Antispastic therapy with botulinum toxin type A in patients with traumatic spinal cord lesion

Botulinumtoxininjektion als antispastische Therapieoption bei Patienten mit traumatischer Rückenmarksläsion

Abstract

Objectives: The purpose of this study was to determine the effect of botulinum toxin injections for the treatment of spasticity after traumatic spinal cord injury.

Methods: 9 patients were included in this prospective designed study, with a follow-up of at least 2 years. All patients suffered from a massive spasticity after traumatic spinal cord lesion. Conservative treatment options did not show satisfying results. All patients were injected a maximal dose of 2,000 units of botulinum toxin A in no more than 6 skeletal muscle groups. Clinical control examinations were performed after 2 weeks and after at least 2 years.

Results: 6 patients reported a good or very good result. One patient offered increasing difficulty in walking for a short time after injection. 2 patients showed no beneficial effects. One patient experienced a modest temporary general weakness for 3 days. After 2 years, 3 patients showed improved function with persistent reduction of spasticity. In the other cases, the beneficial effect lasted for an average of 9 months.

Conclusion: Botulinum toxin A injection seems to be an effective complementary therapy option in the treatment of spasticity of paraplegic patients with complete deficit of their motor function (ASIA A and B) and a spastic distribution pattern, effecting only a limited number of muscle groups. Caution has to be recommended for incomplete paretic patients, who are able to walk.

Keywords: botulinum toxin, spasticity, traumatic spinal cord lesion

Zusammenfassung

Fragestellung: Ziel dieser Arbeit war es, den Effekt von Botulinumtoxininjektionen bei der Behandlung therapieresistenter Spastiken nach traumatischen Rückenmarkläsionen zu evaluieren.

Methode: Es handelt sich um eine prospektive klinische Studie, die insgesamt 9 Patienten mit spastischer Paraplegie/Paraparese nach traumatischer Rückenmarksläsion erfasst. Alle 9 Patienten wiesen ausgeprägte therapieresistente Muskelspastiken auf. Allen Patienten wurden bis zu 2,000 Einheiten von Botulinumtoxin A in nicht mehr als 6 Muskelgruppen injiziert. Eine klinische Nachuntersuchung erfolgte nach 2 Wochen und nach mindestens 2 Jahren.

Ergebnisse: Sechs Patienten berichteten über ein gutes oder sehr gutes Ergebnis und zeigten sich zufrieden. Bei einem Patienten fiel eine Schwäche der angrenzenden Muskulatur auf, wodurch seine Mobilisation im Alltag negativ beeinflusst wurde. Bei 2 Patienten ließ sich keine wesentliche Spastikreduktion nachweisen. Ein Patient entwickelte eine generalisierte Schwäche, die sich spontan nach 3 Tagen zurückbildete. Von den übrigen 6 Patienten wiesen 3 Patienten nach 2 Jahren eine unveränderte zufriedenstellende Spastikreduktion auf, ohne dass eine erneute Therapie erforderlich war. Die übrigen 3 Patienten gaben an, dass der Effekt ca. 9 Monate angehalten hatte. Bei der 2-Jahreskontrolle
wiesen diese eine Spastiksymptomatik entsprechend der vor der Be-
handlung auf.

Fazit: Die Studie zeigt, dass die Injektion von Botulinumtoxin A eine
wirkungsvolle Therapie therapierezisterter Spastiken mit Beteiligung
selektiver Muskelgruppen nach traumatischer Rückenmarksläsion (ASIA
A und B) darstellen kann. Mit Vorsicht sollten die Injektionen bei denje-
nigen Patienten angewendet werden, die eine inkomplette Lähmung
aufweisen und Fußgänger sind.

