Localizador web
Artículo 142.156

Systematic Review: Can Botulinum Toxin Be Recommended As Treatment for Pain in Myofascial Syndrome?

Claudia Alejandra Pereda,[a] Jacqueline Usón Jaeger,[b] and Loreto Carmona[c]

[a]Rheumatology, Clínica Mediterráneo, Almería, Spain.
[b]Rheumatology, Hospital de Móstoles, Madrid, Spain.
[c]Research Unit, Fundación Española de Reumatología, Madrid, Spain.

Myofascial pain syndrome (MPS) may have an intrinsic muscle spasm component.
Aim: Since botulinum toxin has been successfully used to reduce hypertonicity in several neurological disorders, we analyzed the efficacy of botulinum toxin A or B in reducing pain in MPS.
Methods: We performed a systematic review through an electronic search in MEDLINE, EMBASE, and Cochrane Library Plus. All clinical trials of botulinum toxin and regional pain were selected. In addition, the abstracts of the ACR and EULAR meetings in the previous 3 years were searched manually. The studies identified were reviewed and analyzed by 2 independent reviewers.
Results: Eight studies met the inclusion criteria. The methodological quality was generally low. Botulinum toxin was compared to saline solution (6 studies), to steroids (2 studies), and to lidocaine and dry needle (1 study arm). The population studied included persons with neck pain (n=3), low back pain (n=2), piriformis syndrome (n=2), several trigger points (n=1), and healthy volunteers in whom pain was provoked (n=1). Botulinum toxin showed a certain advantage over saline solution and steroids in pain control. A meta-analysis of the 3 studies with efficacy measures that could be combined showed a weighted mean difference in pain on a 0-10 visual analogue scale of -2.72 (95% CI, −3.86 to −1.58). However, botulinum toxin showed no advantage over lidocaine (P>.016).
Conclusions: Currently, there is insufficient evidence to confirm the real efficacy of botulinum toxin A and B in the treatment of MPS. Given the high cost of botulinum toxin, long-term high quality studies are required.

Key words: Botulinum toxin. Myofascial syndrome. Systematic review. Meta-analysis.

Revisión sistemática: ¿es recomendable el empleo de toxina botulínica como tratamiento del dolor en el síndrome miofascial?

El dolor miofascial tiene un posible componente de contractura muscular.
Objetivos: Dado que la toxina botulínica ha resultado beneficiosa en enfermedades asociadas a hipertonía, se quiso evaluar la eficacia de la toxina botulínica en la reducción del dolor en el síndrome miofascial (SM).
Métodos: Se realizó una revisión sistemática con búsqueda en Medline, EMBASE y Cochrane Library Plus de todos los ensayos clínicos de toxina botulínica en dolor regional. Además, se efectuó una búsqueda manual entre los resúmenes de los congresos del ACR y EULAR de los últimos 3 años. Los estudios seleccionados fueron revisados y analizados de forma independiente por 2 revisoras.
Resultados: Ocho estudios cumplían los criterios de inclusión, y la calidad metodológica general fue baja. Toxina botulínica se comparó frente a solución salina fisiológica en 6 estudios, frente a esteroides en 2 y frente a lidocaína y aguja seca en 1 (brazo de 1 estudio). La población estudiada incluía cervicalgia (n = 3), lumbalgia (n = 2), síndrome piriforme (n = 2), puntos gatillo varios (n = 1) y voluntarios sanos a los que se provocaba dolor (n = 1). Toxina botulínica mostró una cierta ventaja sobre placebo y corticoides. Un metaanálisis de los 3 estudios con medidas de eficacia agrupables dio como resultado una diferencia media ponderada en una escala visual analógica de dolor de 0-10 de −2,72 (intervalo de confianza del 95%, −3,86 a −1,58). Sin embargo, toxina botulínica no mostró superioridad frente a lidocaína (p > 0,016).
Conclusiones: La evidencia en esta revisión no permite confirmar la efectividad de toxina botulínica A o B en el tratamiento del SM. Son necesarios estudios rigurosos, de

Funding: Fundación Española de Reumatología.

Correspondence: Dra. C.A. Pereda.
Reumatología. Clínica Mediterráneo.
Nueva Musa, s/n. 04007 Almería. España.
E-mail: pereda1963@hotmail.com

Manuscript received November 3, 2005; accepted for publication April 25, 2006.

mayor calidad y a largo plazo dado el alto coste de la toxina botulínica.

Palabras clave: Toxina botulínica. Síndrome miofascial. Revisión sistemática. Metaanálisis.

