

A Case with Improvement of Blepharospasm by Zolpidem

Munkyoung Sunwoo^a

Junghee Cho^b

Jun Hong Lee^b

Gyu Sik Kim^b

Jong Hun Kim^b

Sun-Ah Choi^b

^aDepartment of Neurology,
Yonsei University College of Medicine,
Seoul, Korea

^bDepartment of Neurology,
National Health Insurance Corporation
Ilsan Hospital, Goyang, Korea

Zolpidem is usually used for the treatment of insomnia as a hypnotic drug. It was also suggested to be effective in the treatment of dystonia in some studies. A 74-year-old woman had been suffering from frequent and intense bilateral spasms of the eyelids for 20 years. She has been treated with botulinum toxin injection and taken some medications. But, she experienced a little effect and was not satisfied with those treatments. Her symptom was improved after taking Zolpidem which had been prescribed for insomnia by her primary physician. She did not show any improvement after placebo injection and neostigmine test. This is the first report which shows improvement of isolated blepharospasm by Zolpidem in Korea. Zolpidem can be one of useful alternative pharmacological treatments for blepharospasm. Further randomized, blinded, placebo- controlled studies are needed to validate this finding.

Journal of Movement Disorders 2011;4:53-54

Key Words: Zolpidem, Blepharospasm, Dystonia.

Zolpidem tartrate is a short acting nonbenzodiazepine hypnotic drug which is useful for the treatment of insomnia.¹ Recently, it has not been rarely reported that Zolpidem improves motor symptom in Parkinson's disease, progressive supranuclear palsy and X-linked dystonia-Parkinsonism syndrome.²⁻⁴ It has been also shown to be effective in the treatment of blepharospasm or the Meige's syndrome.^{5,6} Blepharospasm is a form of focal dystonia characterized by involuntary spasms of orbicularis oculi muscles. Increasing gamma-aminobutyric acid (GABA) activity through GABA agonists that cross the blood-brain barrier can result in reinforce GABA-ergic inhibition on the thalamus and motor cortex and, thus, ameliorate the dystonic symptoms which might have been produced by increased disinhibition. We report a patient whose blepharospasm was improved by Zolpidem.

Case

A 74-year-old woman, previously healthy, had been suffering from frequent and intense bilateral spasms of the eyelids for 20 years. It did not involve any other muscle of the face or neck. She reported an abnormal feeling of tension in the eyelids and subsequently, involuntary excessive blinking developed. These spasms were insuppressible, exacerbated by stress and bright light; furthermore their frequency and severity have been worsening over the years.

She has been treated with botulinum toxin injection (Botox[®], Allergan, Irvine, CA, USA) in the orbicularis oculi muscles (up to 25 Units per eye) and taken some medications (trihexyphenidyl 6 mg, clonazepam 1.5 mg, baclofen 30 mg per day). But, she experienced a little effect and was not satisfied with those treatments. Accidentally, she found that her symptom was improved after taking Zolpidem which had been prescribed for insomnia by her primary physician. When she woke up in the next morning after taking Zolpidem, she felt the best condition which she has ever experienced on her eye lids.

When she came to our hospital, she could not open her both eyes because of severe eyelids spasm. She did not report any history of head trauma, surgical incidents or neurological disease. There was no exposure to neuroleptic medication and no family history of movement disorder. On neurological examination, she did not show any abnormal finding including

Received December 2, 2010

Accepted January 31, 2011

Corresponding author

Sun-Ah Choi, MD, PhD
Department of Neurology,
National Health Insurance
Corporation Ilsan Hospital,
1232 Baekseok-dong, Ilsandong-gu,
Goyang 410-719, Korea
Tel +82-31-900-0230
Fax +82-31-900-0343
E-mail sachoi0416@naver.com

· The authors have no financial conflicts of interest.

bradykinesia, tremor, rigidity. In repetitive nerve stimulation tests, she did not show decremental responses. On the neostigmine test and placebo injection, she showed no improvement. She showed much improvement of blepharospasm after taking Zolpidem 10 mg in 20 to 30 minutes and that effect lasted for average 5 hours. She did not complain much sleepiness which disturbed day time activities.