Schlüsselwörter: Botulinumtoxin, Spastik, traumatische
Rückenmarksläsion

Introduction

Different therapy strategies are used to reduce spasticity
in patients with traumatic spinal cord lesions. These op-
tions consist of conservative management, including
physiotherapeutic and pharmacological approaches, as
well as surgical techniques. Botulinum toxin plays an im-
portant role in the treatment of spasticity of different
diseases [1]. By locally injecting botulinum toxin, an isolated
skeletal muscle inhibition and improved muscle kinemat-
ics can be achieved. Thus, botulinum toxin injection is a
treatment option of particular interest in cases of localized
spasticity [1], [2], [3].

The purpose of this study is to evaluate the effect of
botulinum toxin injections in patients with spasticity
caused by traumatic spinal cord injuries and to determine
favourable patients’ characteristic.

Materials and methods

The study included 9 male patients (mean age 40 y ±
16 y), suffering from a none-acute traumatic lesion of the
spinal cord and chronic spastic paraplegia (Table 1). Eight
patients had a complete spinal cord lesion, defined as
American Spinal Injury Association (ASIA) impairment
scale type A [4]. One patient showed an incomplete
neurologic deficit, defined as ASIA type C. All of them
offered an increased spasticity state of 3 to 4 on the
Ashworth scale modified by Bohannon and Smith [5], [6].
All patients underwent a combination of physiotherapeutic
and oral antispastic therapy for at least three months
without satisfying success. Major spasticity affected not
more than six general muscle groups of the lower limbs.
All patients underwent botulinum toxin A injections in the
affected muscle groups with a dilution of 100 U/ml under
ultrasonographic control. The maximum general injection
dose was limited to 2,000 U. After the injection, all pa-
tients underwent intensive physiotherapy of the affected
muscles for three days to improve the Botox distribution.
All patients underwent clinical control examinations after
3 ± 2 weeks and 34 ± 3 months after botulinum toxin
injections.

Statistics

A descriptive analysis was performed.

Results

Six of the nine patients were satisfied or very satisfied
after botulinum toxin injection and offered a clear reduc-
tion of spasticity in the treated muscle groups to a state
of two or less on the Ashworth scale modified by Bohan-
non and Smith, with an average reduction of 1.9 states
after two weeks (Figure 1). Five of them reported reduced
difficulties during mobilisation including transfers to the
wheel chair as well as getting dressed or undressed. The
patient with incomplete motor function deficit showed a
relevant reduction of the adductor spasticity. However,
he had increasing problems in walking due to additional
muscle weakness for three months and regaining muscle
strength over a period of another three months after-
wards. Another patient reported a temporary general
weakness after injection, which fully recovered after three
days. Two patients experienced no benefit regarding their
spasticity level.

The effect of the botulinum toxin injections started after
two to five days and reached a peak after an average of
two weeks. No signs of infection or allergic reaction were
recordable, particularly at the side of injection. At the final
evaluation, three patients had persistent low spasticity
at the affected muscle groups of state two or less of the
Ashworth scale modified by Bohannon and Smith. Three
patients regained spasticity to a slightly lower level (≤3)
compared to the initial level of spasticity (Figure 1). The
beneficial effect lasted for at least seven months and
decreased subsequently in all of them.

Discussion

Several studies showed the beneficial effect of botulinum
toxin to adults and children in cases of spasticity and
demonstrated it to be safe even after repeated injections
[7], [8]. However, Bakheit et al. described dose-dependent
side-effects in 7% of the patients [9]. The side-effects
consisted of focal or generalized muscle weakness and
urinary incontinence in about 1% of patients. All other
reported adverse events were less common and included
pain at the site of the injection, fatigue, somnolence, in-
fluenza-like symptoms, fever, and purpuric skin rash.
Similarly, one of our patients (11%) complained of mild
Table 1: Patient population