Introduction

The myofascial pain syndrome (MPS) is defined as muscle pain generally localized to the scapular or pelvic areas and is characterized by augmented tone and muscle rigidity, secondary to the contraction of muscle bands, that with digital pressure develop intense, localized pain as well as pain at a distance, a situation that is referred to as "trigger point."[1] It constitutes an important motive of consultation in the primary care setting, in rheumatology and in pain treatment units. In fact, it is estimated that between 30% and 85% of patients in pain treatment units are there due to MPS.[2] Its pathogenesis is not conveniently clear. Though it has been observed that muscle spasm or contraction is present at trigger points, both electric activity and histology are almost always normal.[3] On the other hand, it has an unsatisfactory response to medical treatment and physiotherapy.[4] Botulinic toxin inhibits the muscle contraction by blocking the liberation of acetylcholine to the neuromuscular space and, therefore, produces muscle relaxation in the region of the injected muscle.[5] Since more than a decade ago, it is employed both in adults and children with neurologic disorders that produce spasm, hypertonia and/or muscle dystonia.[6,7] The botulinic toxin has demonstrated a reduction in pain and an improvement in muscle function, increasing the functional capacity of many patients with different neurologic problems.[7] Because MPS evolves with pain summed to a probable component of sustained muscle contraction it was considered that botulinic toxin could be beneficial in its treatment.[9] In daily practice, this drug is employed more every day, in spite of, at least up to this date, the lack of overwhelming evidence that recommends its use in MPS. Our objective was to determine, if possible, the efficacy of botulinic toxin A or B in the treatment of MPS and, if the contrary was true, to identify the degree of evidence for a recommendation. To that effect we carried out a systematic review of the medical literature.

Methods

A systematic review of scientific literature was undertaken, following the habitual protocols to this effect, that include establishing study selection criteria, a search strategy, and a systemic data collection.

Selection Criteria

By study type we decided to include randomized, controlled clinical trials. Regarding the number of participants, it is evident that MPS is a poorly defined pathology. Because of this it was decided that studies which concerned adult patients with MPS would be included, but also those of patients with regional pain of cervical, scapular, lumbar or gluteal localization, including the pyriform syndrome. Cervical pain and chronic headache due to whiplash were excluded, because those are patients normally followed by traumatology reason why patients with temporomandibular affectation were also excluded. Regarding the type of intervention, studies that compared botulinic toxin, A or B, in any preparation (with saline solution or combined with anesthetic) applied intramuscularly, versus placebo (saline solution, dry needle) lydocaine or steroids, were included. We accepted studies with cointerventions, only if they were applied to both groups similarly. By types of outcome measures, studies that measured the reduction in pain by any means, preferably the Visual Analog Scale (VAS) of the physician or the patient, by pain meter or through the patients or physicians global assessment, were selected.

Search Strategies

Searches of Medline (1966-2005), EMBASE Drugs and Pharmacology (1991-2005), and Cochrane Library Plus "All EBM Reviews" (Cochrane DSR, ACP Journal Club, DARE, and CCTR) were conducted and crossed-referenced by 2 researchers (JUJ/CAP) in an independent manner. The time limit of the search was May 2005. Additionally, a manual search of the abstracts presented at the American College of Rheumatology (ACR) and EULAR meetings of the last 3 years were done. Table 1 show the complete strategy used.

Search Methodology

Citations were introduced and manager in Procite 5.1 and were reviewed by title and abstract by 2 independent reviewers (CAP/JUJ), with consensus in the inclusion of each pair and the dissolution of the incongruities of a third researcher (LC). We recovered all articles that by analysis of the abstract seemed to comply with the inclusion criteria or, in those without

TABLE 1. Search Strategy Used in the Systematic Review

	Number Text	Limits	Total References
In Medline			
#1	Muscle pain	Randomized controlled trial	1177
#2	Low back pain	Randomized controlled trial	663
#3	Regional pain	Randomized controlled trial	495
#4	Myofascial pain syndrome	Randomized controlled trial	288
#5	Neuropathic pain	Randomized controlled trial	178
#6	Shoulder pain	Randomized controlled trial	140
#7	Cervical pain	Randomized controlled trial	105
#8	Myofascial pain	Randomized controlled trial	99
#9	Regional pain syndrome	Randomized controlled trial	27
#10	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8, or #9		2738
#11	Botulinum toxin	Randomized controlled trial	212
#12	Botox	Randomized controlled trial	138
#13	#11 or #12		212
#14	#10 and #13		40
#15	#14 not stroke		34
#16	#15 not tension-type headaches		29
#17	#16 not dystonia		18
#18	#17 not anismus		17
In EMBASE			
1	Myalgia	Humans	7812
2	Low back pain	Humans	2820
3	Neck pain	Humans	999
4	Neuropatic pain	Humans	931
5	Shoulder pain	Humans	806
6	Regional pain	Humans	428
7	Myofascial pain	Humans	396
8	Randomized controlled trial		74 054
9	Botulinum toxin A		2986
10	1 or 2 or 3 or 4 or 5 or 6. or 7		13 608
11	10 and 8		157
12	11 and 9		21

an abstract, those in which the title suggested that the criteria were met. All of the recovered studies were evaluated by the independent pair and the data was concentrated in ad hoc data collection sheets, that had been previously piloted and in which Jadad's[10] quality criteria of the studies was met, as well as the number of patients and centers involved, inclusion and exclusion criteria, randomization methods, interventions, and outcome measures. The collected data was introduced afterwards in the Review Manager 4.2.7 software.

