Anatomical look into OnabotulinumtoxinA injection for chronic migraine headache

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Introduction

Migraine headaches (MH) affect one in seven Americans annually, and are a leading cause of outpatient and emergency visits [1] . The migraine spectrum includes episodic migraine (EM) and chronic migraine (CM).

OnabotulinumtoxinA (BoNT-A) injection is a commonly used preventive treatment for Migraine worldwide. In the United States, OnabotulinumtoxinA is the only FDA approved treatment for Chronic Migraine [2] after two large studies called Phase III REsearch Evaluating Migraine Prophylaxis Therapy (PREEMPT) [3,4] .

The mechanism of action of BoNT-A is multifactorial, with several postulated theories. One mechanism is the inhibition of peripheral sensitization by the reduction of neuropeptide and neurotransmitter exocytosis from peripheral sensory neurons, thereby reducing central sensitization.[5] Another purported mechanism is the reduction of local sensitivity of muscle nociceptors and decreased blood glutamate concentration following injection of craniofacial muscles, which has been demonstrated in animal models.[6]

In addition, BoNT-A acts on neuromuscular transmission, particularly involving *SNAP-25* cleavage within the carboxyl-terminus, preventing SNARE-mediated vesicle fusion ultimately leading to inhibition of calcitonin gene-related peptide (CGRP) release, and impairing delivery of transient receptor potential (TRP) channels including TRPV1 or TRPA1 to the terminal membrane.[7,8] BoNT-A also has been shown to inhibit C-, rather than Aδ- type meningeal nociceptors, and it is this inhibition of meningeal and trigeminovascular nociceptors to the spinal trigeminal nucleus which aid in migraine relief [9] .

Injection technique is slightly different among providers, but PREEMT protocol designed based on ***intramuscular*** injection of BoNT-A . We wanted to examine the hypothesis of weather the current technique of injection[10] is going end up ***intramuscular*** in all of the cases. In this study we looked at the distance of the muscles fascia to skin surface in whom BoNT-A is injected in four different body mass index category (BMI).

Methods

- We retrospectively looked at the patients aged 18-89 who have received computed tomography (CT) scans of the head and neck that have been read as normal
- . Then based on BMI, patients were categorized in 4 groups:

(1) normal weight (BMI < 25)
(2) overweight (BMI 25-30)
(3) obese (BMI 30-35)
(4) severely obese (BMI > 35)

Five patients were randomly selected from each of these groups for the measurement in the study.

- Based on published injection protocols for BoNT-A, four standardized locations were chosen in order to obtain measurements in millimeters from the skin surface to the underlying muscle fascia. These sites included: (A) frontalis muscle; (B) temporalis muscles; (C) semispinalis capitis muscles; and (D) trapezius muscles (*Figure 1*).
- For each patient, measurements were taken bilaterally, and data from each facial side was included for analysis.

