

# Effect of pregabalin for the treatment of chronic refractory cough

## A case report

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### Abstract

**Rationale:** Chronic refractory cough (CRC) is a common clinical problem which is more likely associated with some physical problems. Although many patients have received satisfactory treatment, there were still many patients suffered from long-term cough symptoms after standardized treatment.

**Patient concerns:** A patient suffered from postherpetic neuralgia (PHN) and also he complained CRC for more than 20 years.

**Diagnosis:** The patient was diagnosed with PHN and CRC.

**Interventions:** Pregabalin was originally administered to treat PHN.

**Outcomes:** pregabalin not only alleviated her pain of PHN but also relieved chronic cough.

**Lessons:** This report demonstrated the surprising effect of pregabalin on the treatment of CRC.

**Abbreviations:** CRC = chronic refractory cough, PHN = postherpetic neuralgia, VAS = visual analog scale.

**Keywords:** pregabalin, chronic refractory cough, gabapentin, cough

## 1. Introduction

Chronic cough is defined as cough that has been present for more.<sup>[1]</sup> Chronic refractory cough (CRC) is a common clinical problem which is more likely associated with some physical problems such as syncope, chest pain, insomnia, bad mood (anxiety and depression), impaired quality of life, and so on.<sup>[1,2]</sup> Nearly 11% to 16% of patients suffer from it during their life. Although many patients have received satisfactory treatment, there were still 20% to 40% of patients suffered long-term cough symptoms after standardized treatment.<sup>[2]</sup> Thus, an innovative treatment with fewer adverse effects and long-term relief was necessary for CRC.

Recent studies have shown that the sensitivity of the cough reflex is increased in chronic cough.<sup>[3]</sup> The mechanism of CRC showed some similarities with peripheral and central sensitization,

such as neuropathic pain.<sup>[4]</sup> Therefore, drugs for chronic neuropathic pain have attracted widespread interest among clinicians due to the effect treatment for CRC. Gabapentin is commonly used for the adjuvant treatment of neuralgia after herpes zoster. Some previous studies have shown that gabapentin could significantly improve the quality of life-related to CRC and reduced the severity and frequency of cough. It might suggest that gabapentin is effective as a neuromodulator for CRC. However, due to the drug tolerance and serious side effects, the administration had been restricted.<sup>[5]</sup> As a new generation of anti-neuropathic pain drugs, pregabalin is worthy of investigation as a substitute for gabapentin for chronic refractory cough due to its excellent pharmacokinetics and safety. This report described a patient with CRC. Pregabalin was originally administered to treat postherpetic neuralgia (PHN). But it was amazing that the patient's long term CRC was cured. The purpose of report was to report the surprising effect of pregabalin on the treatment of CRC, and its safety, mechanisms, and new clinical application value.

## 2. Case report

Patient has provided written informed consent. A 58-year-old female was diagnosed with PHN in his left chest. The visual analog scale (VAS) was 6 to 7. Pregabalin 75mg bid was administered for PHN. Also, the patients complained with a more than 20 years history of chronic refractory cough. She complained an intermittent daily dry cough without obvious mitigating factors. There was no history of smoking, sinusitis, asthma, and gastro-esophageal reflux. She had been treated with variety of medicine. The physical examination, chest X-ray, routine blood test, electrocardiogram were normal. After 3 months, the patient's VAS decreased to 4 to 5. And surprisingly, the patient complained the cough was cured. The pregabalin 75 mg twice per day was administered for another 3 months. There was no evidence of recurrence and serious side-effect after 2-years of follow-up.

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### 3. Discussion

This report demonstrated a patient with chronic refractory cough who was surprised cured with pregabalin. Chronic cough is defined as cough that has been present for more than 8 weeks with a normal chest X-ray and is refractory to routine treatment. The major causes include upper respiratory cough syndrome (UACS, also known as postnasal drip syndrome), cough variant asthma, gastroesophageal reflux disease, eosinophilic bronchitis, angiotensin-converting enzyme inhibitor (ACEI) drug application, chronic obstructive pulmonary disease (COPD), and so on. Although a standardized treatment based on the anatomic diagnostic protocol can greatly improve the treatment of chronic cough, about 20% to 40% of patients cannot determine the cause and a refractory, idiopathic cough persists.<sup>[6]</sup> Many patients suffered from long-term chest pain, tension urinary incontinence, laryngeal pain, dysphagia, and other complications.<sup>[7]</sup> It seriously affected the quality of life (QoL) and increased the economic burden.<sup>[8]</sup>

Recent studies have shown that the key factor in CRC was the high sensitivity of cough reflexes, including peripheral sensitization and central sensitization.<sup>[9]</sup> The mechanism of CRC is closely related to aggravation and changes of cough reflex (including Peripheral neural activation and peripheral reflex hypersensitivity in the areas innervated by the vagus nerve). It showed some similarities with the clinical features of chronic pain.<sup>[9]</sup> Compared with healthy people, the cough center with increased sensitivity has a stronger cough-stimulation response to the peripheral cough receptor, which is more likely to cause or aggravate cough. Once the reflex center sensitization is formed, the usual cough-independent stimulation can also induce cough.<sup>[10]</sup> Based on the mechanism of CRC, neuromodulation was administered to the patients.

The neuromodulation treatments for CRC mainly include non-pharmacological treatments (such as physical, psychological, and speech pathology treatments), cough suppression therapy, and neuromodulatory drugs.<sup>[11,12]</sup> Cough suppression physiotherapy and speech pathology therapy have a good application prospect in CRC because it can interfere with the sensitivity of cough reflex, cough frequency, and cough impulse, but treatment population has not been well established.<sup>[13]</sup> Gabapentin is a representative of neuromodulatory drugs in recent years, some studies reported that it can significantly improve the quality of life associated with chronic cough, reduce the severity of cough.<sup>[14]</sup> It can also reduce the high sensitivity of cough center by inhibiting the release of synaptic neurotransmitters in the brain, but significant treatment-related adverse effects can also prevent dose escalation of neuromodulatory therapies. However, pregabalin may be better tolerated in CRC than gabapentin because it can be prescribed in lower doses by its pharmacokinetic properties.<sup>[15]</sup>

In this patient, Pregabalin was administered to treat post-herpetic neuralgia at 75 mg twice per day. After using it, she obtained amazing satisfactory results for cough relief. The satisfactory therapeutic effect was still obtained during the course of drug reduction. The patient did not feel cough after 2-years' follow-up. Although it has been proved in the mechanism and individual use that neuromodulatory drugs such as pregabalin

have shown good application prospects in the treatment of CRC, due to the limited number of clinical studies and less data, the optimal dose, the duration of treatment, the in-depth mechanism, and the safety of long-term use are not known. More placebo randomized controlled trials are needed to investigate this therapeutic potential.

CRC is very difficult to treat. There were some similar neuronal pathways in chronic pain and CRC. This provided a basis for neuromodulatory drugs to treat chronic cough.<sup>[16]</sup> Given the limited therapeutic options in patients with CRC, pregabalin maybe a new option for CRC because of its well tolerance, a wide margin of safety, and few significant drug interactions.

### Author contributions

**Conceptualization:** Ling Ye.

**Investigation:** Jun Li.

**Resources:** Jun Li.

**Writing – original draft:** Jun Li, Ling Ye.

**Writing – review & editing:** Ling Ye.

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