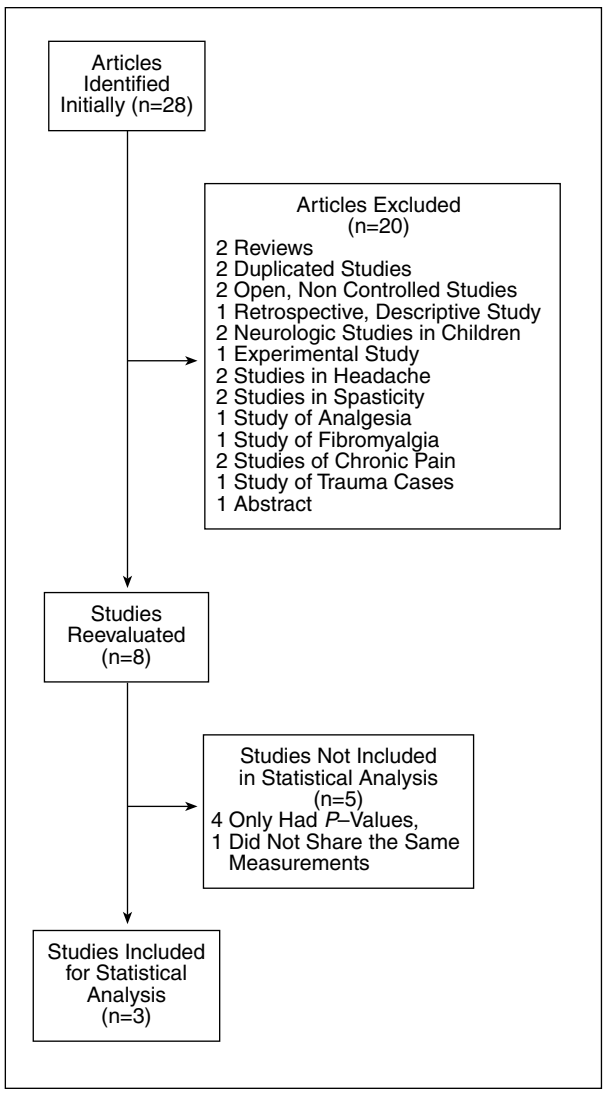


Figure 1. *Flow chart of the analyzed studies in the present metaanalysis. RCT indicates randomized clinical trials.*

Metaanalysis

We planned to perform a metaanalysis in those situations in which homogeneity of the outcome measures was observed, as well as in interventions and study populations. To carry out the metaanalysis we used differences in weighed means in a random effects model. The heterogeneity was evaluated by the statiscal test I^2.

Results

The search in EMBASE and Medline produced 38 references, of which 14 were duplicates between databases. The search in the Cochrane Library resulted negative, both for *"botulinum toxin and myofascial syndrome"* as for *"botox and myofascial syndrome."* The search in meeting abstracts produced 2 results,[11,12] one of which allowed the recuperation of an article not identified previously because it was publeshed posterior to the date in which the Medline and EMBASE database search was done, but sufficiently important to be considered for the review.[13] In all, 26 articles were analyzed, plus another 2 that were localized by the secondary search through the articles. Of the 28 articles analyzed, 11 complied with the inclusion criteria, but in one was found in triplicate, so we included only the most recent reference, and a EULAR abstract was substituted for the complete article,[13] which accounts for 8 included studies (Figure 1).

Study Description

The 8 included studies were double blind clinical trials (n=5), a simple blind (n=1), and crossed (n=2).[13-20] The localization of MPS in which the response to botulinic toxin has been evaluated are: cervical pain (n=3), chronic lumbar pain (n=2), pyriform syndrome (n=2), various trigger points (n=1), and 1 in healthy volunteers in whom pain was induced. The dose of botulinic toxin injected varied enourmously between studies, from 12.5 units to approximately 200. The controls used were mainly saline solution (n=6) and steroids (n=2 [triamcinolone and methylprednisolone]). One study showed a control arm with lydocaine. The median age of the study population is around 40 years, except in studies with healthy volunteers, who were in their twenties. The number of patients was low in all of the studies. The majority of articles were reviews or letters to the director, not formal studies, or had not established the type of pain specified as an inclusion criteria (Table 2).

Methodologic Quality of the Included Studies

The methodologic quality of the 8 included studies is moderate to poor. Two studies, Foster et al[18] and Wheeler et al,[19] both in 2001, surpassed the 3 value (moderate) in the Jadad quality scale for clinical trials.[10] The rest of the studies did not describe the method of randomization or masking, or the blinding method, or were not analyzed as intention to treat, which reveals a low general quality of the studies.

