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Dextromethorphan is Effective for Essential Blepharospasm

Xuesheng Zheng*

Department of Neurosurgery, XinHua Hospital, Affiliated to Shanghai JiaoTong University School of Medicine, Shanghai 200092, China

***Corresponding author:** Xuesheng Zheng, Department of Neurosurgery, Xinhua Hospital, Affiliated to Shanghai JiaoTong University School of Medicine, 1665 Kongjiang Road, Yangpu District, Shanghai, China, Tel: 86-21-25078005; E-mail: zhengxuesheng@xinhuamed.com.cn

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Abstract

Background: Blepharospasm is a focal dystonia presented with continuous involuntary contractions of the muscles surrounding the eyes, causing frequent eyelid closure and visual disturbance. The current treatments for blepharospasm are not very satisfactory. This is a retrospective study of the therapeutic effect of dextromethorphan on blepharospasm.

Methods: This retrospective study included 22 patients with essential blepharospasm, who were treated with dextromethorphan. The effect was evaluated using Jankovic Rating Scale (JRS) and Blepharospasm Disability Index (BSDI).

Results: Before dextromethorphan treatment, the baseline JRS score is 5.55 ± 1.10 points, and the BSDI score was 2.87 ± 0.59 points. After 1 week of dextromethorphan treatment, the JRS score decreased to 2.82 ± 0.85 points, and the BSDI score decreased to 1.36 ± 0.58 points. In the following 3 weeks of treatment, the JRS and BSDI scores kept in a steady state. One week after the dextromethorphan treatment, the JRS score (5.41 ± 1.01 points) and BSDI score (2.63 ± 0.64 points) returned to the pre-treatment baseline level.

Conclusion: We found that dextromethorphan is effective in patients with blepharospasm, and this finding might imply an alternative treatment option to blepharospams.

Keywords: Essential blepharospasm; Dextromethorphan; Focal dystonia; Blepharospasm disability index

Introduction

Blepharospasm is a focal dystonia presented with continuous involuntary contractions of the muscles surrounding the eyes, causing frequent eyelid closure and visual disturbance, and affecting the daily life and word. Severe blepharospasm may cause traffic accidents [1]. Since the etiology and mechanism of essential blepharospasm is unknown, current treatment is mostly directed to relief the symptoms [2]. Many therapies such as biofeedback, hypnosis, acupuncture, psychotherapy have been tried but with little success. Some drugs such as levodopa, tetrabenazine, meprobamate, clonazepam, lithium carbonate, haloperidole, diphenylhydantoin and amantadine hydrochloride have been tried to relieve the spasm symptom, but the effect is very poor [3]. In 2014, a 50-year-old male patient reported to us that he occasionally found his blepharospasm symptoms were released after taking the antitussive drug dextromethorphan when he got an upper respiratory tract infection. Thereafter, we found that dextromethorphan is effective in patients with blepharospasm, and here is a retrospective study for this series. This finding might imply an alternative treatment option to blepharospasm.

Patients and Methods

Patients: During January 2015 to December 2016, 22 patients with essential blepharospasm received oral administration of dextromethorphan, 30 mg three times a day for 4 weeks. Fifteen patients are women, and 7 patients are men. The ages range from 42 to 67 years (mean 58.3). During the period of dextromethorphan administration, no other medicine is prescribed to the patients, except for antihypertensive or antidiabetic agents if necessary. The severity of blepharospasm is evaluated every week during the treatment, one week before treatment and one week after treatment, according Jankovic Rating Scale (JRS) and Blepharospasm Disability Index (BSDI). Any side effects are recorded.

Jankovic Rating Scale (JRS): The patient is evaluated by a neurosurgeon according to JRS [4], a standard physician rating scale for semi-quantification. The scale includes scores of severity and frequency. As to severity, score 0 means no spasm, score 1 means increased blinking present only with external stimuli, score 2 means mild spontaneous eyelid fluttering, score 3 means moderate spasm, and score 4 means severe spasm. As to frequency, score 0 means no spasm, score 1 means slightly increased frequency of blinking, score 2 means eyelid fluttering lasting <1 sec, score 3 means eyelid spasm lasting >1 sec, and score 4 means functional blind due to persistent eye closure. Therefore, the total score of JRS is 8.

