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Full Length Research Paper

Clinical efficacy of Neuronox® botulinum toxin treatment in hemifacial spasm patients

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Hemifacial spasm (HFS) is a disease causing abnormal movement of the face. Treatment with a botulinum toxin injection is effective. Original botulinum toxin is expensive, particularly in developing countries. We evaluated clinical efficacy and safety of generic botulinum toxin in HFS patients. A 16-week, open labeled, prospective study to evaluate Neuronox® treatment at HFS clinic, Khon Kaen University hospital, Thailand was carried out. Peak improvement (PI), time to PI (TPI), and duration of response period (D) were reported by patients every 4 weeks. In total, 50 HFS patients participated in the study; 30 new and 20 previously diagnosed patients. Two patients did not response to Neuronox® treatment; one in each group. For those who responded to Neuronox® treatment, the mean PI, TPI, and D was 73.44%, 9.44 weeks, and 15 weeks, respectively. The PI, TPI, and D were not statistically different between new and previously diagnosed patients. Ptosis and facial paresis were the common side effects and mostly occurred in the first 4 weeks. Treatment of HFS by generic Neuronox® botulinum toxin is an effective alternative treatment with similar rate of side effects to original botulinum toxin. It may be preferable in countries with limited healthcare resources.

Key words: Hemifacial spasm, Neuronox®, botulinum toxin, efficacy, side effects.

INTRODUCTION

Hemifacial spasm (HFS) is a common abnormal movement of the face that affects patient's quality of life. Presently, the most effective treatment is a botulinum toxin injection. Dysport® and Botox® are the two common botulinum toxins in the market and have the efficacy of 80 to 85% (Bentioglio et al., 2009; Jitpimolmard et al., 1998; Poungvarin et al., 1995).

Currently, HFS patients in Thailand are treated with original Dysport® or Botox® injections. The expenses are between 1,794 to 3,488 Baht (60 to 116 USD) per 60 to 120 units of Dysport® or 1,770 to 3,540 Baht (59 to 118 USD) per 15 to 30 units of Botox®. The drug is effective for 3 to 4 months. Hence, a patient needs 3 to 4 injections a year, with an expense around 5,400 to 16,200 (180 to 540 USD) baht to 7,200 to 21,600 (240 to 720 USD) per year. Thailand has recently registered another type of botulinum toxin called Neuronox®. It is a botulinum A toxin and has efficacy equivalent to Botox®, but the cost is around 300 Baht (10 USD) per 5 units or half price of Botox® (Yoon et al., 2009). Therefore, if Neuronox® is used to treat HFS patients, the medical cost will be two-fold reduced. A few studies have shown that Neuronox® is as effective as Botox® in HFS and blepharospasm. In Thailand, there is limited study of Neuronox® in HFS treatment. A previous report showed that Neuronox® treatment in HFS patients had comparable quality of life to original botunilum toxin

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treatment (Kongsengdao and Kritalukkul, 2012). Here, we aim to determine the efficacy and side effect of Neuronox® in HFS treatment.

PATIENTS AND METHODS

We did a 16-week, open labeled, prospective study to evaluate Neuronox® treatment at HFS clinic, Department of Medicine, Faculty of Medicine, Khon Kaen University. Diagnosis of HFS was made clinically by two neurologists (SJ and ST). We included HFS patients aged 20 and above; both either new or previously diagnosed. New patients must never be treated with botulinum toxin. For those previously diagnosed, the patients must have good responses to either Dysport® or Botox® botulinum toxin. The subjectively rated responses to the original botulinum toxin of more than 80% indicated good responses. The exclusion criteria were patients with brain lesion or had other neurological diseases, pregnant women, or allergic to botulinum toxin. Injection of 15 units of Neuronox® (Medytox Inc., Seoul, Korea) was performed on the 3 standard sites; 5 units per site. The three injected sites were the medial and lateral part of the lower eyelid and the lateral part of the orbital orbicularis oculi, just above the lateral eyebrow (Jitpimolmard et al., 1998). An informed consent was obtained from each patient before enrollment. The study protocol was approved by the Ethical Committee for Human Research, Khon Kaen University.