| Pat | Age | Level of neurop def | ASIA | Spastic: initial | Muscle groups involved (side) | Inj units | Spastic: 2 weeks | Effect duration | Adverse effect |
|-----|-----|---------------------|------|-----------------|-------------------------------|-----------|-----------------|----------------|---------------|
| 1   | 45  | L1                  | A    | 4               | Hip flex; add (bil)           | 2,000     | 1               | 9 months       | None          |
| 2   | 31  | L2                  | A    | 4               | Knee flex; Ankle sup+plant fl (bil) | 1,500     | 1+              | 7 months       | None          |
| 3   | 32  | L1                  | A    | 4               | Hip flex; Knee flex; Ankle plant flex (l) | 800       | 1               | ≥35 months     | None          |
| 4   | 20  | L1                  | A    | 4               | Hip flex; add; Knee flex; Ankle sup+plant fl (bil) | 2,000     | 2               | 8 months       | None          |
| 5   | 77  | L1                  | C    | 3               | Hip add; Knee flex (bil)       | 1,200     | 2               | 6 months       | Mobility ↓     |
| 6   | 39  | C7                  | B    | 3               | Hip add; Knee flex; Ankle plant fl (bil) | 2,000     | 3+              | None           | Initial gen weakness |
| 7   | 28  | Th12                | A    | 3               | Hip add (bil)                  | 1,000     | 1               | ≥26 months     | None          |
| 8   | 47  | L1                  | A    | 4               | Hip flex; add; Knee flex (bil) | 2,000     | 4               | None           | None          |
| 9   | 41  | L2                  | A    | 3               | Ankle sup+plant fl (bil)       | 2,000     | 1               | ≥25 months     | None          |

Pat: patient; neurop def: neurologic deficit; Inj: units: units of botulinum toxin injected; ASIA: American Spinal Injury Association; C: cervical spine; Th: thoracic spine; L: lumbar spine; Flex: flexion; Add: adduction; Sup: supination; Plant fl: plantar flexion; gen: general

Figure 1: Depicts the course of spasticity, defined by the Ashworth Scale modified by Bohannon and Smith, on the day prior injection, the day afterwards, after two weeks, and after two years. The mean values and the standard deviation are presented.

(Pri: Injection)

Spastic systemic weakness after injection, lasting for three days. Adverse effects were recorded after administering doses of more than 1,000 U in children and more than 2,000 U in adults [9]. Therefore, our maximal dose of administration was 2,000 U for each adult patient.

The encouraging results of our study are consistent with other studies that showed beneficial effects of botulinum toxin injections in the therapy of spasticity [1], [2], [3], [10]. Similarly, two case reports showed a positive effect of botulinum toxin injections in patients with spinal cord injury and ulcers caused by spasticity [11], [12].

In our study population, 6 of 9 of the patients presented with a significant reduction in their spasticity, reported a better quality of life, and were satisfied or very satisfied. Two of our patients did not benefit from the therapy. One of these patients showed a diffuse pattern of spasticity that affected six functional muscle groups of the upper and lower leg. Thus, this patient seemed to be a poor candidate for this treatment strategy based on the restricted maximal dose of botulinum toxin. Furthermore, this therapy has to be seen very critically in incomplete paretic patients (ASIA C), particularly in those who are...
able to walk. These patients are commonly dependent on maximum strength of all functional muscle groups at their lower limb. Thus, botulinum toxin injection causes weakness of certain muscle groups, which might lead to temporary immobilisation as seen in one of our cases. The strong limitation of this study is its limited patient group, including only nine patients and only one patient with incomplete motor function deficit (ASIA C). Thus, certain patients’ characteristics which might cause limited effectiveness of botulinum toxin injections, such as diffuse spasticity pattern or incomplete motor function deficit are based on single cases only. Thus, the statistics was based on descriptive analysis only. Additionally, the level of spasticity was based on the Ashworth scale modified by Bohannon and Smith that is purely observer dependent, which might lead to bias. Nonetheless, this study includes a very selective patient collective with beneficial effects in the majority of the cases. Future studies are warranted to further evaluate the effects of botulinum toxin and the safety profile of it in the treatment of patients with spasticity after traumatic spinal cord injury.