Blepharospasm Disability Index (BSDI): BSDI is a self-rating scale for patient [4]. It includes 6 items, i.e., driving a vehicle, reading, watching television, shopping, walking and doing everyday activities. For each item, score 0 means no impairment, score 1 means slight impairment, score 2 means moderate impairment, score 3 means severe impairment and score 4 means complete inability to do that activity. If an item is not applicable to a patient, for example, the item "driving a vehicle" for a patient without a driver license, that item

should be deleted. The final score is the average of scores from all applicable activities. Thus, the BSDI score ranges from 0 to 4.

Statistical analysis: Student t-test and ANOVA were used for analyzing quantitative data. $P<0.05$ was accepted as statistically significant.

Result

The JRS and BSDI scores of 22 patients at different time points are listed in Table 1.

Before dextromethorphan treatment, the baseline JRS and BSDI scores are recorded. The mean JRS score was 5.55 ± 1.10 points, and the mean BSDI score was 2.87 ± 0.59 points.

After 1 week of dextromethorphan treatment, the mean JRS score decreased to 2.82 ± 0.85 points, and the mean BSDI score decreased to 1.36 ± 0.58 points. Compared with the pre-treatment baseline, the improvement of JRS score ($P<0.05$) and BSDI score ($P<0.05$) was statistically significant.

As demonstrated in Figure 1, the average JRS score and BSDI score kept in a steady state during the 4-week period of dextromethorphan treatment, and the differences of JRS score ($P>0.05$) and BSDI score ($P>0.05$) among these 4 times points are statistically insignificant.

One week after the dextromethorphan treatment, the JRS score (5.41 ± 1.01 points) and BSDI score (2.63 ± 0.64 points) returned to the pre-treatment baseline level.

There was no serious complication in this series. Two patients had mild dizziness and 1 patient had slight nausea, and these side effects were endurable and did not lead to withdrawn of dextromethorphan.

	Pre-treatment		1 week		2 weeks		3 weeks		4 weeks		Post-treatment	
Case No.	JRS	BSDI	JRS	BSDI	JRS	BSDI	JRS	BSDI	JRS	BSDI	JRS	BSDI
1	7	3.8	2	0.7	2	0.8	2	0.7	2	0.7	7	3.5
2	4	2.2	3	1.3	3	1.4	3	1.4	2	1.3	5	2.3
3	7	3.1	2	1.5	2	1.4	2	1.4	2	1.6	6	3.4
4	6	3.3	3	2.1	3	2.3	3	2.2	3	2	6	3.1
5	5	2.8	3	1.1	2	0.9	3	1.1	3	1.2	5	2.5
6	5	1.9	2	0.8	2	1	2	0.9	2	0.8	5	1.6
7	8	4.2	4	2.6	4	2.5	3	2.5	4	1.5	7	3.6
8	4	2.6	4	1.8	3	1.6	4	1.6	4	1.7	4	2.6
9	6	2.9	3	1.8	3	1.7	3	1.4	3	1.2	6	2.8
10	6	2.7	2	0.8	3	0.9	2	1.1	3	1	5	1.8
11	5	3.1	2	1	2	1.2	2	0.8	2	1.1	5	3.3
12	6	3.8	3	1.2	3	1.1	3	1.1	2	0.8	6	3.8
13	4	2.3	2	0.5	3	0.7	2	0.8	3	0.7	3	2.5
14	6	2.7	4	2.2	3	2.4	4	2.2	4	2.1	6	2.4
15	5	3.2	3	2.2	3	2.1	3	2.1	3	2.2	5	2.8
16	6	2.8	5	1.8	5	1.6	4	1.8	4	1.5	5	2.4
17	5	2	2	0.7	2	0.8	2	0.6	2	1.4	6	2.2
18	5	3.1	3	1.3	3	1.3	3	1.2	3	1.4	5	2.6
19	7	2.5	3	1.4	3	1.4	3	1	3	1.6	7	2.2
20	5	3.2	2	0.9	2	1	3	0.8	3	1.2	5	3.1
21	4	2.1	3	0.8	3	0.8	3	0.9	3	0.8	4	1.8
22	6	2.8	2	1.5	2	1.2	2	1.2	3	1.1	6	1.6

Table 1: JRS and BSDI scores of 22 patients with essential blepharospasm treated with dextromethorphan.

