

Is Botulism Toxin Useful In Myofascial Pain Syndrome

Brian Knight MD, FRCPC
Pain Clinic
Misericordia Hospital
Edmonton, Alberta

Conflict of Interest Disclosure

- I have received honoraria for educational events from:
 - Purdue Pharma
 - Pfizer
 - Janssen-Ortho
 - Allergan
 - Valiante
 - Shire
 - Medtronic
 - Bayer

Problems With Studying Myofascial Pain Syndrome

- We don't really know what it is
- Some of us doubt or flat out don't believe in it
- If it exists it is incredibly common
 - Probably the most common chronic disease
- There is no consensus about the best way to treat it

Problems Involving Studying Any Procedure Involving Needling

- Hard to blind
- Ethical issues about injecting placebo
- Can you have a placebo with needling
 - Acupuncture effect?
 - Systemic endorphin release with needling
 - fMRI, Evoked potential changes
 - Local effect on muscle of needling

Two Different Approaches Trigger Point Injection in MFPS

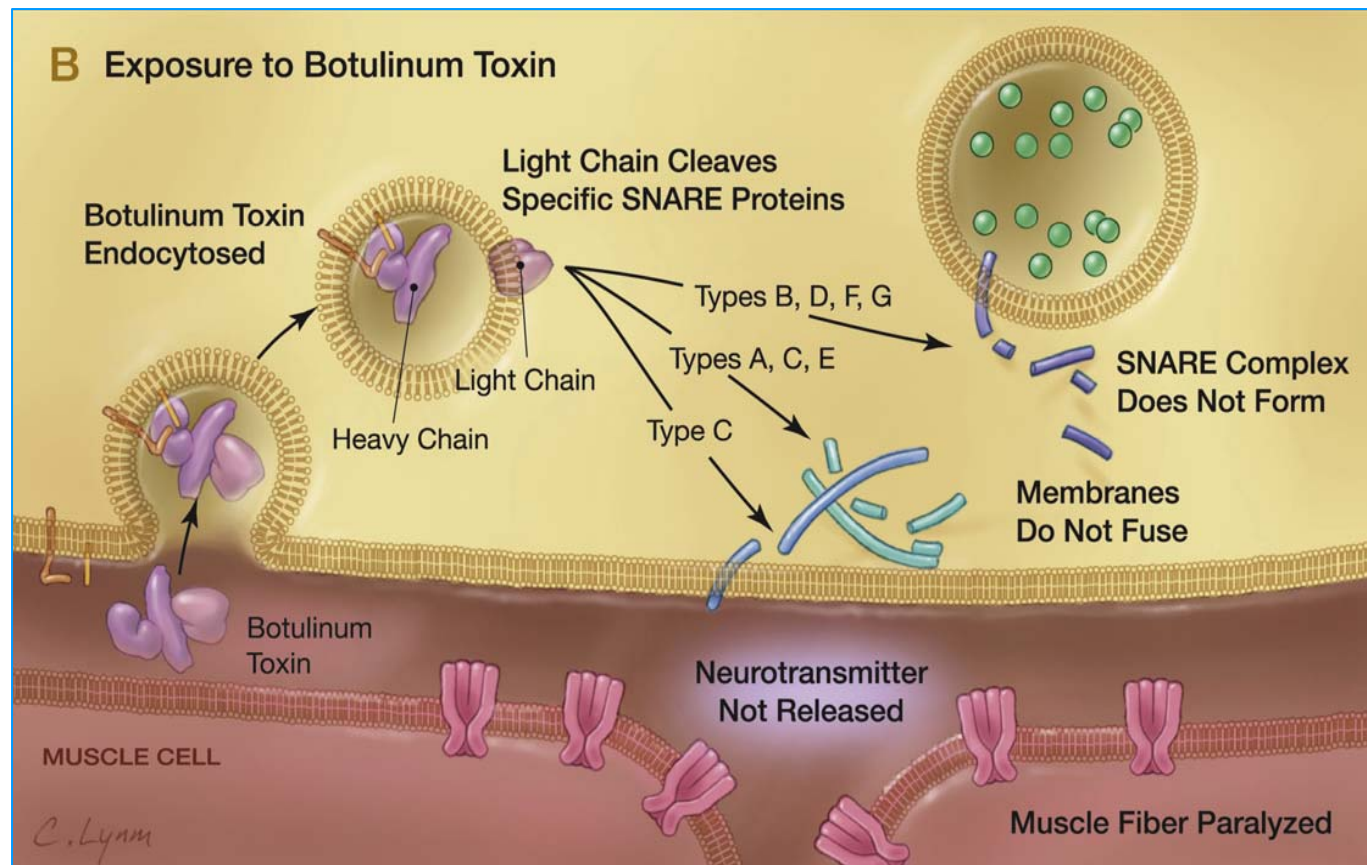
- Stick the needle in the painful point
- Use the needle to relax muscle shortening associated with or causing abnormal posturing