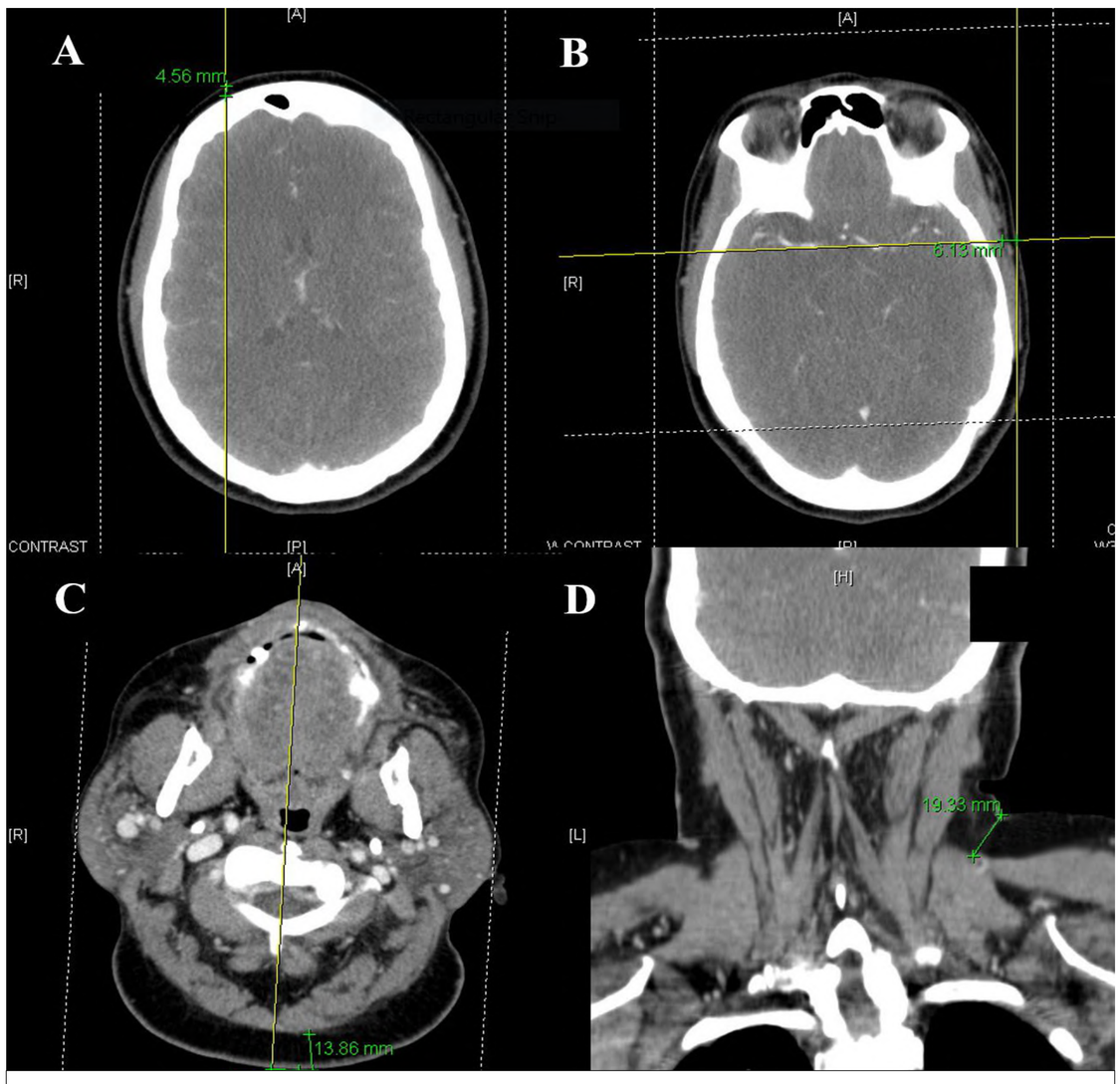

Figure 1 *-Measurement of the depth of muscles in four main injection site of OnabotulinumtoxinA*

Results

Results of the study are shown in *Figure 2*. Basically with increasing BMI, the thickness of the subcutaneous layer increases in the head and neck, resulting in a greater distance between the skin surface and the muscle fascia of muscles that are targeted for injection in standard chronic migraine BoNT-A injection protocols. Because it is a pilot study, it is limited by its small sample size. However, even with the small sample size, significant differences were seen in the distance between the skin surface and the underlying muscle fascia between the different BMI populations at each of the sites studied.

