to use small-volume, high-concentration injections with ultrasound control. The diffusion of BoNT is limited to a few centimeters from the injection site.[11,12] Borodic, et al.,[11] in their study, found that when 10 U of the toxin was injected into the longissimus muscle of rabbits, the BoNT diffusion could spread up to 4.5 cm from the site of injection. Furthermore, it is crucial to acknowledge that upon the nerve's penetration into the muscle, it gives rise to an extensive network of delicate branches that extend distally. It is worth emphasizing that the diffusion of the BoNT has the capacity to adequately encompass a broad area from the injection site, especially within the region exhibiting the highest density of neural branching.

In the present study, we have also shown where the injection should be made within the muscle, as injecting BoNT into the wrong area can lead to the need for larger amounts of the toxin and decreased effectiveness due to the formation of antibodies.[13-15] To avoid these negative effects, it is crucial to inject smaller amounts directly into the correct area.

Currently, there is no agreed upon location for administering BoNT injections in the adductor pollicis muscle. Our study employed the Sihler staining technique, which can potentially overcome the limitations of traditional dissection methods. We have demonstrated that using this method on the adductor pollicis muscle allows for accurate and comprehensive understanding of the muscle's nerve distribution.

ACKNOWLEDGEMENTS

The authors sincerely thank those who donated their bodies to science so that anatomical research could be performed. Results from such research can potentially increase mankind's overall knowledge that can then improve patient care. Therefore, these donors and their families deserve our highest gratitude.

This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korean government (MSIP) (NRF-2020R1A2B5B0100223811).

AUTHOR CONTRIBUTIONS

Conceptualization: Kyu-Ho Yi and Kang-Woo Lee. Data curation: Yousun Hwang and Min Ho An. Formal analysis: Hyo-Sang Ahn and Hyewon Hu. Funding acquisition: Hyo-Sang Ahn and Hyewon Hu. Investigation: Ji-Hyun Lee and Hyung-Jin Lee. Methodology: Kyu-Ho Yi. Project administration: Kyu-Ho Yi. Resources: Kyu-Ho Yi. Software: Kyu-Ho Yi. Supervision: Kyu-Ho Yi. Validation: Kyu-Ho Yi. Visualization: Kyu-Ho Yi. Writing—original draft: Kyu-Ho Yi and Kang-Woo Lee. Writing—review & editing: Ji-Hyun Lee and Hyung-Jin Lee. Approval of final manuscript: all authors.

ORCID iDs

Kyu-Ho Yi https://orcid.org/0000-0001-5572-1364
Kang-Woo Lee https://orcid.org/0000-0001-8654-8306
Yousun Hwang https://orcid.org/0000-0001-5688-1992
Min Ho An https://orcid.org/0000-0003-2773-9756
Hyo-Sang Ahn https://orcid.org/0009-0003-3564-5562
Hyewon Hu https://orcid.org/0000-0001-5460-6428
Ji-Hyun Lee https://orcid.org/0000-0003-3732-2698
Hyung-Jin Lee https://orcid.org/0000-0002-3082-935X

REFERENCES

1. Childers MK, Brashear A, Jozefczyk P, Reding M, Alexander D, Good D, et al. Dose-dependent response to intramuscular botulinum toxin type A for upper-limb spasticity in patients after a stroke. Arch Phys Med Rehabil 2004;85:1063-9.
2. Gracies JM, Lugassy M, Weisz DJ, Vecchio M, Flanagan S, Simpson DM. Botulinum toxin dilution and endplate targeting in spasticity: a double-blind controlled study. Arch Phys Med Rehabil 2009;90:9-16.e2.
3. Van Campenhout A, Verhaegen A, Pans S, Molenaers G. Botulinum toxin type A injections in the psoas muscle of children with cerebral palsy: muscle atrophy after motor end plate-targeted injections. Res Dev Disabil 2013;34:1052-8.
4. Oddy MJ, Brown C, Mistry R, Eastwood DM. Botulinum toxin injection site localization for the tibialis posterior muscle. J Pediatr Orthop B 2006;15:414-7.
5. Chang L, Blair WF. The origin and innervation of the adductor pollicis muscle. J Anat 1985;140(Pt 3):381-8.

6. Caetano EB, Nakamichi YDC, Alves de Andrade R, Sawada MM, Nakasone MT, Vieira LA, et al. Flexor pollicis brevis muscle. anatomical study and clinical implications. Open Orthop J 2017;11:1321-9.
7. Wall SA, Chait LA, Temlett JA, Perkins B, Hillen G, Becker P. Botulinum A chemodenervation: a new modality in cerebral palsied hands. Br J Plast Surg 1993;46:703-6.
8. Autti-Rämö I, Larsen A, Taimo A, von Wendt L. Management of the upper limb with botulinum toxin type A in children with spastic type cerebral palsy and acquired brain injury: clinical implications. Eur J Neurol 2001;8 Suppl 5:136-44.
9. Fehlings D, Rang M, Glazier J, Steele C. Botulinum toxin type A injections in the spastic upper extremity of children with hemiplegia: child characteristics that predict a positive outcome. Eur J Neurol 2001;8 Suppl 5:145-9.
10. Russman BS, Tilton A, Gormley ME Jr. Cerebral palsy: a rational approach to a treatment protocol, and the role of botulinum toxin in treatment. Muscle Nerve Suppl 1997;6:S181-93.
11. Borodic GE, Ferrante R, Pearce LB, Smith K. Histologic assessment of dose-related diffusion and muscle fiber response after therapeutic botulinum A toxin injections. Mov Disord 1994;9:31-9.
12. Ramirez-Castaneda J, Jankovic J, Comella C, Dashtipour K, Fernandez HH, Mari Z. Diffusion, spread, and migration of botulinum toxin. Mov Disord 2013;28:1775-83.
13. Kinnett D. Botulinum toxin A injections in children: technique and dosing issues. Am J Phys Med Rehabil 2004;83(10 Suppl):S59-64.
14. Hsu TS, Dover JS, Arndt KA. Effect of volume and concentration on the diffusion of botulinum exotoxin A. Arch Dermatol 2004;140:1351-4.
15. Lepage D, Parratte B, Tatu L, Vuiller F, Monnier G. Extra- and intramuscular nerve supply of the muscles of the anterior antebrachial compartment: applications for selective neurotomy and for botulinum toxin injection. Surg Radiol Anat 2005;27:420-30.