REVIEW ARTICLE (META-ANALYSIS)

Effectiveness of Botulinum Toxin for Shoulder Pain Treatment: A Systematic Review and Meta-Analysis

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Abstract

Objective: To evaluate the current evidence of the effectiveness of botulinum toxin (BTX) treatment for shoulder pain.

Data Sources: Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Web of Science, and Scopus were searched from inception through week 18 of 2015.

Study Selection: Randomized controlled trials comparing the clinical efficacy (pain intensity and shoulder range of motion [ROM]) of BTX injection to conventional therapy (steroid or placebo injection) were included.

Data Extraction: Two reviewers independently screened abstracts and full texts. The results of the pain intensity and shoulder ROM were extracted and presented in the form of mean and SD. We constructed random-effects models and calculated the mean difference (MD) for continuous outcomes. A total of 219 articles were identified, of which 9 articles were eligible for the final analysis.

Data Synthesis: The analysis indicated a statistically significant decreased pain score in the BTX therapy group compared with the control group, with the MD$=1.35$ (95% confidence interval [CI], .80−1.91; $P<.001$; $I^2=81$%). Patients who received BTX therapy were more likely to have a significant increase in shoulder abduction ROM than patients in the control group, with the MD$=8.02$ (95% CI, 1.17−14.88, $P=.02$, $I^2=89$%).

Conclusions: Compared with conventional (steroid or placebo injection) therapy, BTX injections have beneficial effects for adult patients with shoulder pain, evidenced by improved pain scores and ROM.

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Shoulder pain is one of the most common musculoskeletal disorders affecting the adult population, with an estimated prevalence of 7% to 25% in the general population.[1] Without proper treatment, chronic shoulder pain and limitation of the shoulder's range of motion (ROM) can have a strong disruptive impact on an individual's physical activity[2] and cognitive function.[3] Traditional therapeutic approaches for shoulder pain include pharmacotherapy, injection therapy, physical therapy, and behavioral modification.[4] Unfortunately, these therapeutic methods may not be effective in many patients,[5] and long-term benefit after treatment is transient. The pain relief may also be incomplete or nonexistent, with varying degrees of improvement.[6]

During the past few decades, botulinum toxin (BTX) has been shown to be an analgesic, with direct antinociceptive effects in an inflammatory pain model.[7] BTX injection may offer advantageous treatment for shoulder pain because its effects are prolonged compared with traditional modalities. Many case reports and clinical trials have been published showing that shoulder pain can be treated efficiently and simply using BTX injection.[8,9] Many nonrandomized or retrospective studies focused on the effectiveness of BTX for shoulder pain but without comparisons to the control group and with small sample sizes. So, the clinical efficacy of BTX injection therapy in the treatment of shoulder pain is still unclear. We therefore conducted this systematic review to synthesize all the evidence on BTX as a therapeutic intervention in the management of shoulder pain. The objective of this review was to assess the benefit of BTX for shoulder pain as compared with placebo or steroid injection.

Methods

The study protocol was finalized in advance of any data collection, which defined objectives, search strategy, inclusion/exclusion criteria, data extraction, outcomes of interest, and analytical approaches. This systematic review is in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[10]

Search strategy and study selection

The search was performed on Ovid MEDLINE In-Process and Other Non-Indexed Citations, Ovid MEDLINE, Ovid EMBASE, Web of Science, and Scopus from database inception through week 18 of 2015. Search terms were broad and without language or country restrictions. Controlled vocabulary supplemented with keywords was used to search for studies of shoulder pain with BTX. Relevant studies were identified using the following search terms: (*BTX* or *BoNT* or *botulinum toxin*) and (*shoulder pain* or *arthritis* or *neck pain* or *limb pain* or *joint pain*) as keywords or text words or Medical Subject Headings. Two reviewers, working independently and then double checking each other's findings (T.W., Y.F.), reviewed titles and abstracts and then full texts in order to exclude irrelevant studies. All conflicts were discussed and resolved with a third author (J.L.). The reference sections of the included articles were used to identify additional relevant articles.

