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# Targeted Botulinum Toxin Protocol for Refractory Chronic Headache Attributed to TMD: A Preliminary Case Series

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## OBJECTIVE

To evaluate the feasibility and preliminary outcomes of a targeted 100-unit BoNT-A protocol in patients with refractory chronic headache attributed to TMD, focusing on:

- Pain (Visual Analogue Scale - VAS)
- TMD-related Quality of Life (OHIP-TMD)
- Central Sensitization (CSI)
- Sleep Quality (PSQI)

## INTRODUCTION

- Chronic headache attributed to Temporomandibular Disorder (TMD) that is unresponsive to standard treatments causes significant disability.
- This condition is frequently associated with central sensitization, a state where the nervous system becomes hypersensitive to pain.
- Botulinum toxin type A (BoNT-A) has shown efficacy in TMD and primary headaches, but its specific role in this refractory condition remains unclear.

## METHODS

### Study Design

- A prospective, pilot case series.

### Participants

- Seven patients diagnosed with refractory chronic headache attributed to TMD.

### Intervention: 100U BoNT-A Protocol (Fig. 1)

- A standardized 100U protocol of BoNT-A (Botox®) was administered bilaterally.
- Masseter: 25U per side
- Temporalis: 10U per side
- Temporalis Tendon: 5U per side
- Corrugator: 4U per side
- Frontalis: 6U per side

### Assessments

- Performed at Baseline, 2 weeks, and 2 months post-treatment using VAS, OHIP-TMD, CSI, and PSQI.

## POSSIBLE MECHANISM OF ACTION

BoNT-A may alleviate pain through multiple pathways:

- Neuromuscular Blockade: Inhibits acetylcholine release, reducing muscle tension.
- Inhibition of Neuropeptides: Blocks the release of pro-inflammatory mediators like CGRP and Substance P.
- Reduction of Neuroinflammation: Attenuates microglial activation in the central nervous system.
- Axonal Transport: Evidence suggests BoNT-A may be transported to central ganglia (e.g., trigeminal), exerting a wider effect.

## CONCLUSIONS

This targeted 100U BoNT-A protocol appears to be a safe and highly promising therapeutic option for refractory chronic headache attributed to TMD.

The protocol achieved complete pain relief in all participants and showed significant improvements in quality of life, central sensitization, and sleep quality. Larger controlled studies are required to validate these preliminary findings.

## RESULTS

### Pain Control

- All patients (100%, n=7) completed the protocol and follow-up.
- The treatment was well tolerated with only mild, transient adverse effects.

Mean scores show improvement across all measures (Table 1).