Mandatory Botox Joke

...THE MANY FACES OF THE BOTOX BABE...

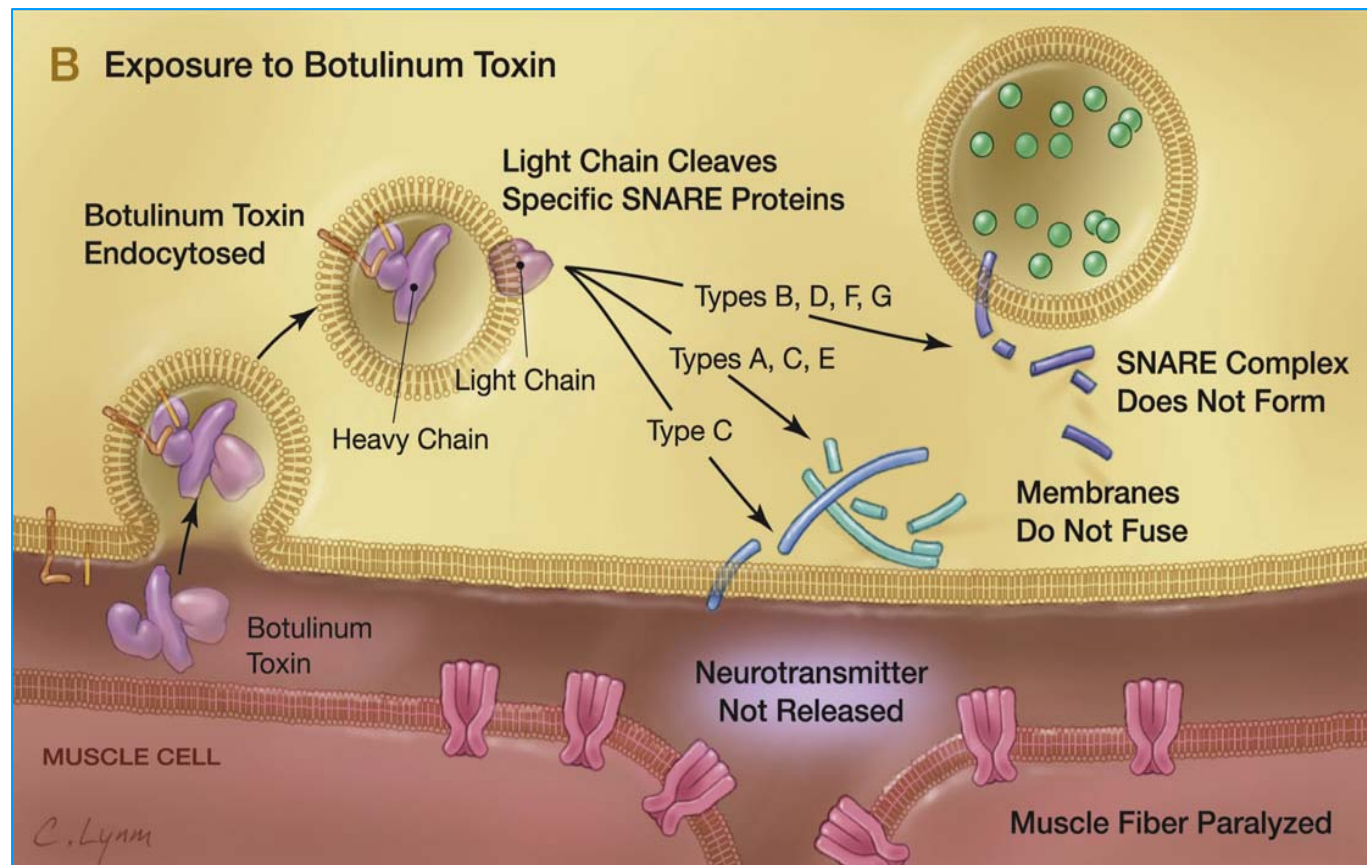


Botulinum Toxin Mechanisms of Action: Current Hypothesis



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Botulinum Toxins in Clinical Use

- Botulinum toxin type A (BTX-A)
 - BOTOX®
 - Dysport®
- Botulinum toxin type B
 - Myobloc™

Antinociceptive Effects Beyond Muscle Relaxation

- Blockade of neuromuscular transmission to relax muscle and reduce spasms is insufficient to explain levels of pain relief achieved¹
- Antinociceptive benefits of botulinum toxin therapy may indicate alternate/additional mechanisms of action¹⁻³
- Botulinum toxin A may directly affect synaptic activity in the CNS (animal studies)³

1. Hallett M. *Ann Neurol.* 2000;48:7-8.