Clinical messages

• Botulinum toxin injection for the treatment of spasticity after traumatic spinal cord lesion has the potential of a very promising treatment strategy.
• It seems to be particularly effective in patients with complete lower limb motor function deficit and spasticity pattern limited to few muscle groups.
• Caution has to be recommended in incomplete paretic patients, who are still able to walk, in order to avoid immobilizing effects.
• Further studies are necessary to find parameters, which might affect the antispastic therapy with botulinum toxin.

Notes

Competing interests

The authors declare that they have no competing interests.

References

1. Rekand T. Clinical assessment and management of spasticity: a review. Acta Neurol Scand Suppl. 2010;(190):62-6. DOI: 10.1111/j.1600-0404.2010.01378.x
2. Koman LA, Mooney JF 3rd, Smith BR, Walker F, Leon JMD. Botulinum toxin type A neumoskeletal blockade in the treatment of lower extremity spasticity in cerebral palsy: a randomized, double-blind, placebo-controlled trial. BOTOX Study Group. J Pediatr Orthop. 2000 Jan-Feb;20(1):108-15. DOI: 10.1097/01241398-200001000-00022
3. Lamping N, Roche N, Carne P, Cheze L, Pradon D. Effect of botulinum toxin injection on length and lengthening velocity of rectus femoris during gait in hemiparetic patients. Clin Biomech (Bristol, Avon). 2013 Feb;28(2):164-70. DOI: 10.1016/j.clinbiomech.2012.12.006
4. American Spinal Injuries Association. ASIA Classification – Standards for neurological and functional classification of spinal cord injury. Chicago: American Spinal Injuries Association; 1992.
5. Ashworth B, Grimbly L, Kugelberg E. Comparison of voluntary and reflex activation of motor units. Functional organization of motor neurones. J Neurol Neurosurg Psychiatr. 1967 Apr;30(2):91-8. DOI: 10.1136/jnnp.30.2.91
6. Bohannon RW, Smith MB. Interrater reliability of a modified Ashworth scale of muscle spasticity. Phys Ther. 1987;67(2):206-7. Available from: http://ptjournal.apta.org/content/67/2/206
7. Dressler D. Routine use of Xeomin in patients previously treated with Botox: long term results. Eur J Neurol. 2009 Dec;16 Suppl 2:2-5. DOI: 10.1111/j.1468-1331.2009.02877.x
8. Guarany FC, Picon PD, Guarany NR, dos Santos AC, Chiella BP, Barone CR, Fendt LC, Schesatatsky P. A double-blind, randomised, crossover trial of two botulinum toxin type A in patients with spasticity. PLoS ONE. 2013;8(2):e56479. DOI: 10.1371/journal.pone.0056479
9. Bakheet AM, Severa S, Cosgrove A, Morton R, Roussouns SH, Doderein L, Lin JP, Roussou SH. Safety profile and efficacy of botulinum toxin A (Dysport) in children with muscle spasticity. Dev Med Child Neurol. 2001 Apr;43(4):234-8. DOI: 10.1111/j.1469-8749.2001.tb00195.x
10. Corry IS, Cosgrove AP, Duffy CM, Taylor TC, Graham HK. Botulinum toxin A in hamstring spasticity. Gait Posture. 1999 Dec;10(3):206-10. DOI: 10.1016/S0966-6362(99)00037-5
11. Naiker AS, Rooshi SA, Chan JL. Botulinum toxin type A for rehabilitation after a spinal cord injury: a case report. J Orthop Surg (Hong Kong). 2009 Apr;17(1):96-9. Available from: http://www.josonline.org/pdf/v17ip96.pdf
12. Intioso D, Basciani M. Botulinum toxin type A in the healing of a chronic buttock ulcer in a patient with spastic paraplegia after spinal cord injury. J Rehabil Med. 2009 Nov;41(13):1100-2. DOI: 10.2340/16501977-0460

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