Table 1: Results

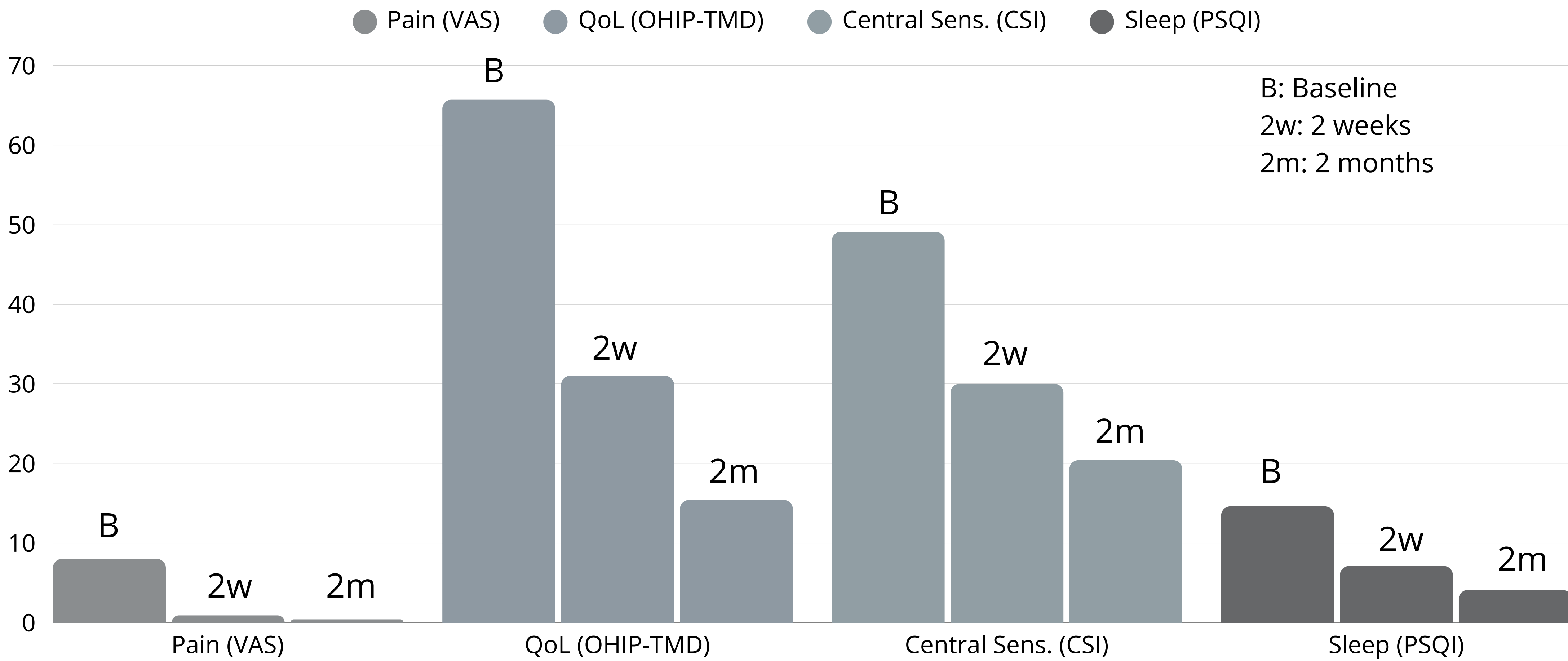


Fig.1. BoNT-A Protocol

1 Yoshida K. Sphenopalatine Ganglion Block with Botulinum Neurotoxin for Treating Trigeminal Neuralgia Using CAD/CAM-Derived Injection Guide. J Oral Facial Pain Headache. 2020;34(2):135-40. 2 Peck J, Zeien J, Patel M, Cornett EM, Berger AA, Hasoon J, et al. Review of Interventional Therapies for Refractory Pediatric Migraine. Heal Psychol Res. 2022;10(5). 5 Morenilla-Palao C, Planells-Cases R, García-Sanz N, Ferrer-Montiel A. Regulated Exocytosis Contributes to Protein Kinase C Potentiation of Vanilloid Receptor Activity \*. J Biol Chem [Internet]. 2004 Jun 11;279(24):25665-72. Available from: <https://doi.org/10.1074/jbc.M311515200> 6 Chen W-J, Niu J-Q, Chen Y-T, Deng W-J, Xu Y-Y, Liu J, et al. Unilateral facial injection of Botulinum neurotoxin A attenuates bilateral trigeminal neuropathic pain and anxiety-like behaviors through inhibition of TLR2-mediated neuroinflammation in mice. J Headache Pain [Internet]. 2021;22(1):38. Available from: <https://doi.org/10.1186/s10194-021-01254-2> 7 Matsuka Y, Yokoyama T, Yamamoto Y, Suzuki T, Dwi Fatmawati NN, Nishikawa A, et al. Application of Purified Botulinum Type A Neurotoxin to Treat Experimental Trigeminal Neuropathy in Rats and Patients with Urinary Incontinence and Prostatic Hyperplasia. Ahmed SA, editor. J Toxicol [Internet]. 2012;2012:648384. Available from: <https://doi.org/10.1155/2012/648384> 8 Pearl C, Moxley B, Perry A, Demian N, Dallaire-Giroux C. Management of Trigeminal Neuralgia with Botulinum Toxin Type A: Report of Two Cases. Dent J. 2022;10(11). 9 Waskitho A, Yamamoto Y, Raman S, Kano F, Yan H, Raju R, et al. Peripherally Administered Botulinum Toxin Type A Localizes Bilaterally in Trigeminal Ganglia of Animal Model. Vol. 13, Toxins. 2021.