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Case Report

Gabapentin in Treatment of Two Parkinson's Disease Patients with Pain: A Case Report

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ABSTRACT

Background: Pain is one of the most common and disabling non-motor symptoms in Parkinson's disease (PD), 85% of individuals in early/moderate PD stages have pain, and the most reported type of pain was pain around joints (81.5%). Compared with motor symptoms, pain causes more problems to the quality of life in PD patients. However, effective pharmacological treatment for PD pain remains poor. There are few reports about long-term use of gabapentin (GBP) in the treatment of PD pain.

Case: We present two cases of PD, case 1 developed severe pain around the joints all over the body, case 2 developed moderate pain around her temporomandibular joints. Both patients derived benefit from long-term using of GBP with no adverse effect.

Conclusion: PD pain is a very difficult clinical problem to deal with, we think GBP can be the choice of some patients: with female sex, and PD pain with dyskinesia, and especially in moderate/advanced PD stages.

Keywords: Gabapentin; Parkinson's; Pharmacological

INTRODUCTION

Pain is one of the most common and disabling non-motor symptoms (NMS) in Parkinson's disease (PD), 85% of individuals in early/moderate PD stages have pain, and the most reported type of pain was musculoskeletal pain (pain around joints, 81.5%) [1,2]. Compared with motor symptoms, pain causes more problems to the quality of life in PD patients [1]. However, the exact mechanism of pain underling PD is unclear, and effective pharmacological treatment for PD pain remains poor.

Gabapentinoids, including pregabalin and gabapentin (GBP), are first-line treatments for neuropathic pain (such as hyperalgesia and ongoing pain), but only less than 3% of PD patients with pain benefit from gabapentinoids (pregabalin and GBP), and their application in patients with PD pain was limited by the adverse effect of dizziness and drunkenness [1,3]. We reported two PD patients with pain, derived benefit from long-term using of GBP with no adverse effect.

CASE PRESENTATION

Case 1 was a 74-year-old Han Chinese woman with a 6-year history of PD. She was bedridden for more than 1 year and extremely emaciated, visiting our hospital with complaints of paroxysmal pain around the joints and back of the body and severe dyskinesia in recent 3 months. The onset time was irregular, and lasted for about 5 minutes each time, with an interval of 10-120 minutes. On admission, she was taking Benserazide-levodopa (625 mg/day), pramipexole (0.875 mg/day), selegiline (10mg/day). The neurological examination on admission revealed the following: she had mask-like face, normal eye movements, slow and slurred speech, atrophy and curling of limbs, involuntary twisting of the whole body, cogwheel rigidity in the limbs, and no pathologic reflexes. Tendon reflex in the limbs decreased dominantly. She said that every joint was painful. There were painful groans in every pain attack. The other admission manifestations are shown in Table 1. Based on the above drugs, we added Carbidopa-levodopa 375mg/day for the first three days, symptom of pain wasn't improved, so we added GBP on the 4th day, the dosage was titrated from 300 mg/day to 600 mg/day. On the 5th day after adding GBP

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(DAG), pain was diminished, and interval was prolonged. On the 11th DAG, visual analogue scale (VAS) was 2, and dyskinesia was improved. She was able to stand on the 16th DAG, walk for a short distance and take food without help on the 36th DAG, and we found no adverse effect. However, on the 81st DAG, she got up at night for toilet and fell down, resulting in right femoral neck fracture.

	Age (y)	Age of onset (y)	Age of initial treatment(y)	Initial response to levodopa	Tremor	Rigidity
Case1	74	68	68	good	Bilateral limbs	Bilateral limbs
Case2	63	56	57	good	Left limb	Bilateral limbs
	Bradykinesia	HY stage	VAS	HAMA(14 items)	HAMD(24 items)	ADL(Barthel Index)
Case1	Bilateral limbs	5	10	16	13	5
Case2	Left limb	2.5	6	18	25	85

Table 1: Demographic and clinical data of both patients at admission.

Case 2 was a 63-year-old Han Chinese woman with a 7-year history of PD. She was diagnosed with lung cancer and thoracic vertebral metastases 6 years ago, there was no abnormality on head MRI at that time. She visited our hospital with complaints of pain around her temporomandibular joints and opening her mouth involuntarily in the last six months. These symptoms occurred mostly 3-5 hours after taking dopaminergic drugs (several times per day), and lasted 3-15 minutes. On admission, she was taking Benserazide-levodopa (625 mg/day), pramipexole (1.125 mg/day), amantadine (200 mg/day), rasagiline (1 mg/day). The neurological examination on admission revealed the following: she had mask-like face, normal eye movements, normal muscle strength of limbs, no arm swing in left upper limb, cogwheel rigidity in the limbs, and no pathologic reflexes. Tendon reflex in the limbs decreased mildly. The other admission manifestations are shown in Table 1. Based on the above drugs, we added GBP to patient, the dosage was titrated from 300mg to 900mg per day. After 10 days of treatment, her pain and involuntary mouth opening were significantly reduced. Now she has been taking GBP for more than one year, VAS is 2, and no obvious adverse effects were found, and involuntary mouth opening appeared only once every 1-3 months.