Results

Table 3 shows in detail the characteristics of the 8 studies included. For statistical analysis effects, only 4

TABLE 2. Excluded Studies and Cause

Studies	Exclusion Motive
Acquadro and Borodic, 1994[21]	Review, not clinical trial
Balague, 1996[22]	Review, not clinical trial
Barwood et al, 2000[23]	Concerns the action of botulinic toxin A in children with neurologic disease
Blersch et al, 2002[24]	Experimental study. Evaluates nociceptive receptors in humans responding to botulinic toxin
Boyd, 2001[23]	Evaluation study of general mobility, hip dysplasia and its progresión to surgery in children with infantile paralisis treated with botulinic toxin A
Carrasco et al, 2003[25]	Descriptive retrospective study
De Andrés, 2002[26]	Descriptive retrospective study
De Andrés et al, 200[32]	Open, uncontrolled study
Freund and Schwartz, 2000[27]	Use of botulinic toxin A in patients with cervical pain secondary to whiplash
Freund and Schwartz, 2002[28]	Headache of osteomuscular origin
Grazko et al, 1995[29]	Measures spasticity and rigidity, but not pain
Hyman et al, 2000[30]	Study of hip spasticity
Mahowald, 2004[11]	Referrs to intraarticular botulinic toxin effectivity in chronic refractory pain
Nixdorf et al, 2002[31]	Estudio de efectividad de la toxina botulínica para dolor crónico mandibular
Paulson 1996[32]	Evaluation of the effectivity of botulinic toxin in fibromyalgia
Porta, 1999[33]	Duplicated in Porta 2000 (included)
Porta, 1999[34]	Duplicated in Porta 2000 (included)
Rollnick et al, 2000[35]	Effectivity in tension headache, not cervical pain
Sarifakioglu and Sarifakioglu, 2004[36]	Evaluation of the application of ice as analgesia in the site of application of botulinic toxin

had the minimum requirements to be evaluated, this when detailing the results in a numeric fashion and not only with the *P*-values.[13,15,16,19] This notwithstanding, only 3 studies had the same measures 3 that were the ones finally metaanalyzed[13,15,16] (Table 4). The metaanalysis showed Benedit of botulinic toxin A, both when compared to saline solution or needle[13,16] or when compared to methylprednisolone,[15] being the median weighed difference before and after treatment in a VAS of pain from 0 to 10 of −2.42 (95% confidence interval [CI], −3.54 to −1.30). Curiously, the difference in efficacy of the botulinic toxin when compared to methylprednisolone is higher than when the control is saline solution. In the Kamanli et al[13] study, there is no superiority in the botulinc toxin against lydocaine (*P*>.016). If this study arm is included in the metaanalysis, the median weighed difference in favor of the botulinic toxin disappears (−1.3 [−3.67 to 1.42]) (Table 5). The Wheeler et al[19] study, of good quality (Jadad of 4), did not find significant differences between the botulinic toxin and saline solution in a mixed pain scale and function of 0 to 100 (median difference between active and control of 36.2 [95% CI, 26.9-45.4], in favor of placebo), nor in the patients global assessment by Likert scale (−0.30 [−1.30 to 0.70]), nor in the physicians global (−0.20 [−1.00 to 0.60]), nor in the pain meter punctuation (0.00 [−1.37 to 1.37]).

Discussion

Certain drugs are frequently used in clinical practice even when information about their benefit is limited. In our case, the clinical trials regarding the use of botulinic toxin that were analyzed are scarce. There are also, among the selected studies only a few that have expressed their results in a clear enough matter to be analyzed in an objective form. For example, 4 of the included studies[14,18,20,33] conclude that botulinic toxin is more effective than saline solution or triamcynolone in MPS. None of the studies, through their results, permit an objective interpretation, nor are they metaanalizable. This casts doubt on the effectivity of real treatment. On the other hand, studies done in general are characterized