Discussion

Blepharospasm is a form of focal dystonia characterized by involuntary spasms of orbicularis oculi muscles. Dystonia might be due to basal ganglia dysfunction associated with globus pallidus interna hypoactivation and cortical overactivation.⁷ Basso and colleagues revealed that reduced basal ganglia dopamine levels causes a decrease in nucleus raphe magnus inhibition of the blink circuit that increases trigeminal blink excitability.⁸

Some reasons for the improvement of blepharospasm by Zolpidem in this case can be suggested. Firstly, Zolpidem is an imidazopyridine with high selectivity for the benzodiazepine-1 subtype receptor, which is a part of the -aminobutyric acid (GABA)-receptor complex. Abundant GABAergic Zolpidem-binding sites lie in the output structures of the basal ganglia; ventral globus pallidus, substantia nigra pars reticulatae, subthalamic nucleus. By binding to these sites, Zolpidem could reinforce the GABAergic hypofunction influence on the thalamus and motor cortex, which could regulate the blink circuit that reduces trigeminal blink excitability.⁹ Secondly, anxiolytic effect, not related to a direct action on the basal ganglia, may be another possible mechanism. Lastly, the possibility of a placebo effect when this patient took the Zolpidem can be considered. Thus, we observed the placebo effect not Zolpidem in this patient. But, she did not show any improvement of her blepharospasm after administration of placebo, which meant this effect was not due to a placebo effect.

Blepharospasm can start as an isolated movement of the eyelids, and occasionally it remains confined to the eyelids or other cranial structures eventually become involved. Marsden point-

ed out that if blepharospasm occurs alone, without the involvement of other craniocervical structures, then the label essential blepharospasm may be appropriate.¹⁰ This patient showed isolated blepharospasm without the involvement of other muscles. There are a few reports which show dystonic condition improved by Zolpidem. Garretto et al. reported on 3 patients, 1 with blepharospasm and 2 with Meige's Syndrome whose symptoms were improved by Zolpidem.⁵ In Korea, there is one case report that Zolpidem is effective in the treatment of Meige's syndrome.⁶ This is the first report which shows improvement of isolated blepharospasm (essential blepharospasm) by Zolpidem in Korea. Zolpidem may be one of useful alternative pharmacological treatments for blepharospasm. Further randomized, blinded, placebo-controlled studies are needed to validate the action of this drug on dystonic condition.

REFERENCES

1. Holm KJ, Goa KL. Zolpidem: an update of its pharmacology, therapeutic efficacy, and tolerability in the treatment of insomnia. *Drugs* 2000; 59:865-889.
2. Daniele A, Albanese A, Gainotti G, Gregori B, Bartolomeo P. Zolpidem in Parkinson's disease. *Lancet* 1997;349:1222-1223.
3. Daniele A, Moro E, Bentivoglio AR. Zolpidem in progressive supranuclear palsy. *N Engl J Med* 1999;341:543-544.
4. Evidente VG. Zolpidem improves dystonia in "Lubag" or X-linked dystonia-parkinsonism syndrome. *Neurology* 2002;58:662-663.
5. Garretto NS, Bueri JA, Rey RD, Arakaki T, Nano GV, Mancuso M. Improvement of blepharospasm with Zolpidem. *Mov Disord* 2004;19: 967-968.
6. An JY, Kim JS, Kim YI, Lee KS. Successful treatment of the Meige Syndrome with Oral Zolpidem Monotherapy. *Mov Disord* 2008;23: 1619-1621.
7. Evinger C. Animal models of focal dystonia. *NeuroRx* 2005;2:513-524.
8. Basso MA, Powers AS, Evinger C. An explanation for reflex blink hyperexcitability in Parkinson's disease. I. Superior colliculus. *J Neurosci* 1996;16:7308-7317.
9. Chen L, Xie JX, Fung KS, Yung WH. Zolpidem modulates GABA (A) receptor function in subthalamic nucleus. *Neurosci Res* 2007;58:77-85.
10. Marsden CD. Blepharospasm-omandibular dystonia syndrome (Brueghel's syndrome). A variant of adult-onset torsion dystonia? *J Neurol Neurosurg Psychiatry* 1976;39:1204-1209.