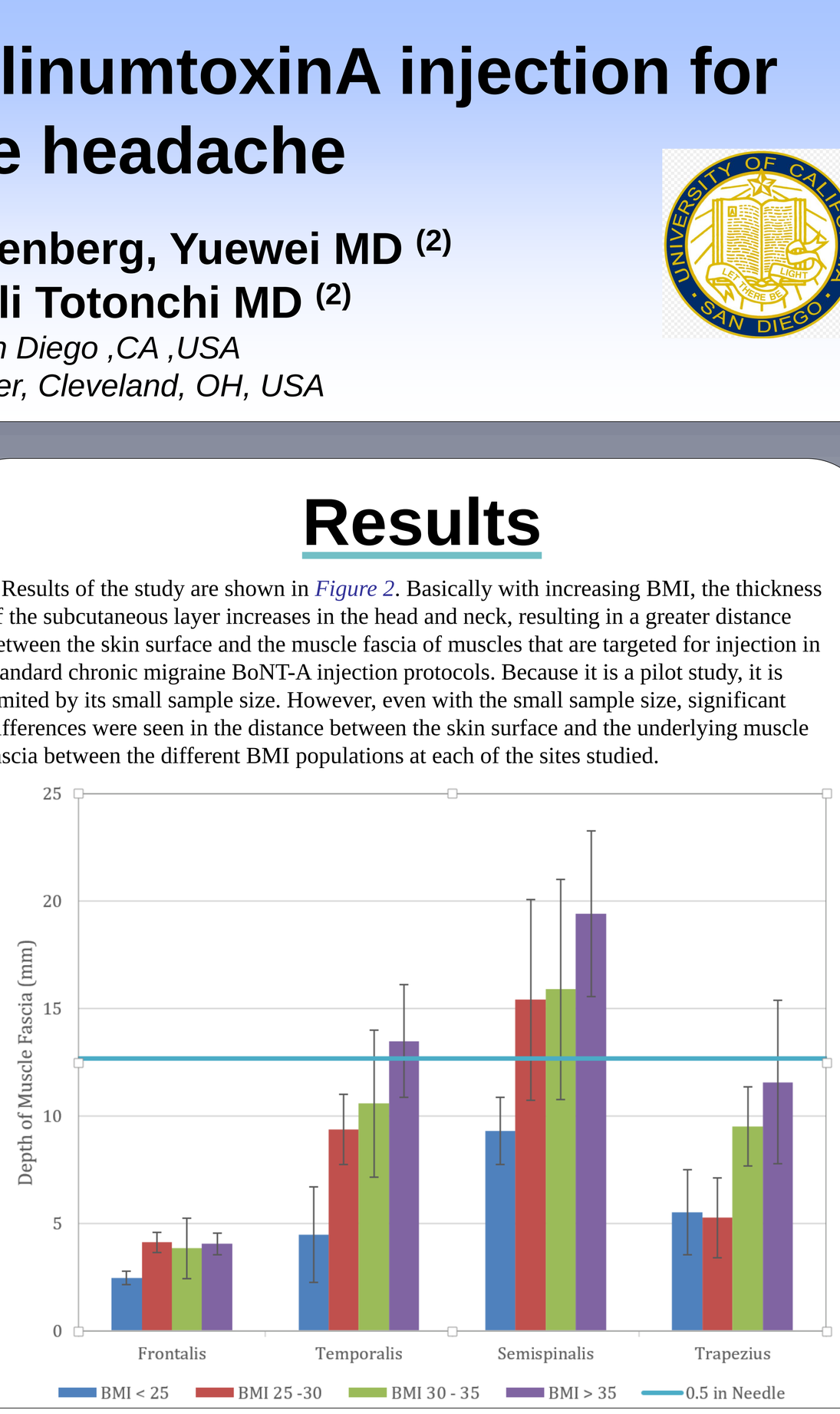

Figure2 - *Comparison of muscle depths of frontalis, temporalis, semispinalis capitis, and trapezius muscles in different BMI to the length of a 0.5in needle typically used to administer botulinum toxin in standard chronic migraine injection protocols.*

Conclusions

Although mechanism of action for the BoNT-A in migraine treatment is still matter of debate, FDA approved intramuscular injection as standard treatment based on PREEP trials . The recommended needle size for injection is 0.5 inch (12.7 mm) which most of injectors use it.[10]

Based on our study, at least in some patients (higher BMI) and some locations (cervical paraspinal and temporalis), using a 0.5-inch needle will not provide full intramuscular access of BoNT-A. We believe the treatment paradigm should also take into account body habitus and BMI as certain muscles may not have complete intramuscular uptake of toxin. Based on our observations in clinical practice, by implementing this simple technical change regarding the needle length, response rates to BoNT-A for the treatment for CM may be improved while limiting some of the most common reported complications in cervical paraspinal (neck) muscles , including neck pain after injection . Plus intramuscular injection causes less pain and discomfort compare to superficial injections. More importantly until a newer randomized control trials show the potential efficacy of superficial injection of BoNT-A(e.g. subcutaneous) , we need to follow the ***intramuscular*** injection which approved by PREEMT trials .

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