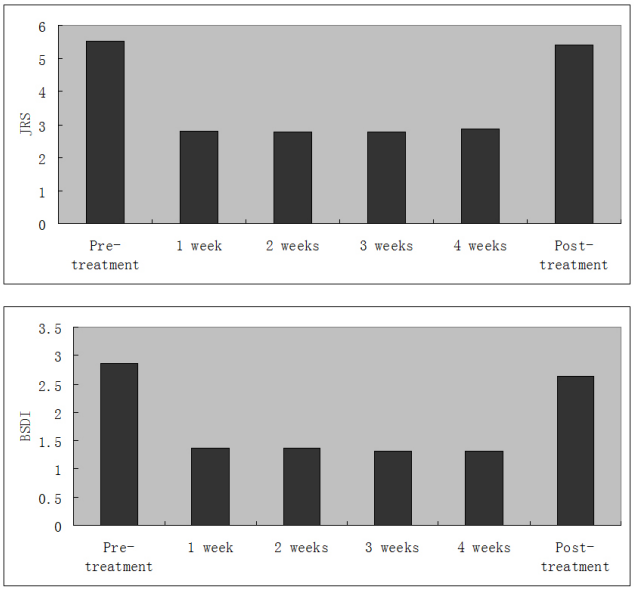

Figure 1: The average JRS and BSDI scores essential blepharospasm patients treated with dextromethorphan.

Discussion

Since the pathogenesis of essential blepharospasm is not clear now, all current treatments for this disorder aim to relieving the spasm symptoms.

The most common treatment is Botulinum neurotoxin type A (Botox) injection. Botox treatment for essential blepharospasm is successful in short-term performance, and its adverse events are infrequent. But the botulinum neurotoxin is an exogenous antigen to the immune system, and will trigger the production of specific antibodies. At last, the botulinum neurotoxin will be neutralized. Therefore, botulinum neurotoxin injection is generally effective at first but will be resisted in several years [5].

The effect of surgical treatments is not satisfactory. Deep brain stimulation (DBS), differential sectioning of the facial nerve, frontalis sling, and myectomy have been attempted with some degree of symptom relief, but not cure [6].

As mentioned above, many oral drugs have been reported to have very limited symptom relief effect limited. Our finding that the antitussive drug dextromethorphan is capable of inhibiting blepharospasm came occasionally from the clinical practice. It might turn out a new option of non-surgical treatment, which requires prospect clinical trials in the future.

As an antitussive drug, dextromethorphan is probably acting in the central nervous system to elevate the cough threshold [7]. It can attenuate the glutamate-induced neurotoxicity and has a neuroprotective property against the ischemia-induced brain damage [8]. Dextromethorphan has many other medical applications, such as pain relief, psychological application, and the treatment of addiction [9].

Pharmacological effects of dextromethorphan are very extensive. It is a nonselective serotonin reuptake inhibitor and a sigma-1 receptor agonist, and also a low-affinity noncompetitive N-methyl-D-aspartate receptor (NMDAR) antagonist [10]. It can inhibit glutamate release from the presynaptic terminals projecting to the second-order neurons [11].

Although dextromethorphan has many actions in the central nervous system, the exact acting sites and mechanisms are not fully understood. Different brain regions have been shown to function abnormally in the blepharospasm, including the basal ganglia, the cortex, and the cerebellum. However, it is unclear whether the functional changes in these sites are the cause or outcome of the disease [2]. The precise neural circuitry involved in the pathogenesis of essential blepharospasm is not clear either. Therefore, there is plenty of room for research as to how dextromethorphan may act to blepharospasm.

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