2. Foster L, et al. *Neurology.* 2001;56:1290-1292.

3. Gobel, et al. *Pain.* 2001;91:195-199.

Antinociceptive Effects Beyond Muscle Relaxation

- Substance P
- Calcitonin Gene Related Peptide (CGRP)

Antinociceptive Effects of Botulinum Toxin Type A in Clinical Trials

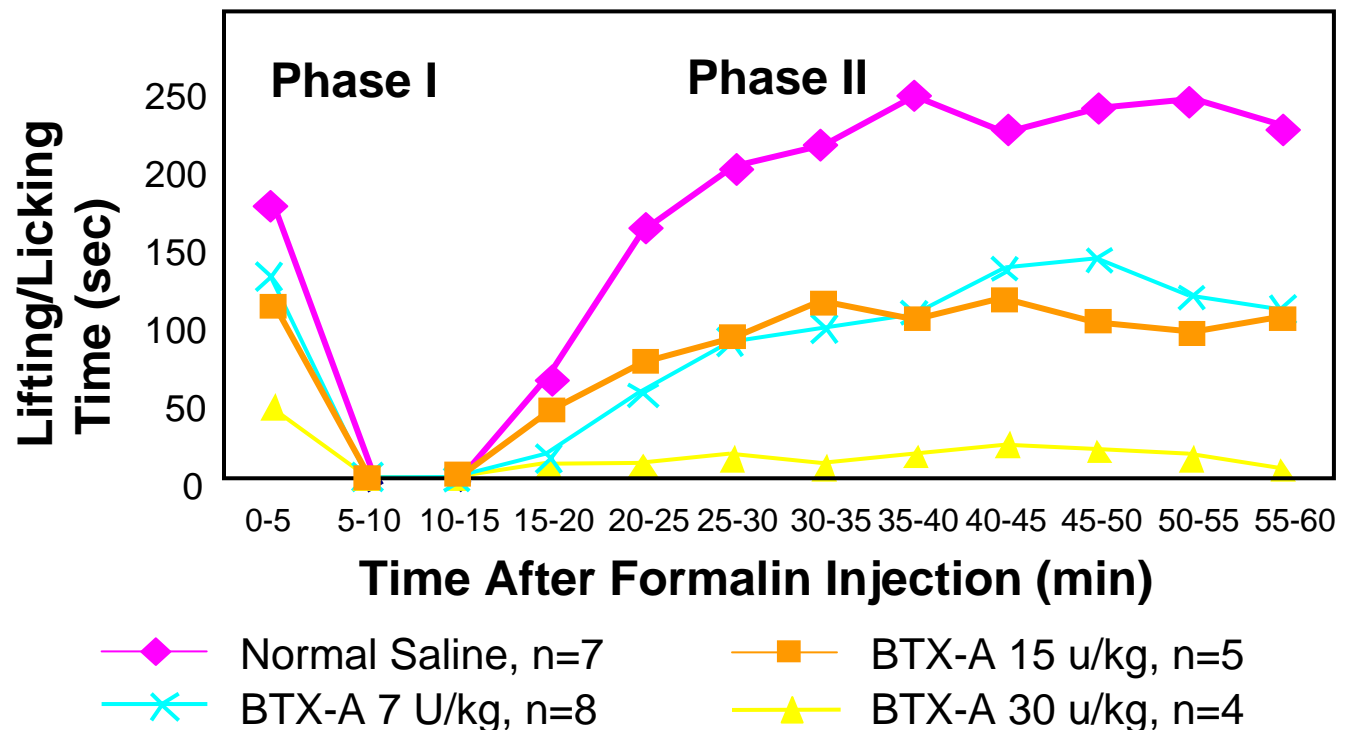
- Pain relief was a major treatment benefit in therapy for patients with movement disorders
 - Odergren et al. *Scand J Rehabil Med.* 1994
 - Greene et al. *Neurology.* 1990
 - Brin et al. *Adv Neurol.* 1988
 - Tsui et al. *Can J Neurol Sci.* 1987
- Myoclonus-associated pain relief
 - Polo and Jabbari. *Mov Disord.* 1994
- Adductor-release surgery pain prophylaxis
 - Barwood et al. *Dev Med Child Neurol.* 2000
- Whiplash-associated neck pain
 - Freund and Schwartz. *Headache.* 2000

