P-51

Time-dependent Effects of Botulinum Toxin on Functional Recovery in Sciatic Nerve Injured Rats

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Introduction

- Botulinum neurotoxin A (BoNT/A) has recently gained traction in the field of regenerative medicine due to reports of its effectiveness in regeneration following peripheral nerve injury.
- Our previous study has shown that peripheral nerve regeneration is best achieved at a BoNT/A concentration of 7 U/kg.
- However, the proper timing of injections has not yet been studied.
- This study compared the degree of functional recovery by injecting BoNT/A immediately after injury or one week after injury.

Methods

- Twenty 6-week-old rats with sciatic nerve injury were randomly divided into four groups including the immediately treated (IT) group, delay treated (DT) group, the control group and the sham group.
- IT group received a single session of intraneural BoNT/A (7 U/kg) injection immediately after a nerve-crushing injury.
- DT group received a single session of intraneural BoNT/A (7 U/kg) one week after sciatic nerve injury.
- One week following sciatic nerve injury, the control group was treated with an intraneural injection of normal saline.
- The sham group received only skin and muscle incision.
- For functional assessment, electrophysiological studies and serial sciatic functional index (SFI) analysis were performed every week for 9 weeks.

Result

- The electrophysiological study results demonstrated an increase in compound muscle action potential amplitude (CMAP) in IT, DT and control groups, indicating a gradual recovery of motor function.
- Comparing IT and control group, IT group showed a significantly greater CMAP two weeks after a nerve-crushing injury ($p < 0.05$).
- In the DT group, there was no significant difference from the control group until week 7, but there was a significant difference in CMAP from week 8.
- When comparing the IT and DT groups, the IT group had a significantly greater CMAP starting at week 5.
- Even though time passed by week 9, all groups had considerably lower CMAP values than the sham group.

Result

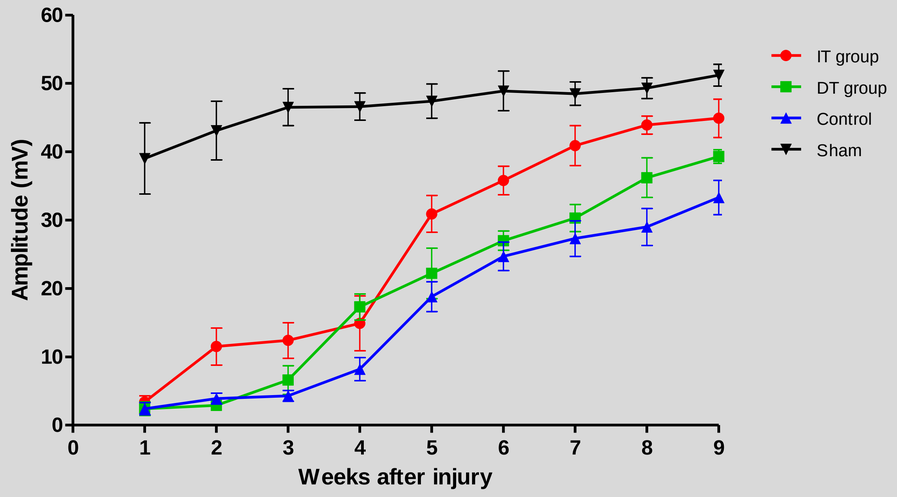

Figure 1. CMAP amplitude of each group, weekly

- The SFI results showed similar trends to the CMAP results.
- When compared to the control group, both IT and DT group had significantly higher SFI score from week 8 ($p < 0.05$).
- When comparing the IT and DT groups, the IT group showed greater SFI throughout the experiment, with statistically significant peaks at weeks 3 to 5 and after week 8.
- While the CMAP results fell short of the sham group, the SFI results showed that the IT group was not statistically significantly different from the sham group at week 9.

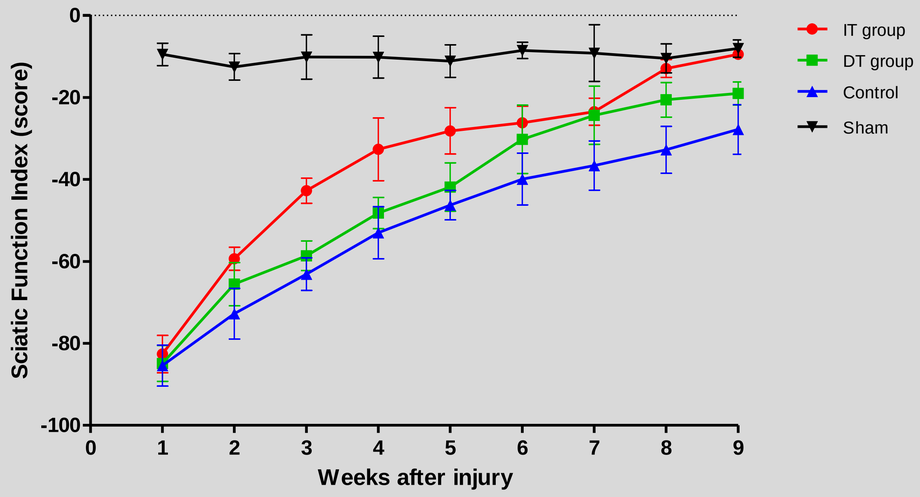

Figure 2. SFI score result of each group, weekly

Conclusion

- Our research showed that BoNT/A injections immediately after nerve injury were most effective. Injections a week after injury resulted in faster recovery than the control group.
- In conclusion, it seems that BoNT/A injections should be administered as soon as possible for recovery after nerve damage. Furthermore, as it was effective even when injected a week later, we suggest that injecting during the subacute phase is still effective.

Reference

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