Table 3. Included Studies

Study	Methods	Participants	Interventions	Results	Comments
Chesire et al, 1994[14]	Clinical trial crossed controls, 8 weeks. Self financing	N=6 (median age, 43; 67% women). Inclusion criteria: cervical paraspinal pain or in scapular girdle. Exclusión criteria: diffuse pain or neurologic deficit	1. Botulinic toxin A 50 U in 4 mL of saline IM (n=6) on 2 separate occasions for 8 weeks. 2. IM saline (n=6) 2 twice with 8 weeks in between applications	Of the 6 patients, 4 responded, one of them in the 5 variables and 3 patients in 4 variables	No abandonment of treatment. No adverse effects. Limitations: low number of patients. Short follow-up. Quality: Jadad 2
Porta, 2000[15]	Clinical trial, randomized, simple blind, 60 days. Self-financing	N=40 (median age 47, 68% women). Inclusion criteria: chronic myofascial pain with chronic muscle spasm in the pyriform, ilopsoas or anterior scalenus muscles >6 months and <2 years. Exclusión criteria: discal or bone disease, disk surgery, abdominal tumor, anatomical problem, rheumatoid arthritis, root compression	Botulinic toxina A 80-100 U + saline solution 2 mL +2 mL bupivacaine 0, 5% (n=20). Methylprednisolone 80 mg +2 mL saline solution +2 mL bupivacaine (n=20). Physiotherapy 30 days alter intervention	VAS (0 to 10) evaluation 30 and 60 days. After 30 days neither botox nor methylprednisolone showed any significant differences when compared to baseline. Alter 60 days: botox median −5.5 (±0.3) ≤0.0001 when compared to methylprednisolone	No patients abandoned treatment. Adverse events: in 9 patients there was an increment or recurrence of pain, in 2 dysphonia (lasting 2-3 hours) anterior scalenus weakness in legs (group unknown), 19 patients pain upon extensión, 3-4 days postinjection. Limitations: adverse events re not segregated by group. Jadad: 2
Childers et al, 2002[16]	Clinical trial, crossed, double blind, 20 weeks. Self financing	N=9 (median age, 42; 100% women). Inclusion criteria: Buttock pain, hip and coger extremity (pyriform muscle syndrome) of ≥3 months, pain >5/10 in VAS in 3 consecutive evaluations. Exclusión criteria: pregnancy, lumbar disk hernia, root compromiso, pathologic EMG	Botox A: 100 U i.m. (n=9) 1 application Solution saline (dose not specified) (n=9), in both cases the intervention was fluoroscopically guided as well as electromyographically	Weekly for 10 weeks. VAS improved in a few patients, with botox activity and intensity as well as spasm improved, but not distress	Patient abandonment (1/10). Adverse effects: not mentioned. Limitations: crossed trial with difficult analysis, without a description of adverse effects, without a description of placebo dose applied. Number of patient cointerventions was not specified. Jadad: 3 (poor)
Wheeler, 1998[17]	Clinical trial, randomized, double blind, 4 months. Financing: Allergan Corp	N=33 (no demographic description). Inclusion criteria: refractory pain, unilateral, cervicothoracic, paraspinal, myofascial. Exclusión criteria: less than 21 years of age, diffuse pain, pregnancy, allergy to botox, fibromyalgia, illness that interferes with neuromuscular transmission, systemic inflammation, steroid infiltration in trigger point in the 4 previous weeks	Botulinic toxin A: 50 U in 2 mL saline. Botuilinic toxin 100 U in 2 mL of saline. Placebo = saline solution. Eleven patients received a second injection of botulinic toxin in the same region and 2 patients in an adjacent region	Basal, 1, 3, 6, 9 weeks and 3, and 4 months. There was no significant difference among the 3 groups in the global evaluation of pain nor in pain measured by the pain meter	Abandonment: none. Adverse effect: 2 patients with paresthesias and a heavy sensation on the ipsilateral arm, 2 patients with a discrete discomfort in site opposing the injection, 2 changes in the site of pain alter the injection. Limitations: low patient number, lack of. Standard deviation in the measurements, no discrimination by gender. Jadad: 2
Foster, 2001[18]	Clinical trial, randomized, double blind, 8 weeks self financing	N=31 (mean age, 46; 52% women). Inclusion criteria: lumbar pain L1 to S1 ≥6 months, uni or bilateral. Exclusión criteria: lumbar pain <6 months, <18 years of age, inflammatory illness	Botox A 40 U IM. Saline solution: dose not specified. Only 1 application in treatment and control groups	Three and 8 weeks. Visual analog scale 0-10 and OLBPQ (0-5 item questionnaire on functional ability)	Abandonment: 1 patient botox and 2 in saline. Adverse effects: postinjection pain in 2 patients with saline. Limitations: low patient number. Amount of saline used is not specified. Jadad: 5 (very good quality)

Continued next page

Table 3. Included Studies (*Continued*)