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Dose-Dependent Pain Perception in Rats After BTX-A Injection

Dose-Dependent Pain Perception as Measured by Peripheral Injections of BTX-A or Saline

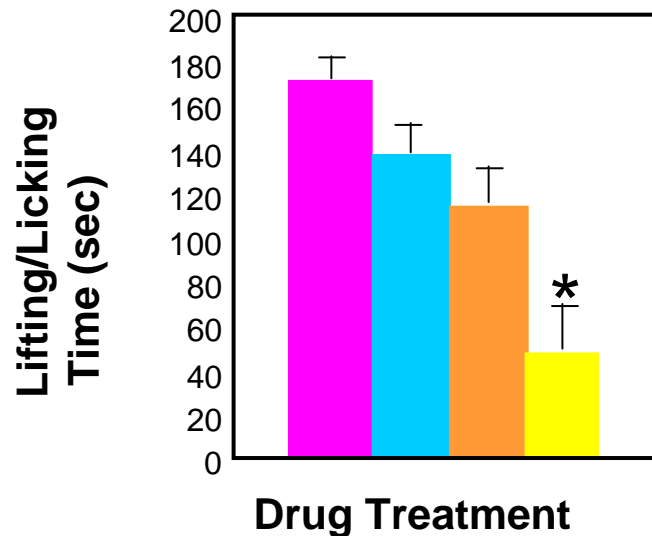


*BTX-A = botulinum toxin type A.

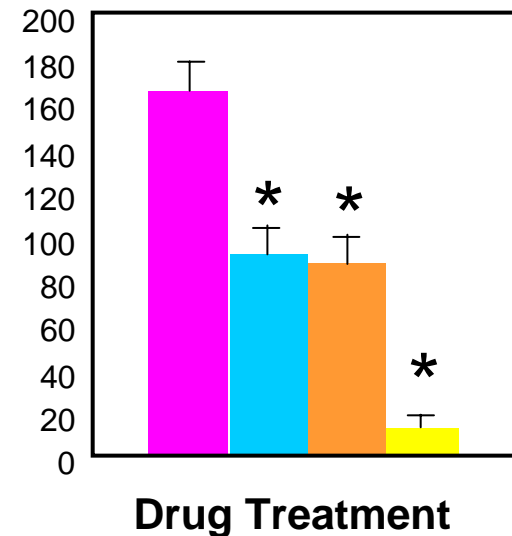
Aoki KR. *J Neurol.* 2001;248(Suppl 1):1/3-1/10.