Evaluation

We assessed the patients' peak improvement (PI), time to PI (TPI), duration of response period (D), and quality of life by using Thai HFS-30 (Setthawatcharawanich et al., 2008) form (data not presented). The HFS-30 is a Thai version of HFS-30 that is used to evaluate quality of life in HFS patients. The assessment was done every 4 weeks for 4 times and then every 4 weeks until the patient needed another treatment. If the symptoms worsened before the appointment, the neurologists evaluated and treated the patients properly. These patients were defined as non-responders to treatment.

At each visit, the patients reported PI, TPI if presented, D, and side effects (Jitpimolmard et al., 1998). PI defined by the maximum percentage of improvement after Neuronox® injection in percentage (0 to 100%). Response to treatment was identified if PI was more than 20%. D is the duration of being free of symptom. Any side effects including skin irritation, ptosis, facial paresis, inability to close eyes firmly, and other symptoms are recorded.

Sample size calculation

Base on previous study (Poungvarin et al., 1995), 40 and 80% of patients' response to placebo and botulinum toxin, respectively. With type I error of 0.05, two-tailed, and 80% of power, the sample size of patients required was found to be 40 and 10 patients were added for loss to follow up or to account for those who do not complete the study. The total sample size was 50.

Statistical analyses

PI, D, and side effects were reported by descriptive statistics. PI and D were compared between new and previously diagnosed patients by Wilcoxon rank sum test. The statistical significant was declared if the p-value was less than 0.05. Patients who did not response to Neuronox® treatment were excluded from the statistical analyses. All statistical analyses were done by STATA software Version 10.1, Texas, USA.

RESULTS

In total, 50 HFS patients participated in the study; 30 new and 20 previously diagnosed patients. There were no patients with previous treatment of Neuronox®. Of these, 48 patients (96%) responded to treatment and only 2 patients did not respond to Neuronox® treatment; one in each group. For those who responded to Neuronox® treatment (Table 1), the mean (SD) PI was 73.44 (17.51%) with the range of 20 to 100%. The earliest and latest PI was 4 and 19 weeks, respectively. The mean (SD) TPI was 9.44 (4.48) weeks. The mean (SD) D was 15 (2.12) weeks. The PI, TPI, and D were not statistically different between new and previously diagnosed patients (Table 1).

Side effects of Neuronox® injection (Table 2) were reported in 18, 17, 9, and 1 patient at week 4, 8, 12, and 16, respectively. The most common side effect was ptosis. Four patients had facial paresis and ptosis at week 4; one patient reported persistence of this side effect until week 12. One patient developed facial paresis in week 12 and the symptom remained till the end of study. Facial paresis was also found with lacrimation, dizziness, or tension headache. The duration of side effects were found to last from 5 to 81 days.

DISCUSSION

The botulinum A toxin widely used for HFS treatment in Thailand are Botox® and Dysport®. The efficacy and side effects of the botulinum toxin are shown in Table 3. The response rates were 80% or more with the maximum side effect rate of 34%. Our study found that Neuronox® injection had good response rate (48/50 patients; 96%). All outcomes variables were comparable to either Botox® or Dysport® treatment including the mean PI, TPI, and D as shown in Tables 3 and 4 (Dutton and Buckley, 1988; Elston, 1992; Flanders et al., 1993; Kollewe et al., 2010; Poungvarin et al., 2001; Rieder et al., 2007; Setthawatcahrawanich and Ovartlanporn, 2007; Suputtitada et al., 2004; Taylor et al., 1991; Van den Bergh et al., 1995). The treatment responses were not different between newly and previously diagnosed HFS patients.

The side effects of Neuronox® injection were found more common during week 4 of treatment but the incidences of all side effects were found to be less along with the continuation of treatment. The overall side effects from Neuronox® were not different from previous study using original botulinum toxin (36 versus 34%) as shown in Table 3. At week 16, only 1 patient (2%) had side effect from Neuronox® injection. In clinical practice, physicians may optimize the dose of botulinum toxin treatment to reduce side effects.