Study	Methods	Participants	Interventions	Results	Comments
				Pain reduction in 73% of patients with botox at 3 weeks weeks and 60% OLBPQ: 67% at 8 weeks of patients improved at 8 weeks	
Wheeler 2001[19]	Clinical trial, randomized, double blind, controlled, 4 months. Self financing	N=50 (mean age, 43). Inclusion criteria: chronic cervical pain in the last 3 months, without medial or psychological problems. Exclusion criteria: other illness, without muscular disease	Botox A: 231 U (mean) i.m., once a week for 4 months (n=25). Saline solution: once a week for 4 weeks (n=25)	0, 4, 8, 12, and 16 weeks. There was no significant difference in the NPAD questionnaire, patient global assessment, physicians global assessment, pain meter, Beck, SF mental, and SF Physical	Abandonments: 4 patients with botox and 1 with saline. Adverse effects: muscle weakness, pain at the site of injection, cold symptoms. No specification as to which episode. Limitations: does not distinguish number of patients according to outcome. Jadad: 4
Voller, 2003[20]	Clinical trial, randomized, double blind, 28 days. Financed by Allergan Inc.	N=16 (mean age, 28; 50% women). Objective: to establish the analgesic efficacy of botox on C and A fibers. Inclusion criteria: healthy volunteers, right handed, between 19 and 40 years of age, no medications including analgesics 4 weeks prior to start	1. Botulinic toxin A 50, Botox A 30 U intradermic in 4 points of the forearm on one occasion. Saline solution: 0.12 mL in 4 points in the forearm on one occasion	3, 14, 28 days. No significant differences between groups in pain due to heat, tolerant to pain and VAS posterior to the capsaicin test	Abandonments: none. Adverse effects: none. Limitations the studied population is not specified, no crude results in results section (nor means nor percentages). Jadad 2
Kamanli, 2005[13]	Clinical trial, simple blind, 4 weeks, self financing	N=29 (age not specified, 23 women and 6 men). Objective: to compare analgesic efficacy of botox, lydocaine and simple needle in trigger points. Inclusion criteria: patients with SM in a physiotherapy program	Lydocaine 0.5%-1 mL: one application. Botox A: 10-20 U one application in trigger point. Simple needle: one application	4 weeks. Botox was superior to 2 comparators in anxiety and depression scales. Lydocaine was superior to botox and needle in fatigue VAS. Lydocaine and botox were equally effective in VAS pain being botox the most expensive procedure	Abandonment: not described. Adverse effects in the 3 groups: cold or burning sensation, 30%; paresthesia, 30%; fatigue, 55.6%; muscle pain, 33%; headache, 10%, and malaise predominated in 80% with dry needle. Limitations: age is not clear in the study group. Jadad: 1

*FADIR test: prolongation of the Achilles tendon reflex with a flexed leg, adduction and internal rotation of at least 1.86 msg.

by a poor registry of adverse effects and a reduced number of patients. The metanalysis shows a statistical difference in favor of botulinic toxin against saline solution or methylprednisolone, but not if lydocaine is included as a control. Apart from the metaanalysis, a study of great quality,[19] there was no evidence of an advantage of botulinic toxin over saline solution. It has to be said that there is no evidence of a publication tendency, because there is the same number of studies in favor of as against the intervention.

Weaknesses in our study have a basis on the limitations of primary studies in which it is based, especially due to the general low quality and the low number of patients included. It is true that the comparative characteristics chosen, it cannot be stated, alter this review, that employing botulinic toxin A or B in MPS can produce

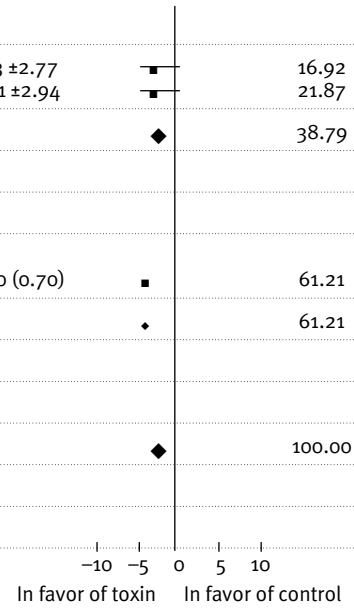
TABLE 4. Botulinic Toxin Efficacy Metaanalysis Alter 1 Week Versus Placebo or Steroids in the Myofascial Pain Syndrome

Review: botox efficacy

Comparison: botulinic toxin versus comparator

Efficacy measures: differences in VAS pain 0-10

Study or subcategory	N	Botulinic toxin, Mean±SD	N	Mean control ±SD	WMD (random), 95% CI	Weight, %	WMD (random) 95%
Control: placebo							
Childers 2002	9	−1.74 ±2.26	9	0.23 ±2.77		16.92	−1.51 (−3.85 to 0.3)
Kamanili 2005	9	−3.41 ±1.04	10	−1.91 ±2.94		21.87	−1.50 (−3.44 to 0.44)
Subtotal (95% CI)	18	19				38.79	−1.50 (−3.00 to −0.01)
Heterogeneity test: χ^2=0.00, df=1 (*P*=.99), I^2=0%							
Total effect test: Z=1.97 (*P*=.05)							
Control: methylprednisolone							
Porta 2000	20	−5.50 (0.30)	20	−2.50 (0.70)		61.21	−3.00 (−3.33 to −2.67)
Subtotal (95% CI)	20		20			61.21	−3.00 (−3.33 to −2.67)
Heterogeneity test: not applicable							
Total effect test: Z=17.62 (*P*<.00001)							
Total (95% CI)	38	39				100.00	−2.42 (−3.54 to −1.30)
Heterogeneity test: χ^2=3.67, df=2 (*P*=.16), I^2=45,4%							
Total effect test Z=4.24 (*P*<.0001)							



WMD indicates weighed median difference; IC, confidence interval.

better results than non steroidal antiinflammatory drugs or muscle relaxants, due to the lack of direct physical comparisons confronting other interventions apart from parenteral.