Dose-Dependent Pain Perception in Rats After BTX-A Injection (Cont'd)

The Effect of BTX-A (s.c.) on Formalin Pain Phase I



The Effect of BTX-A (s.c.) on Formalin Pain Phase II



Data represent mean \pm SEM.
* P <0.05.

Aoki KR. *J Neurol*. 2001;248(Suppl 1):1/3-1/10.

- Normal Saline, n=7
- BTX-A 7 U/kg, n=8
- BTX-A 15 U/kg, n=5
- BTX-A 30 U/kg, n=4

Botulinum Toxin Type A: Recent Clinical Trials in Neck and Back Pain

Study, Year	Type	Patient N	Diagnosis	Comparator (if applicable)
Cheshire, 1994	Randomized	6	MPS (cervical paraspinal/shoulder girdle)	Normal saline
Wheeler, 1998	Randomized	33	MPS (cervicothoracic)	Normal saline
Porta, 2000	Randomized	40	MPS, chronic muscle spasm	Methylprednisolone
Lang, 2000	Open label	72	MPS	—
Barwood, 2000	Randomized	16 (children)	Spastic type cerebral palsy (postoperative)	Normal saline
Wissel, 2000	Open label	60	Pain related to spasticity	—
Freund, 2000	Randomized	26	Whiplash	Normal saline
Wheeler, 2001	Randomized	50	Chronic neck pain	Normal saline
Foster, 2001	Randomized	31	Chronic low back pain	Normal saline

Botulinum Toxin Type A in Refractory Cervicothoracic MPS: A Randomized Study

Wheeler, 1998

- 33 patients with chronic unilateral neck pain
- BTX-A (50 or 100 U in 2 cc of saline) or 2 cc saline injected into single most sensitive trigger point
- Outcomes measured:
 - Pressure threshold
 - NPAD score
 - Patient's subjective assessment
 - Clinical improvement

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Botulinum Toxin Type A in Refractory Cervicothoracic MPS: A Randomized Study

Wheeler, 1998

- No significant differences between the 3 treatment groups at baseline
- Among all patients who received a follow-up 100 U BTX-A injection
 - 80% and 75%, respectively, of the initial 50 and 100 U BTX-A groups became asymptomatic
 - 25% of the initial placebo injection group became asymptomatic
- Enough patients became asymptomatic after a 2nd injection to warrant additional studies

Pilot Study of Botulinum Toxin Type A in MPS

Lang, 2000

- Open-label study of global efficacy of BTX-A (N=72)
- Novel injection technique (20-600 U at 20 U/mL)
 - Midbelly of affected muscles
 - Upper trapezius injected in grid pattern
 - Levator and suboccipital paraspinals received 2 infiltrations
- Improvement rated by physician as excellent, good, fair, poor

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Pilot Study of Botulinum Toxin Type A in MPS: Global Symptomatic Improvement



Botulinum Toxin Type A and Chronic Low Back Pain: A Randomized Study

Foster, 2001

- Randomized, double-blind trial involving 31 patients
- Lateralized chronic low back pain (≥ 6 months duration)
- BTX-A vs. normal saline
- 40 U into 5 sites
- Outcome measures:
 - Oswestry Low Back Pain Questionnaire (OLBPQ)
 - Visual analog scale (VAS)

