行政院國家科學委員會專題研究計畫
"精簡報告"
肉毒桿菌素對肌膜激痛點治療效果之探討 (2/2)
The Study of Therapeutic Effect of Botulinum Toxin Type A on Myofascial Trigger Point (2/2)
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中文摘要

藉由對周遭肌肉神經交感處之間乙
醣胺素釋放的阻斷，使 A 型肉毒桿菌素
(Botulinum toxin type A; BTX-A)能達到抑
制肌肉收縮的效果，可能對於肌膜激痛
點也有治療的效果。先前的動物與人體實
驗顯示，一個肌膜激痛點區域內含有許多敏
感小點。每個敏感小點都含有感應部分(感
覺小點 sensitive focus)，與運動部分(活動
小點 active locus)。活動小點 stimulating of
的自發性電位活動(SEA)，是確認人類肌膜激
痛點(MTrP)或頸肌激痛點(MTrS)的重
要客觀性發現，這可能有助於我們用來做
為肌膜激痛症治療的有性評估。

本研究是要用客觀性的指標，來確認
評估 A 型肉毒桿菌素治療肌膜激痛症的效
果，同時確認乙醣胺素適量釋放對激痛點
的病理生成機制。在第一年的研究裡，18
隻紐西蘭成兔被分為三組，分別接受單劑
量的 BTX-A 5u, BTX-A 10u, 和 BTX-A
15u，來測試不同劑量對 SEA 影響的效果。
另有十隻兔子接受 BTX-A 的多點式小劑
量注射，來比較不同注射方式的影響。實
驗結果顯示，BTX-A 15u 或 10u 都能顯著
地降低 SEA 的盛行率，而 BTX-A 5u 就不
行；然而，15u 和 10u 與 5u 之間無顯著地
差別。單點式注射和多點式注射的效果也
沒有達到顯著性差異，但多點式注射對於
SEA 降低的效果有較為持久的趨勢。本研
究顯示 BTX-A 能夠確實降低兔子激痛
點(MTrS)裡 SEA 的盛行率，不同劑量與不
同注射方式所造成的影響，尚未達到顯著
有意義地差別。

第二年研究的目標是，將第一年動物
實驗的效果應用在人體上，以確認 BTX-A
對於人類肌膜激痛點(MTrP)的確實療效。
我們以 SEA 在激痛點裡的盛行率，做為
BTX-A 治療肌膜激痛症候群的客觀性評估
指標。本研究也將有助於我們對 SEA 之病
理生理學機制的瞭解。由於肉毒桿菌素價
格非常昂貴，而且此地的病人對於肉毒桿
菌素仍抱持著存疑審慎的觀望態度，這使得
我們在招募病人進行研究時，遇到阻礙。
目前只有五位肌膜激痛症的病人接受過肉
毒桿菌素的治療，並沒有發現到明顯的副
作用，初步的治療結果評估起來還算不
錯。我們希望在實驗結束前，能努力招募
到足夠數目的病人，以確實地驗證肉毒桿
菌素在肌膜激痛點的治療效果。

關鍵詞：A 型肉毒桿菌素、肌膜激痛症候
群，肌膜激痛點，自發性電位活動。

ABSTRACT

Botulinum toxin type A (BTX-A),
which inhibits muscle contraction by
blocking the release of acetylcholine from
peripheral neuromuscular junction, may
inactivate MTrP activity. The concept of
multiple small sensitive loci in a myofascial
trigger point (MTrP) has been wildly
accepted based on recent animal and human
studies. Recording of spontaneous
electrical activity (SEA) from many active loci is an important objective finding to identify an MTrP in human or myofascial trigger spot (MTrS) in rabbit. This study is designed to assess the effect of BTX-A on SEA prevalence in rabbit MTrS and human MTrP in order to confirm the role of excessive acetylcholine release on the pathogenesis of MTrP. In our first year experiment, Eighteen New Zealand rabbits were divided into three groups (a single bolus of BTX-A 5u, BTX-A 10u, and BTX-A 15u) to delineate the dose effect of BTX-A on the SEA. Another 10 rabbits were grouped as receiving multiple point injection to delineate the different injection technique effect. It was found that injection of BTX-A 15u or BTX-A 10u, but not BTX-A 5u, significantly reduced the prevalence of SEA. However, there was no significant difference in the effectiveness between the injection dose of 10u and 15u. No significant difference between single bolus injection and multiple point injection were noted, although there was a tendency that multiple point injection might maintain the SEA decreasing effect much longer than single injection. The result of the first year study demonstrated the suppressive effect of BTX-A on SEA prevalence in a rabbit MTrS region.

The goal of our second year study is, based on the results of our first year, to evaluate the effect of BTX-A on SEA in human MTrPs. Prevalence of SEA in the MTrP region may be an useful objective indicator to evaluate the therapeutic effectiveness of BTX-A injection to treat MTrPs. Due to the very high cost of BTX-A, and the somewhat bad feeling of patients about BTX-A, we had difficulty in recruiting many patients into our study. There were 5 patients who had received BTX-A for their MTrPs. No major complication was noted. The preliminary results showed BTX-A was effective in decreasing the SEA prevalence in human MTrP. We hope we can recruit more patients to better elucidate the therapeutic effect of BTX-A on myofascial pain syndrome.