Conclusions

– Implications for practice. This systematic review does not constitute sufficient evidence to confirm the effectivity of botulinic toxin. The poor quality of the studies, the inadequate size of the sample and the lack of trial replication make it impossible to draw conclusions.
– Implications for research. There is an important necessity to do methodologically strict studies that describe the real effectivity of the botulinic toxin in MPS.

Recommendations

The existing evidence does not allow us to recommend or contraindicate the use of botulinc toxin A or B in the treatment of MPS of any localization. It is necessary to do prospective studies with a larger number of patients and an appropriate design. Grouping the patients with MPS by localization, localizing the muscles to be injected by ecography and comparing in a crossed manner the botulinic toxin with local anesthetic without postinjection physiotherapy will help to know if botulinic toxin A or B is really effective. The authors relieve that these studies are needed due to the high cost of botulinic toxin.

References

1. Travell JG, Simons DG. Myofascial pain and dysfunction. The trigger point manual. Baltimore: Williams & Wilkins; 1983.
2. de Andrés J, Cerdá-Olmedo G, Valia JC, Monsalve V, López-Alarcón MD, Mínguez A. Use of botulinum toxin in the treatment of chronic myofascial pain. Clin J Pain. 2003;19:269-75.
3. Pearce JM. Myofascial pain, fibromyalgia or fibrositis? Eur Neurol. 2004; 52:67-72.
4. Wheeler AH. Myofascial pain disorders: theory to therapy. Drugs. 2004; 64:45-62.
5. Mense S. Neurobiological basis for the use of botulinum toxin in pain therapy. J Neurol. 2004;251 Suppl 1:I1-7.
6. Berardelli A, Carta A, Stocchi F, Formica A, Agnoli A, Manfredi M. Botulinum A toxin injection in patients with blepharospasm, torticollis and hemifacial spasm. Ital J Neurol Sci. 1990;11:589-93.

TABLE 5. Efficacy Metaanalysis of Botulinic Toxin Alter One Week Versus Any Comparator in Myofascial Pain Syndrome*

Review: botox efficacy

Comparison: botulinic toxin versus comparator

Efficacy measures: differences in VAS pain 0-10 (with lydocaine)

Study or Subcategory	N	Botulinic Toxin Mean ±SD	N	Mean Control	WMD (Random)	Weight, %	WMD (Random) 95%
Control: placebo							
Childers, 2002	9	−1.74±2.26	9	0.23±2.77		22.49	−1,51 (−3.85 to 0.83)
Kamanili, 2005	9	−3.41±1.04	10	−1.91±2.94		23.8	−1.50 (−3.44 to 0.44)
Subtotal (95% CI)	18		19			46.37	−1.50 (−3.00 to −0.01)
Heterogeneity test: χ^2=0.00; df=1 (*P*=.99), I^2=0%							
Total effect test: Z=1.97 (*P*=.05)							
Control: methylprednisolone							
Porta 2000	20	−5.50±0.30	20	−2.50±0.70		27.60	−3.00 (−3.33 to −2.67)
Subtotal (95% CI)	20		20			27.60	−3.00 (−3.33 to −2.67)
Heterogeneity test: not applicable							
Total effect test: Z=17.62 (*P*<.00001)							
Control: lydocaine							
Kamanli, 2005	9	−3.41± 1.04	10	−4.95±1.67		26.3	1.54 (0.30-2.87)
Subtotal (95%)	9		10			26.3	1.54 (0.30-2.87)
Heterogeneity test: not applicable							
Total effect test: Z=2.44 (*P*=.01)							
Total (95% IC)	47		49			100.00	−1.13 (−3.67 to −1.42)
Heterogeneity test: χ^2=50.47; df=3 (*P*=.00001); I^2=94.1%							
Total effect test Z=0.87 (*P*<.039)							