Botulinum Toxin Type A and Chronic Low Back Pain: Results

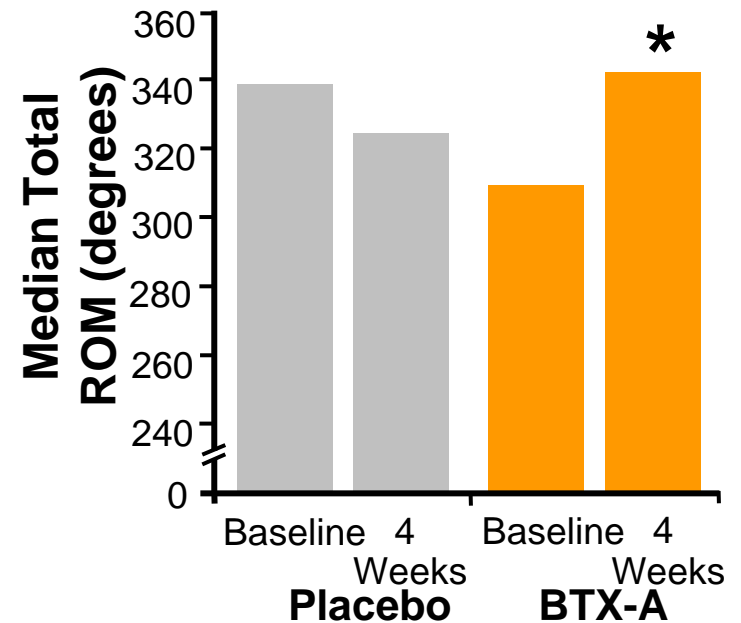
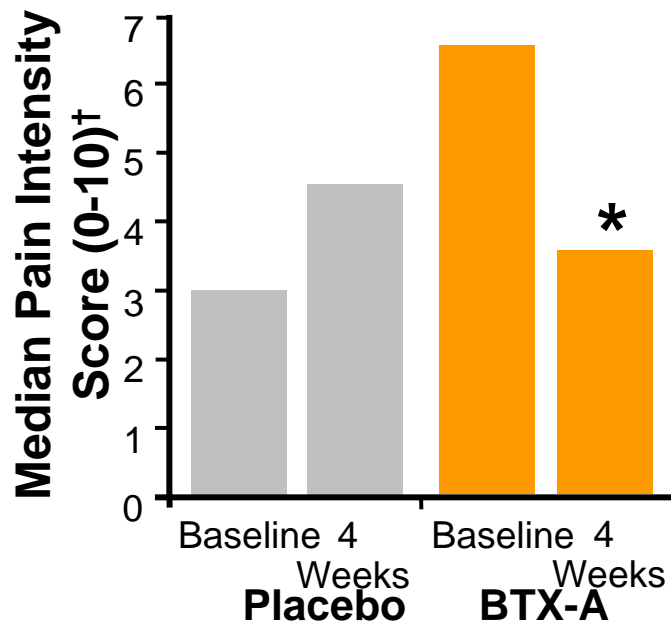
- More patients reported >50% pain relief on VAS with BTX-A than with placebo
 - At 3 weeks: 73.3% vs. 25% ($P=0.012$)
 - At 8 weeks: 60% vs. 12.5% ($P=0.009$)
- Improvement at 8 weeks in OLBPQ: BTX-A, 66.7% vs. placebo, 18.8% ($P=0.011$)

Botulinum Toxin Type A in Whiplash

Freund and Schwartz, 2000

- Randomized, double-blind, placebo-controlled
- 26 patients with chronic whiplash-associated headache
- 5 trigger points injected with either 100 units (10 U/mL) of BTX-A or normal saline
- Outcome measures:
 - Subjective pain (VAS for headache)
 - Objective, composite, active neck ROM

Botulinum Toxin Type A in Whiplash: Results



* $P < 0.01$ vs. baseline.

