

# A literature review exploring the use of botulinum toxin A injection therapy for chronic exertional compartment syndrome treatment

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Chronic exertional compartment syndrome (CECS) is a rare condition typically affecting runners. It has been speculated that the cause of CECS is due to a transient ischemia occurring during exercise compromising blood flow and leading to increased intramuscular pressure. The first line of treatment for patients is cessation of the aggravating activity which some individuals are less inclined to follow. If conservative treatment fails, the next option is a fasciotomy with a recurrence risk of 44.7%. A review of current literature on treatment options for CECS illustrates preliminary studies of the use of botulinum toxins A injection therapy. The use of botulinum toxin A as a non-surgical option for CECS has been theorized due to the analgesic properties and muscle hypotonia to improve blood flow. The objective of this review was to search the current literature on the use of botulinum toxin A as a treatment option for patients with CECS. A thorough search of the literature via PubMed concerning botulinum toxin as a treatment option for patients with CECS was completed. Botulinum toxin A injections demonstrate a statistically significant decrease in intramuscular pressure in the anterior and lateral compartments of the leg. A high correlation is noted in patients experiencing no exertional pain extending to fourteen months following the injections with no reported adverse effects. Patients were able to resume and continue pre-injections level of activity without any residual effects. Our goal was to investigate the current literature for non-surgical treatments for CECS. The effectiveness of this potential therapy both short term and long term are not fully understood as of yet, however future large prospective randomized controlled studies are needed.

**Keywords:** Chronic exertional compartment syndrome, botulinum toxin A

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Chronic exertional compartment syndrome (CECS) is a rare condition typically affecting runners. It has been speculated that the cause of CECS is due to transient ischemia during exercise compromising blood flow and leading to increased intramuscular pressure in the lower extremities [1]. CECS is considered to be a clinical diagnosis. Patients often

present with an intolerable dull, achy pain in their legs after running a consistent distance with no history of trauma. Neurological symptoms such as paraesthesia, numbness, and transient slap-foot are commonly seen clinically with patients with CECS [1]. The first line of treatment for patients is the cessation of the aggravating activity that some individuals are less

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inclined to follow or unable to follow due to occupational demand. If conservative treatment fails, the gold standard is a fasciotomy with a recurrence risk of 44.7% [1,3]. A review of current literature on treatment options for CECS illustrates preliminary studies of the use of botulinum toxins A injection therapy. The use of botulinum toxin A as a non-surgical option for CECS has been theorized due to the analgesic properties and muscle hypotonia to improve blood flow [2,3]. The objective of this review was to search the current literature on the use of botulinum toxin A as a treatment option for patients with CECS.

## Methodology

A thorough search of the literature via PubMed concerning botulinum toxin A as a treatment option for patients with CECS was completed.

## Results

Isner-Horobeti, et. al., performed a preliminary investigation on the effects of botulinum toxin A injections in the anterior and lateral compartments of the leg in patients diagnosed with CECS [3]. The intramuscular pressure (IMP), exertional pain, and muscle strength was monitored before and after injections. A total of 25 anterior leg compartments and 17 lateral compartments in 16 patients with CECS was studied. Specifically, IMP was measured before the injection and 3–9 months after injection.

The follow-up visit showed that there was a statistically significant decrease of IMP at one minute and five minute intervals following the cessation of running protocol in both the anterior and lateral compartments. The anterior and lateral compartments illustrated a reduction of 63% and 68% of IMP over the five-minute interval following cessation of activity, respectively. By five minutes following activity the anterior compartment was  $\leq 20$  mm Hg in 88% of patients and 93% of patients in the lateral compartment [3].