Table 1. Results of treatment of HFS by Neuronox® botulinum toxin.

Patient	Number	Non-response	TPI (week) Mean (SD)	PI (%) Mean (SD)	Duration (week)
New	30	1	9.95 (±4.31)	72.89 (±17.27)	14.68 (±1.887)
Former	20	1	9.10 (±4.62)	73.79 (±17.96)	15.21 (±2.274)
Total	50	2	9.44 (±4.48)	73.44 (±17.51)	15.00 (±2.12)

PI, Peak improvement.

Table 2. Side effects from Neuronox®.

Symptom	N (%)			
	Week 4	Week 8	Week 12	Week 16
Facial paresis	2 (4)	4 (8)	2 (4)	1 (2)
Ptosis	7 (14)	7 (14)	3 (6)	-
Facial paresis and ptosis	4 (8)	1 (2)	1 (2)	-
Facial paresis, inability to close eyelid firmly, and eye itch	1 (2)	-	-	-
Facial paresis, ptosis and tension headache	1 (2)	-	-	-
Facial paresis and lacrimation	-	1 (2)	1 (2)	-
Facial paresis, ptosis and dizziness	-	1 (2)	-	-
Ptosis and dysarthria	-	1 (2)	-	-
Lacrimation	2 (4)	1 (2)	1 (2)	-
Numbness at brow corner	1 (2)	1 (2)	-	-
Wrinkles at nose	-	-	1 (2)	-
Total	18 (36)	17 (34)	9 (18)	1 (2)

Table 3. Efficiency of treatment and side effects of botulinum toxin on HFS.

Type	Author	Follow-up (years)	Patients (n)	No. of treatment	Mean dose	Onset (weeks)	Response rate (%)	PI (%)	Duration of response to treatment (week)	Side effect (%)
Botox®	Dutton	4	60	1044	-	-	97	-	15.4	23
	Fanders	8	65	336	-	-	100	-	16.9	8
	Taylor	-	130	336	-	-	98	-	16.9	32
	Poungvarin	10	875	3061	25	-	98	-	16.2	24.4
	Suputtitada	8	112	874	25	-	98	-	18.7	8.13
	Setthawatcahra-wanich	9	45	521	30.2	0.97	100	92	17.3	5.4
	Rider	12 week		-	-	1.35	86.2	-	10.1	34.6
	Kollewe	12	53	-	22	1	92	GCI 2.6	12	5.2

Table 3. Contd.

Dysport®	Elston	7	73	-	120 - 160	-	75		11.2 - 14	19 - 33
	Berrgh	5	40	144	53	-	100	90	21.1	22
	Jipimolmard	7	175	883	92	-	97	77.2	14.6	29
	Kollewe	12	44	-	51	1	92	GCI 2.6	12	5.8

Other generic botulinum toxins are also effective in blepharospasm and HFS (Table 4). Meditoxin® had efficacy of 95% in blepharospasm, which did not differ from the use of Botox®. The use of Prosigne® to treat HFS and blepharospasm had the mean global assessment of change score of 73.46% (Rieder et al., 2007). This current study showed the efficacy of another generic botulinum toxin with larger sample size. However, further randomized controlled trial may be needed.

There are some limitations in this study. First, the D often becomes shorter with repetitive injection and each drug may have different stability of duration of response. This limitation was not evaluated in this study. Second, our results represented only new HFS patients and previously diagnosed HFS who had good response to original botulinum toxin. The results may not be applied for those patients with response to original botulinum toxin less than 80%. Lastly, the evaluation was subjectively rated by the patients. However, the evaluations may not be overrated because all patients knew that Neuronox® is a generic botox (open-labelled study design).

Conclusion

Treatment of HFS by generic Neuronox® botulinum toxin is an effective alternative treatment with similar rate of side effects to original botulinum toxin. It may be preferable in countries with limited healthcare resources.

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