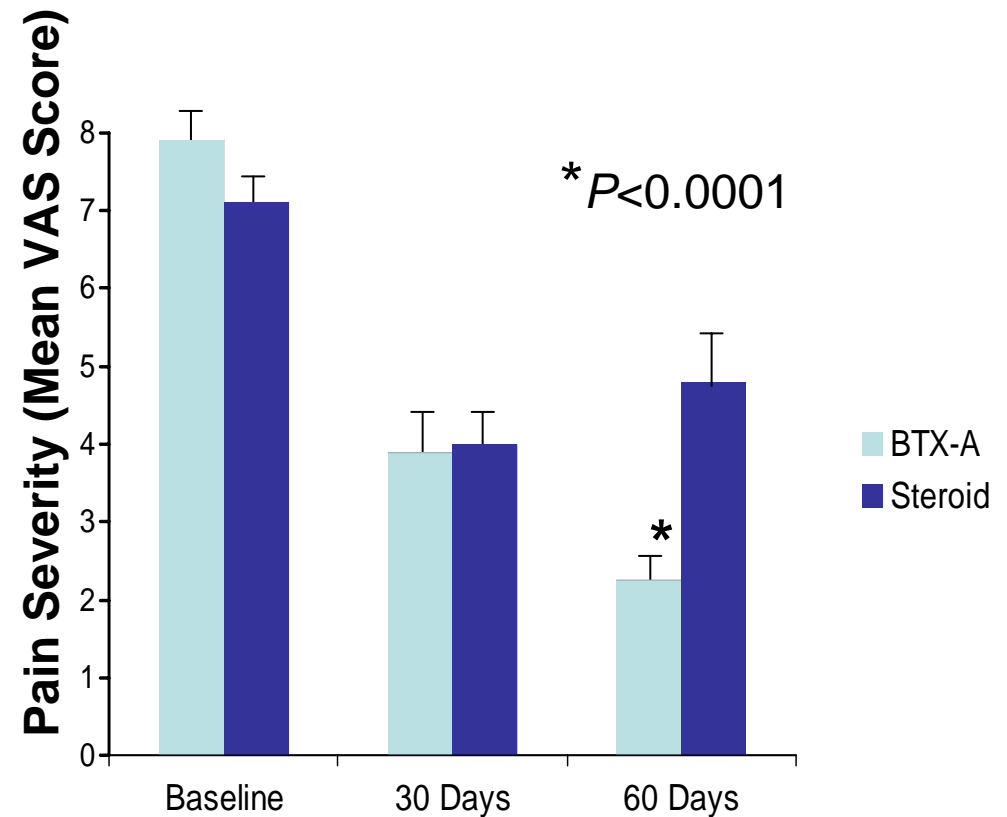
†Median baseline pain score was significantly higher ($P < 0.01$) in the botulinum toxin type A group than in the placebo group.

Freund BJ, Schwartz M. *Headache*. 2000;40:231-236.

Botulinum Toxin Type A and Methylprednisolone in Treatment for MPS and Pain From Muscle Spasm

Porta, 2000

- 40 patients with chronic MPS and muscle spasm
- Random assignment to depot methylprednisolone (80 mg) or BTX-A (80-150 U) in 2-3 cc saline + 2 cc bupivacaine
- Injection into single site in affected muscle, followed by intensive physiotherapy
- Outcome measure: pain (VAS)





Pain 99 (2002) 465–473

PAIN

www.elsevier.com/locate/pain

Randomized controlled trial of botulinum toxin A for chronic myogenous orofacial pain

Donald R. Nixdorf^{a,*}, Giseon Heo^b, Paul W. Major^c

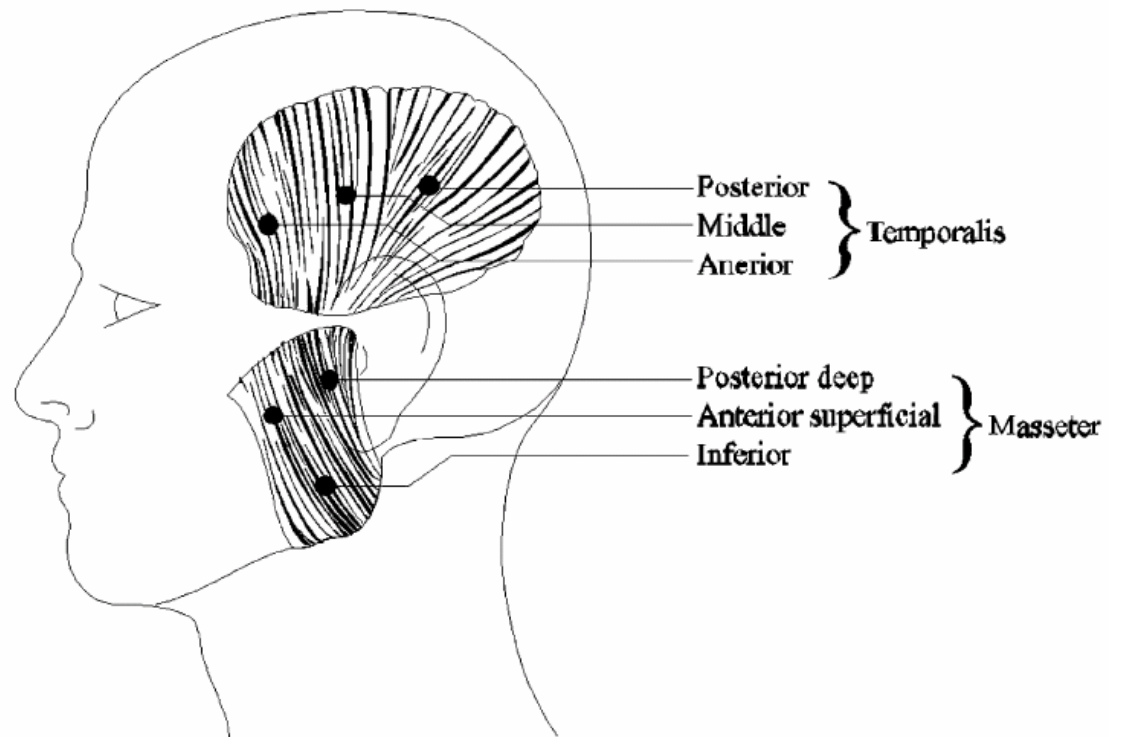
^a*Orofacial Pain Clinic, Department of Dentistry, Faculty of Medicine and Dentistry, University of Alberta, 4048 Dentistry/Pharmacy Centre, Edmonton, Alberta, Canada T6G 2N8*

