Use of botulinum toxin to improve upper limb spasticity and decrease subsequent carer burden in long-term care residents: a randomised controlled study

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KEY MESSAGES

1. Infirmary patients who were treated with intramuscular injection of botulinum toxin A for upper limb spasticity had significant improvement in muscle tone and joint mobility, and caregivers were able to perform basic upper limb care more easily.
2. A basic stretch programme was also beneficial in improving joint mobility, or at least prevented further deterioration of limb contracture in such patients.

Hong Kong Med J 2016;22(Suppl 2):S43-5
HHSRF project number: 07081271

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Introduction

Spasticity leads to decreased range of motion of joints, increased pain, spasm, functional disability, and contractures. Limb spasticity also increases the burden on carers in the provision of nursing and personal care. The use of botulinum toxin to treat spasticity has increased. It blocks acetylcholine release at the neuromuscular junction, thereby inhibiting muscle contraction and decreasing spastic muscle tone. Its antispastic effect usually lasts approximately 3 months. It is safe, with few (usually transient and localised) adverse effects. Since 2008, the American Academy of Neurology has recommended that botulinum neurotoxin be offered as a treatment option for spasticity in adults and children. Nonetheless, its effect on immobile infirmary patients has not been studied. This study aimed to evaluate the role of botulinum toxin A for treating upper limb spasticity in debilitated infirmary patients and the decrease in carer burden when given as a supplement to conventional physiotherapy and occupational therapy.

Methods

This double-blind, placebo-controlled study was conducted from November 2009 to March 2011. The sample size calculation was based on the proportion of subjects in each group attaining a clinically significant four-point improvement in carer burden scale at 6-week post injection. Based on the data from a pilot study, the total sample size was calculated to be 70.

Patients aged >16 years who had (1) upper limb spasticity for >1 year, (2) shoulder adductor, finger flexor, or elbow flexor spasticity >2 on the Modified Ashworth Scale (MAS),[1] (3) at least moderate difficulty with two out of four items defining carer burden scale,[1] and (4) were able to tolerate limb stretching exercises and limb splints for treating spasticity were recruited from four infirmary units and five care and attention homes in Hong Kong. Patients were excluded if they had (1) functionally useful movement in the spastic limb, (2) rigid affected elbow and finger joints that were unlikely to respond to botulinum toxin injection, (3) severe swallowing difficulties and no tube-feeding support, (4) unstable medical conditions, or (5) peripheral motor neuropathic diseases or neuromuscular junctional disorders.

Patients were randomised to receive botulinum toxin or saline injection by a clinician. The maximum total dose of intramuscular botulinum toxin type A (Dysport) used was 1000 units for one patient. Dose selection for individual muscles was based on clinical judgment of spasticity by the injection team. Electrical stimulator-guided or ultrasound-guided method was used for deep muscles in the region of the forearm. All patients received concurrent standardised physiotherapy of passive limb stretching exercises twice a week, in addition to splinting of the affected upper limb for 3 hours/day, 5 days/week. The assessor, patients, and their care-givers were blinded to the injection material.

The primary outcome was carer burden scale at 6 weeks post intervention. Secondary outcomes included Goal Attainment Scaling, degree of spasticity using the Tardieu scale and MAS, resting angular positions of the shoulder and elbow joints using a plastic goniometer with a 360° scale, passive range of movement of shoulder abduction, elbow extension, finger position at rest and at maximal passive finger extension as recorded by a five-point scale, pain assessment using the Pain Assessment

in Advanced Dementia (PAINAD) Scale[2] observed while performing carer burden scale, and incidence of osteoporotic fracture, pressure sores and skin infections in the affected limb. Serial assessments were made at baseline and 2, 6, 8, 12, 16, 20, and 24 weeks post injection.

Results

A total of 21 males and 34 females (mean±standard deviation age, 69±18 years) were randomised to the botulinum toxin A or saline injection group. The two groups were comparable in baseline demographics (Table 1). The mean Charlson's comorbidity index was 3.5, indicating a high number of comorbidities. More than 90% of patients were bedbound or chairbound; all had chronic spasticity, and the mean duration of spasticity was >9 years. Most patients already had some degree of joint contractures at baseline; the mean passive range of movement in the affected joints was less than half that of the normal value.