−10 −5 0 5 10

In favor of toxin In favor of control

*WMD indicates weighed median difference; IC, confidence

7. Snow BJ, Tsui JK, Bhatt MH, Varelas M, Hashimoto SA, Calne DB. Treatment of spasticity with botulinum toxin: a double-blind study. Ann Neurol. 1990;28:512-5.
8. Durette MR, Rodríguez AA, Agre JC, Silverman JL. Needle electromyographic evaluation of patients with myofascial or fibromyalgic pain. Am J Phys Med Rehabil. 1991;70:154-6.
9. Porta M, Perretti A, Gamba M, Luccarelli G, Fornari M. The rationale and results of treating muscle spasm and myofascial syndromes with botulinum toxin type a. Pain Digest. 1998;8:346-52.
10. Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials. 1996;17:1-12.
11. Mahowald ML. Long term of intra-articular botulinum A toxin for refractory joint pain. San Antonio: ACR; 2004.
12. Kamanli A, Kaya A, Ozgocmen S, Bayik Y, Ardicoglu O. A comparative study of lidocaine, botulinum toxin type A injection and dry needling in the treatment of myofascial pain syndrome. Lisbon: EULAR Congress; 2003.
13. Kamanli A, Kaya A, Ardicoglu O, Ozgocmen S, Zengin FO, Bayik Y. Comparison of lidocaine injection, botulinum toxin injection, and dry needling to trigger points in myofascial pain syndrome. Rheumatol Int. 2005;25:604-11.
14. Cheshire WP, Abashian SW, Mann JD. Botulinum toxin in the treatment of myofascial pain syndrome. Pain. 1994;59:65-9.
15. Porta M. A comparative trial of botulinum toxin type A and methylprednisolone for the treatment of myofascial pain syndrome and pain from chronic muscle spasm. Pain. 2000;85:101-5.
16. Childers MK, Wilson DJ, Gnatz SM, Conway RR, Sherman AK. Botulinum toxin type A use in piriformis muscle syndrome: a pilot study. Am J Phys Med Rehabil. 2002;81:751-9.
17. Wheeler AH, Goolkasian P, Gretz SS. A randomized, double-blind, prospective pilot study of botulinum toxin injection for refractory, unilateral, cervicothoracic, paraspinal, myofascial pain syndrome. Spine. 1998;23:1662-6 [discussion, 1667].
18. Foster L, Clapp L, Erickson M, Jabbari B. Botulinum toxin A and chronic low back pain: a randomized, double-blind study. Neurology. 2001;56:1290-3.
19. Wheeler AH, Goolkasian P, Gretz SS. Botulinum toxin A for the treatment of chronic neck pain. Pain. 2001;94:255-60.
20. Voller B, Sycha T, Gustorff B, Schmetterer L, Lehr S, Eichler HG, et al. A randomized, double-blind, placebo controlled study on analgesic effects of botulinum toxin A. Neurology. 2003;61:940-4.
21. Acquadro MA, Borodic GE. Treatment of myofascial pain with botulinum A toxin. Anesthesiology. 1994;80:705-6.
22. Balague F. Injections and low back pain: outcome and randomized controlled trials. Bull Hosp Joint Dis. 1996;55:185-90.

23. Barwood S, Baillieu C, Boyd R, Brereton K, Low J, Nattrass G, et al. Analgesic effects of botulinum toxin A: a randomized, placebo-controlled clinical trial. Dev Med Child Neurol. 2000;42:116-21.
24. Blersch W, Schulte-Mattler WJ, Przywara S, May A, Bigalke H, Wohlfarth K. Botulinum toxin A and the cutaneous nociception in humans: a prospective, double-blind, placebo-controlled, randomized study. J Neurol Sci. 2002;205:59-63.
25. Carrasco AT, Wescoat L, Román A. A retrospective review of botulinum toxin type a compared with standard therapy in the treatment of lumbar myofascial back pain patients. Pain Clin. 2003;15:205-11.
26. de Andrés J. New advances in botulinum toxin therapy for pain. Expert Rev Neurotherap. 2002;2:791-9.
27. Freund BJ, Schwartz M. Treatment of chronic cervical-associated headache with botulinum toxin A: a pilot study. Headache. 2000;40:231-6.
28. Freund BJ, Schwartz M. Relief of tension-type headache symptoms in subjects with temporomandibular disorders treated with botulinum toxin-A. Headache. 2002;42:1033-7.
29. Grazko MA, Polo KB, Jabbari B. Botulinum toxin A for spasticity, muscle spasms, and rigidity. Neurology. 1995;45:712-7.
30. Hyman N, Barnes M, Bhakta B, Cozens A, Bakheit M, Kreczy-Kleedorfer B, et al. Botulinum toxin (Dysport) treatment of hip adductor spasticity in multiple sclerosis: a prospective, randomised, double blind, placebo controlled, dose ranging study. J Neurol Neurosurg Psychiatry. 2000;68:707-12.
31. Nixdorf DR, Heo G, Major PW. Randomized controlled trial of botulinum toxin A for chronic myogenous orofacial pain. Pain. 2002; 99:465-73.
32. Paulson GW, Gill W. Botulinum toxin is unsatisfactory therapy for fibromyalgia. Mov Disord. 1996;11:459.
33. Porta M. Botulinum toxin type a injections for myofascial pain syndrome and tension-type headache. Eur J Neurol. 1999;6 Suppl 4:S103-9.
34. Porta M. A comparative trial of botulinum toxin type a and methylprednisolone for the treatment of tension-type headache. Pain Digest. 1999;9:303-6.
35. Rollnik JD, Tanneberger O, Schubert M, Schneider U, Dengler R. Treatment of tension-type headache with botulinum toxin type A: a double-blind, placebo-controlled study. Headache. 2000;40:300-5.
36. Sarifakioglu N, Sarifakioglu E. Evaluating the effects of ice application on the pain felt during botulinum toxin type-a injections: a prospective, randomized, single-blind controlled trial. Ann Plast Surg. 2004;53:543-6.