^b*Department of Mathematical and Statistical Sciences, Faculty of Science, University of Alberta, 487 Central Academic Building, Edmonton, Alberta, Canada T5G 2G1*

^c*Department of Dentistry, Faculty of Medicine and Dentistry, University of Alberta, 1045 Dentistry/Pharmacy Centre, Edmonton, Alberta, Canada T6G 2N8*

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- Randomised double blind crossover
- 25 units per temporalis muscle
- 50 units per masseter muscle
- 3 sites in each muscle
- No difference in pain intensity, pain unpleasantness or muscle tenderness
- 15 patients started on 10 completed



The Effect of Small Doses of Botulinum Toxin A on Neck-Shoulder Myofascial Pain Syndrome: A Double-Blind, Randomized, and Controlled Crossover Trial

Tuula Ojala, MD, Jari P. A. Arokoski, MD, PhD,† and Juhani Partanen, MD, PhD**

Clin J Pain Volume 22 Number 1, January 2006

- 31 patients, MFPS
- Randomized double blind cross-over
- Botulism toxin A vs Saline, 2 sets of injection 4 weeks apart
- 5 units of Botox each point 15-35 units total
- No difference in changes in pressure pain threshold or neck pain between saline and botulism toxin
- After 1st injections subjective results better for botox (P= .008)
- No difference after second injections

Evidence against Trigger Point Injection Technique for the Treatment of Cervicothoracic Myofascial Pain with Botulinum Toxin Type A

F. Michael Ferrante, M.D.,* Lisa Beam, M.S.,† Robert Rothrock, P.A.-C,‡ Laurence King, P.A.-C‡

- 132 patients with MFPS
- Randomized double blind, placebo controlled
- Saline, botulism toxin 10, 25 or 50 units per point up to 5 points
- Followed by active release physiotherapy, ibuprofen, acetaminophen/propoxyphene for breakthrough
- Pain scores, pressure thresholds and propoxyphene use
- No difference between saline and various doses of botulism toxin
- All groups had differences in pain and pressure thresholds from baseline.

Why the Difference?

- ?Different patient populations
- Different techniques
- Different doses
- Different co-existing therapy
- Small difference might have become more obvious with longer term therapy
- ?Subgroups that responded better
- Is it really surprising to see conflicting results in MFPS patients?

Conclusion

- On the current evidence the widespread use of botulism toxin for MFPS cannot be supported.
- Botulism toxin may be useful:
 - In patients who get short-term response to needling
 - In the treatment of muscle shortening associated with pain
 - To treat postural imbalances associated with muscle shortening and pain.
 - As part of a multidisciplinary treatment program

Conclusion

- Given the strong response to needling, this therapy needs to be looked at more rigorously
- Myofascial pain syndrome as a condition needs more study