TABLE 1. Baseline characteristics of the botulinum toxin and saline groups

Characteristics	Mean±SD or No. (%) of patients	
	Botulinum toxin (n=30)	Saline (n=25)
Age (years)	68.5±18.1	69.0±19.2
No. of males	12 (40.0)	9 (36.0)
Severe spasticity	12 (40.0)	9 (36.0)
Baseline carer burden score	10.9±1.7	10.3±1.9
Charlson's co-morbidity index	3.9±2.0	3.1±1.5
Duration of spasticity (years)	9.5±4.2	9.8±4.6
Spasticity caused by brain problem	30 (100)	25 (100)
Taking oral antispasticity medications	12 (40.0)	8 (32.0)
Rancho cognitive functioning ≥level V	11 (36.7)	11 (44.0)
Modified Functional Mobility Categories of lier or sitter	30 (100)	24 (96.0)
Received baseline limb stretching exercise	6 (22.0)	4 (16.0)
Received baseline splinting	4 (13.3)	2 (8.0)

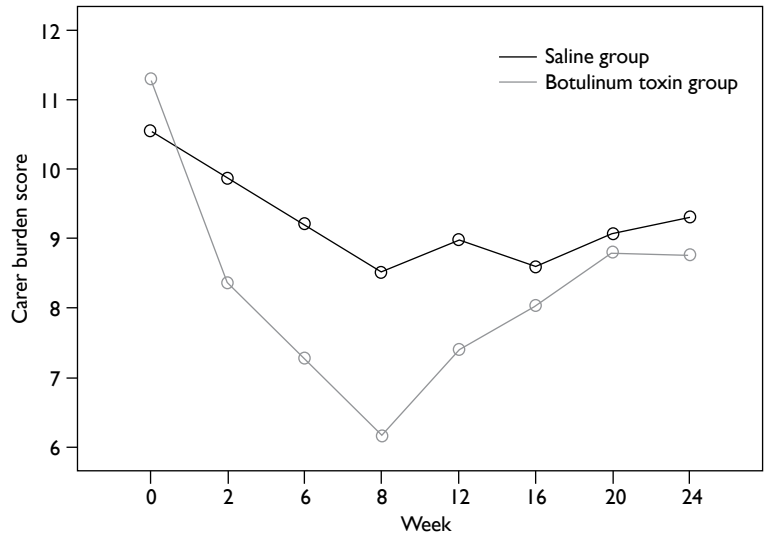

FIG. Carer burden score of the botulinum toxin and saline groups (P<0.001)

At 6 weeks post injection, compared with the placebo group, the botulinum toxin group had a significant decrease in the carer burden scale (2/25 (8%) vs 18/30 (60%) patients had a four-point reduction, P<0.001, Fig) and simultaneous improvement in resting PAINAD (-1.0, P=0.013), PAINAD during basic care procedures (-1.8, P<0.001), MAS of shoulder adductors (-1.47, P<0.001), MAS of elbow flexors (-1.63, P<0.001), and MAS of finger flexors (-0.83, P<0.001), as well as passive range of movement for shoulder abduction (+15°, P<0.001), elbow extension (+19°, P<0.001), and finger extension (+0.47 as recorded by a five-point scale, P=0.006). The trend in improvement in carer burden scale, PAINAD, passive range of movement, and MAS scores in the botulinum toxin group peaked or plateaued at week 8; thereafter improvements gradually diminished in magnitude.

Compared with the saline group, the botulinum toxin group had a significantly greater magnitude of improvement in their Goal Attainment Scaling score (12.65, P=0.001). Most goals pertained to improving the resting position of the limbs (40%) and the range of movement of the joints (32%), followed by decreasing pain during limb stretching (16%) and promoting healing of skin (11%). The botulinum toxin group patients had a significantly greater magnitude of improvement in all four goals, particularly for decreased pain during limb stretching (38% vs 100%, P=0.007).

The botulinum toxin group had clinically significant improvement in muscle spasticity of the affected upper limb (as measured by Tardieu scale and MAS) over the 24-week study period, as well as in the upper limb position (resting angles of both shoulder and elbow joints) The botulinum toxin group also had a trend of improvement in joint mobility in terms of shoulder abduction and elbow extension.

In the saline group, one patient had spasticity in both arms with the right arm being more severely affected, and only the right arm was given interventions including passive stretching and splinting. This patient developed a humeral fracture in his left upper arm (Table 2). In the botulinum toxin group, three patients died of pneumonia: two at week 13 and one at week 20 (Table 2). The two groups did not differ significantly in the cumulative incidence of pneumonia, fever, soft tissue swelling, pressure points, or death.