Key Words: Botulinum toxin type A, myofascial pain syndrome, myofascial trigger point, spontaneous electrical activity.

Background and Objective

A painful myofascial trigger point (MTrP) is a important characteristic of myofascial pain syndrome (MPS). An MTrP is a highly localized hyperirritable spot in a palpable taut band of skeletal muscle fibers. During MTrP injection, it has been recommended that the needle should be inserted into multiple sites in the entire region in order to eliminate tenderness in the entire MTrP region. Hong and Torigoe developed an animal model and found it very useful in studying pathophysiology of MTrP. Based on their experiments, Hong had proposed a model of multiple small sensitive loci in an MTrP region. The most sensitive spot to elicit a local twitch response (LTR) in a taut band in rabbit muscle was defined as a myofascial trigger spot (MTrS), which corresponds to the human MTrP in many aspects. Simons and colleagues found spontaneous and continuous low-amplitude action potentials (10 to 50 µV, occasionally up to 80 µV) in human MTrPs, which were similar to the observation of Hubbard and Berkoff. To be distinguished from the intermittent spike activity (100 to 600 µV, biphasic, initially negative), this continuous low-amplitude activity was originally defined as spontaneous electrical activity (SEA). The minute locus from which SEA can be recorded is defined as an active locus of an MTrP. Based on both human and animal studies, it has been further confirmed that SEA is actually endplate noise as described by electromyographers. Since Botulinum toxin type A (BTX-A) can inhibit muscle contraction by blocking the release of acetylcholine from peripheral nerves, it should block SEA, and thus, might inhibit MTrP or MTrS activity.

The introduction of BTX-A into clinical use started from early 1980s. Through binding irreversibly to presynaptic
cholinergic nerve terminals, BTX-A blocks the exocytosis of the neurotransmitter, acetylcholine, and then inhibits muscle contraction. BTX-A has been approved by the Food and Drug Administration (FDA) in the United States for the management of strabismus, blepharospasm, and hemifacial spasm in patients 12 years of age or older. However, there are only a few studies regarding the management of MPS with BTX-A, their sampled size were small, and most of the therapeutic effects were evaluated by subjective parameters, not by objective parameters.

Our first-year study in rabbits showed that the effect on the decrease of SEA prevalence was significantly more in Groups II (BTX-A 10u) or III (BTX-A 15u) than in Group I (BTX-A 5u). We found no significant difference in the effects on SEA prevalence between Groups II and III (BTX-A 10u and 15u). This might be due to the small muscle volume of rabbit biceps femoris. However, it was apparent that the effect on the decrease in SEA prevalence was dose-dependent.

The purpose of this second-year study includes: (1) to assess the effect of BTX-A on SEA in human MTrP. If effective, it would indicate that excessive acetylcholine release is a factor in the pathogenesis of MTrPs. (2) to develop an objective indicator of the effectiveness of BTX-A in the treatment of MTrPs. Our hypothesis is that BTX-A is capable of decreasing the occurrence of SEA in an MTrP region. The results of different doses of BTX-A and different injection techniques were also compared.

Results and Discussion

In the second year, thirty patients with defined myofascial pain syndrome (clinical characteristics noted in the "Background section") will be recruited if they have not responded to traditional forms of treatment, have a chronic, refractory problem for three months or longer. Those patients with the following conditions will be excluded: (1) acute or serious medical problems; (2) other neurological disorders; (3) coagulopathy or any other bleeding disorders; (4) hepatitis B or AIDS; (5) severe cognitive impairment or psychiatric disorders.

We divided these patients into two groups: Gr I receiving a single bolus BTX-A injection; Gr II receiving multiple injections (on SEA locus guided by EMG) of BTX-A. The same procedures will be performed on the opposite side without BTX-A as a control group. SEA will be searched before BTX-A injection, 3 weeks after, and 6 weeks after BTX-A injection.

There has been 5 patients who participated in our study and received BTX-A for their MTrPs. No major complications, such as ecchymosis, muscle weakness, dysphagia, and allergic reaction were noted. The preliminary results showed BTX-A was effective in decreasing the SEA prevalence in human MTrP. However, due to the very high cost of BTX-A, and the somewhat bad feeling of patients about BTX-A, we had difficulty in recruiting many more patients into our study. This study is still on-going. We hope we can recruit more patients to better elucidate the therapeutic effect of BTX-A on myofascial pain syndrome.

Our study revealed that injection of BTX-A to an MTrP region could reduce the prevalence of SEA, which might be an objective evidence of therapeutic effect of BTX-A on MPS. Since SEAs were recorded more often from an MTrP region than from non-MTrP sites, SEA can be an objective indicator for the existence of an MTrP, and probably may be used as a reference for the degree of MTrP activity. This important finding supports Simons’ conclusion that SEA is abnormal endplate potentials due to excessive leakage of acetylcholine.

We also expected this SEA-guided multiple point injection would be more efficient for MPS patients, since the usual dose for single bolus injection for human muscle was 50–100u, which is higher than the dose needed for this multiple injection procedure. The results from our first year
study also support our hypothesis that multiple injection will be better effective than a single bolus injection.

References

Preliminary Results

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