DISCUSSION

Both of our patients were suffering from pain and dyskinesia for a long time, and their lives were extremely painful, especially for case 2, she was afraid that she would open her mouth at any time, which would make her feel embarrassed and dare not go out of the house. The pain type was pain around joints in both patients. After adding GBP, both patients achieved amazing results. Case 1 recovered to be able to walk after staying in bed for more than one year.

Unlike a previous study (400 mg three times a day) [3], we chose a dose of 300 mg two or three times a day, because both patients were not tall or strong, especially case 1 was very thin. This helps to reduce the side effects of GBP. And we didn't find any side effects of GBP (such as dizziness or drunkenness).

Pain is a common NMS of PD, the occurrence of PD pain is related to the changes of anatomical structure or function at different levels, such as Lewy body formation and neuronal loss in cerebrum [4], decreased threshold of the nociceptive flexion reflex at the spinal cord [5], and loss of epidermal nerve fibres and Meissner corpuscles [6]. Different levels of neurodegeneration in PD affect the structures of dopaminergic and nondopaminergic pathways, which are associated with pain [7]. And several studies have found that dopaminergic drugs can improve PD pain (reviewed by Rukavina et al. [7]). So we added additional levodopa to case 1 firstly, and pain wasn't improved. We believe that nondopaminergic drugs may be the better way to treat PD pain, especially in patients with advanced PD.

As a synthetic GABA analogue, GBP was mainly released for use in epilepsy, however, a double-blind, placebo-controlled, crossover trial has firstly found that GBP can improve rigidity, bradykinesia, and tremor in PD patients [3]. We also found the improvement of motor symptoms in our patients. Its therapeutic mechanism for PD pain is unclear. It is suggested that GBP can promote the release of GABA and increase the level of GABA in striatum, thus acting on the indirect pathway of basal ganglia, reducing the signal output of indirect pathway, and improving the symptoms of PD. Moreover, an animal study has found that GBP can act directly in the spinal cord to inhibit evoked nociceptive signaling and indirectly through supraspinal sites including opioid circuits in the rostral anterior cingulate cortex to relieve ongoing pain and motivate behaviors. Another study (using diffusion tensor imaging, and resting-state functional MRI) found that pain in PD patients is associated with supraspinal structural and functional changes. Therefore, to a certain extent, it can predict the effectiveness of GBP in the treatment of PD pain.

Our two PD patients had pain and dyskinesia, and both symptoms were improved dominantly after adding GBP, it can be seen that GBP has multiple targets. We think that the function of dopaminergic pathway may be in a state of decompensation in patients with advanced PD, and the use of nondopaminergic drugs may achieve good results at this stage.

PD pain is a very difficult clinical problem to deal with. According to our study, we think GBP can be the choice of some patients: with female sex, and PD pain with dyskinesia, and especially in moderate/advanced PD stages.

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study was approved by the Ethics Committee of the Affiliated Hospital of Hangzhou Normal University.

Disclosure

There are no conflicts of interest.

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REFERENCES

1. Silverdale MA, Kobylecki C, Kass-Iliyya L, Martinez-Marin P, Michael L, Sarah C, et al. A detailed clinical study of pain in 1957 participants with early/moderate Parkinson's disease. Parkinsonism Relat Disord. 2018; 56: 27-32.
2. De Mattos DC, Meziat Filho NA, Pedron CA, Vasconcellos LF, Nogueira LAC,et al. Pain characteristics and their relationship with motor dysfunction in individuals with Parkinson disease-A cross-sectional study. Pain Pract. 2019; 19:732-739.
3. Olson WL, Gruenthal M, Mueller ME, Olson WH. Gabapentin for parkinsonism: a double-blind, placebo-controlled, crossover trial. Am J Med. 1997; 102:60-66.
4. Todorova A, Jenner P, Ray Chaudhuri K. Nonmotor Parkinson's: integral to motor Parkinson's, yet often neglected. Pract Neurol. 2014; 14:310-322.
5. Mylius V, Brebbermann J, Dohmann H, et al. Pain sensitivity and clinical progression in Parkinson's disease. Mov Disord. 2011; 26: 2220-2225.
6. Rukavina K, Leta V, Sportelli C, Buhidma Y, Duty S, et al. Pain in Parkinson's disease: new concepts in pathogenesis and treatment. Curr Opin Neurol. 2019; 32: 579-588.
7. Loscher W, Honack D, Taylor CP. Gabapentin increases aminooxyacetic acid-induced GABA accumulation in several regions of rat brain. Neurosci Lett. 1991; 128: 150-154.