Discussion

Infirmary patients with limb spasticity seldom receive appropriate treatment, despite its high prevalence and great impact on daily care and quality of life. In our study, only 18% and 11% of patients received limb stretching and splinting, respectively, at baseline, and only 36% were given oral anti-spastic drugs.

Botulinum toxin significantly improved the rating on the carer burden scale in patients

with moderate-to-severe upper limb spasticity, mainly due to its effect on reducing limb spasticity and improving the joint range of movement. In patients with severe cognitive impairment and high dependence on carers for activities of daily living, the carer burden has been shown to be an indicator of patient prognosis and well-being. For totally dependent infirmary patients who are unable to communicate, the carer burden is an objective measure of how severely the patient is disabled by limb spasticity and contractures. The carer burden also indirectly reflects the patient's quality of life. If the carer burden is high, the patient will likely be subjected to difficult and possibly painful care procedures on a daily basis, sometimes more often. The results of our study are in accordance with previous studies showing that botulinum toxin effectively decreases disability and carer burden in patients with post-stroke arm spasticity.[1,3]

The botulinum toxin and saline groups did not differ significantly in pain level (as measured by the PAINAD scale). Pain relief after botulinum toxin treatment may be due to a decrease in severe spasticity of the affected muscles and increased joint mobility. Botulinum toxin may also act as an analgesic by blocking the effect of neurotransmitters that have been implicated in the pain pathway.[5] Nonetheless, the results of previous studies with patients who were able to communicate varied with regard to pain improvement after botulinum toxin injection for upper limb spasticity.[1,3,4] Our study evaluated the impact of botulinum toxin in patients who were unable to communicate, so an observation scale for pain (PAINAD) was used. Nevertheless, it cannot differentiate pain from discomfort or negative affect in such patients. Apart from pain, a high PAINAD scale may indicate that the patient is resistant to care, or is experiencing negative emotions or anxiety.[2] Other external factors could have simultaneously affected the patients' pain level, so it would be difficult to determine degree of pain relief directly due to relief of spasticity.

It should be noted that the saline group also showed improvements in spasticity and passive range of movement of the affected joints, with a mean reduction in carer burden scale score of 1.2 (P=0.002) at 24 weeks post-intervention. This implies that passive stretch and splinting alone can improve joint mobility, or at least prevent further deterioration of the limb contracture.

One patient in the saline group with bilateral upper limb spasticity developed a spontaneous humeral fracture in his left upper arm, although he only received passive stretch and splinting in his right upper arm. It is likely that this humeral fracture was related to difficult basic care procedures due to the bilateral upper limb spasticity. During passive transfer or lifting of bed-bound infirmary patients, their joint contractures act as a supporting point of leverage to exert any external force on the nearby fragile bone, thereby causing the fracture.

Three patients in the botulinum toxin group died of pneumonia at least 3 months post injection when the effects of botulinum toxin had already begun to fade; these deaths were not considered to be related to botulinum toxin type A treatment.

TABLE 2. Cumulative incidence of complication in the botulinum toxin and saline groups at week 24

Complication	No. (%) of patients	
	Botulinum toxin (n=30)	Saline (n=25)
Pneumonia	4 (13.3)	2 (8.0)
Fever	8 (26.7)	6 (24.0)
Soft tissue swelling	4 (13.3)	1 (4.0)
Skin breakdown at pressure points	5 (16.7)	6 (24.0)
Long bone fracture	0	1 (4)
Death	3 (10.0)*	0

* Two patients died at week 13 and one patient died at week 20 due to pneumonia

Conclusions

Infirmary patients who were treated with intramuscular injection of botulinum toxin A for upper limb spasticity had significant improvement in muscle tone and joint mobility, and carers were able to perform basic upper limb care more easily. The treatment was also associated with improved scores for patient-centred outcome measures. The dosage of 1000 U was safe in these frail infirmary patients.

Acknowledgements

This study was supported by the Health and Health Services Research Fund, Food and Health Bureau, Hong Kong SAR Government (#07081271). We thank all clinical staff and patients who took part in this study.

Results of this study have been published in: Lam K, Lau KK, So KK, et al. Can botulinum toxin decrease carer burden in long term care residents with upper limb spasticity? A randomized controlled study. J Am Med Dir Assoc 2012;13:477-84.

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