Inclusion and exclusion criteria

We included clinical randomized controlled trials (RCTs) that evaluated the effect of BTX injection on shoulder pain in humans. We did not restrict the type of intervention in control groups. We also did not restrict language or study country. Studies focusing on the therapeutic effect of BTX injection for myofascial pain syndrome were excluded. Case reports, case series, reviews, notes, letters, errata, commentaries, and studies published only as abstracts were also excluded.

Data extraction and quality assessment

Study details were extracted from the full texts. The following data were extracted: author, year published, sample size, patients' age, population, injection route, study design, main evaluation index, and follow-up time. The outcomes of interest were pain score (visual analog scale [VAS] and numeric rating scale [NRS]) and shoulder ROM.

We used the Cochrane risk-of-bias tool to assess the methodological quality of the included study in terms of sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting, and other sources of bias.[11]

List of abbreviations:

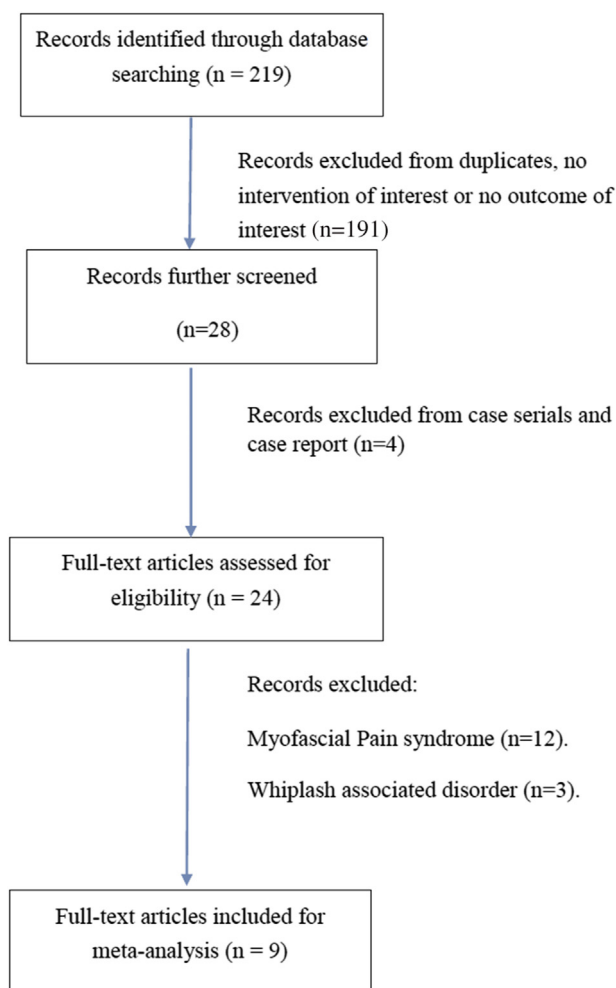|	
BTX	botulinum toxin
MD	mean difference
NRS	numeric rating scale
RCT	randomized controlled trial
ROM	range of motion
SASD	subacromial and subdeltoid
SB	subacromial bursitis
SIS	shoulder impingement syndrome
VAS	visual analog scale

Fig 1 Flow of participants through trial.

Statistical analysis

For the continuous outcomes, we combined the mean differences (MDs) from the included studies using the DerSimonian and Laird random-effect models. We used the I^2 statistic to measure the heterogeneity across the included studies, in which $I^2 > 50\%$ suggests high heterogeneity. All analyses were performed using the generic inverse variance method (RevMan version 5.3[a]). The significance level was defined as $P < .05$.

Results

Study characteristics

We identified 219 articles, of which 9 RCTs (268 patients) were eligible for this review (fig 1). Characteristics of the enrolled studies are described in table 1. Six studies[8,9,12-15] used intramuscular BTX injections, 2 studies[16,17] used intra-articular BTX injections, and 1 study[18] used ultrasound-guided BTX injections to treat subacromial bursitis (SB) or shoulder impingement syndrome (SIS). All the patients in control groups received non-BTX therapy such as steroid or placebo injection. The mean follow-up time was 11.1 weeks (4–24wk). All the studies assessed pain