Over the course of the follow-up period, 94% of patients reported complete eradication of pain. Additionally, patients who presented with no pain were shown to have an increase in running performance of the protocol at follow-up visits. In regards to muscle strength, there was a noticeable loss of muscle grade in the tibialis anterior muscle at the

one-month follow-up visit in 69% of subjects, with the minimum muscle grade 4/5 in 19% of subjects. Patients demonstrated no permanent functional loss despite decrease in muscle strength; muscle strength returned to normal in all patients at following visits. The authors concluded that reduction of IMP and pain could be due to muscle hypotonia leading to muscle atrophy and improved blood flow, however, the effects of botulinum toxin A are not yet fully understood [3].

Since the Isner-Horobeti initial article, there have been two additional case studies utilizing the Isner-Horobeti's methodology to treat a twenty-year-old female recreational runner with a one-year history of CECS and a twenty-three-year-old male in the active military with a seven-year history of CECS [4,5].

In 2016, Baria and Sellon utilized the methodology of Isner-Horobeti (2013) to treat a twenty-year-old female recreational runner [4]. The patient's symptoms were progressively worsening to the point that even walking provoked her pain with noted paresthesia bilaterally in her legs. The patient reported intense pain with running which resolved after ten minutes of rest with failed interventions with ice and heat. The patient was not interested in surgical interventions; thus an alternative approach was needed. Ultrasound and electrical stimulated guided botulinum toxin injections were performed in the tibialis anterior, extensor digitorum longus, extensor hallucis longus, fibularis longus, and fibularis brevis [4].

Following the botulinum toxin A injections, there was a time period of fourteen-month follow-ups. The patient reported decreased pain and no noted paresthesia with activity at one week following the injections. Pain relief continued through the 14-month period with no reported loss in muscle strength and no adverse effects. In this study, the authors measured muscle bulk and sonographic echotexture that illustrated within normal limits at the final fourteen-month visit indicating no loss in muscle mass. They concluded that chemically induced muscle atrophy from the botulinum toxin A injections was not the cause of the reduction in intramuscular pressure and further studies to investigate the pharmacological effects need to be investigated [4].

In 2019, a twenty-three-year-old male on active military duty presented with continuous, bilateral lower leg pain with exertional activity. Due to the worsening symptoms and failed conservative treatments [5]. The clinical presentation noted that after ten minutes of running there was paresthesia to the dorsum of the feet and tearing, burning pain to the anterior lower legs that lasted up to twenty minutes following cessation of activity despite the application of ice and heat. CECS was confirmed in this patient utilizing a Stryker intracompartmental pressure monitor device noted >30 mm Hg in the anterior and lateral compartments bilaterally following one minute of exercise [5].

Due to occupational physical demand, worsening symptoms, failed conservative treatments, and noted high risk of recurrence after a fasciotomy, the patient opted for botulinum A toxin injections therapy for treatment. Following the methodology of Isner-Horobeti, the patient underwent a series of botulinum A toxin injections in the anterior and lateral compartments of the lower leg bilaterally. The initial side effect reported at the patient's one-week follow-up is initial soreness at injection sites and mild foot drop bilaterally. After the two-week follow-up, the patient denied any pain and soreness in the lower legs; after the 6 months follow up the mild foot drop previously noted bilaterally resolved and the patient reported eradication of pain and paresthesia with activity [5].

## Discussion

Our goal was to investigate the current literature for non-surgical treatments for CECS. These case studies are preliminary first steps toward evaluating botulinum toxin A injections as a potential form of therapy. The results from these studies illustrated eradication of pain and paresthesia seen following the injections in patients with CECS. Most importantly, there was no permanent functional loss and no evidence of recurrence in patients which are

associated risk factors with current surgical treatment options for CECS. Interestingly, the primary theory of the effects of botulinum toxin A injections in decreasing intramuscular pressure was not supported in following case studies after Isner-Horobeti et. al. initial study. Investigating the muscle bulk and sonographic echotexture of injected muscles noted unchanged following injection therapy suggesting an alternative theory to muscle hypotonia leading to establish blood flow from transient ischemia [4]. The effectiveness of this potential form of therapy both short term and long term are not fully understood as of yet, however, future larger prospective randomized controlled studies are needed.

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