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Case Series

Oncology Section

# Exploring Rare Off-label Applications of Gabapentin in Palliative Care: A Series of Five Cases

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## ABSTRACT

Gabapentin, a structural analogue of γ-aminobutyric acid, is conventionally used for neuropathic pain; however, its broader role in symptom modulation within palliative care remains insufficiently characterised. Patients with advanced illness frequently experience distressing, non-pain symptoms - such as persistent hiccups, refractory cough, uraemic pruritus, vasomotor hot flashes, and Restless Legs Syndrome (RLS) - that are often resistant to standard therapies or limited by adverse effects. Although emerging evidence suggests a wider neuromodulatory potential of gabapentin, its off-label use for these indications is rarely reported in real-world palliative care practice. We describe a case series of five patients receiving specialist palliative care in whom gabapentin was employed specifically for refractory non-neuropathic symptoms after failure or intolerance of conventional treatments. Notably, gabapentin led to complete resolution of intractable hiccups in a patient with advanced gastroesophageal carcinoma, significant relief of refractory cough in metastatic lung cancer, marked improvement of chronic uraemic pruritus in End-Stage Renal Disease (ESRD), clinically meaningful reduction of tamoxifen-associated hot flashes in a breast cancer survivor, and alleviation of severe RLS impairing sleep in advanced pancreatic cancer. Symptom control was achieved within days to weeks of initiation, and treatment was well tolerated, with only mild, transient somnolence or dizziness observed. This case series underscores the underrecognised versatility of gabapentin as a single-agent strategy for managing multiple refractory symptoms in palliative care. Beyond pain control, gabapentin may offer a pragmatic approach to symptom palliation, reduction of polypharmacy, and improvement in quality of life in patients with advanced disease.

**Keywords:** Off-label use, Refractory symptoms, Symptom management

## CASE SERIES

### Case 1: Intractable Hiccups in Advanced Gastroesophageal Cancer

A 58-year-old man with metastatic gastroesophageal carcinoma was admitted for symptom management, with his most distressing complaint being persistent hiccups lasting more than 10 days. The hiccups occurred every 1-2 minutes, severely impairing sleep and oral intake. On the Edmonton Symptom Assessment Scale (ESAS), he rated the distress as 9/10.

Conventional treatments were trialed sequentially. Metoclopramide (10 mg TDS) offered negligible benefit. Baclofen, titrated to 10 mg TDS, provided partial relief but caused disabling dizziness. Chlorpromazine induced sedation and hypotension. Supportive non-pharmacological measures were ineffective. Given the refractory nature of symptoms, gabapentin was considered as an alternative.

Gabapentin was initiated at 300 mg once daily and titrated to 300 mg three times daily over 48 hours. Within 24 hours, hiccup frequency reduced by nearly 50%, enabling the patient to sleep. By day 3, hiccups had resolved completely. He reported improved appetite and oral intake, and the ESAS distress score decreased to 1/10. Mild initial somnolence resolved without intervention. No other adverse effects were noted, and renal and hepatic parameters remained stable.

Gabapentin was administered during hospitalisation and continued for a total duration of two weeks following discharge. At follow-up, the patient remained asymptomatic with complete resolution of hiccups, along with improved nutritional intake and quality of life.

### Case 2: Refractory Cough in Advanced Lung Cancer

A 64-year-old woman with stage IV adenocarcinoma of the lung presented to the palliative care service with a persistent, distressing dry cough lasting over three months. The cough occurred throughout the day and night, interfering with sleep, communication, and overall quality of life. Despite optimised oncological management, symptom burden remained high, with a distress score of 8/10 on the ESAS.

Multiple pharmacological agents had been trialed. Codeine linctus provided only transient relief and induced constipation. Low-dose oral morphine reduced cough intensity but caused intolerable nausea and sedation. Benzodiazepines offered minimal benefit. Non-pharmacological strategies, including humidification and breathing techniques, were ineffective. Given the refractory nature of symptoms, gabapentin was considered based on emerging evidence supporting its role in chronic cough.

Gabapentin was initiated at a dose of 100 mg three times daily and gradually titrated to 300 mg three times daily over one week, based on symptom severity, patient tolerability, and available evidence supporting its use in refractory cough. Symptomatic improvement was noted within 72 hours, with a reduction in cough frequency of approximately 40%. By the end of the first week, cough intensity had decreased by more than 50%, accompanied by improvement in sleep quality and social interaction. Mild, transient somnolence occurred initially but resolved without dose modification. Gabapentin was continued at a maintenance dose of 900 mg/day for four weeks, with sustained clinical benefit.

### Case 3: Uraemic Pruritus in End-stage Renal Disease (ESRD)

A 45-year-old man with ESRD on thrice-weekly haemodialysis was referred to the palliative care unit for management of intractable pruritus. He described generalised itching, most severe at night, leading to frequent scratching, excoriations, and sleep disruption. On a Visual Analogue Scale (VAS), itch intensity was rated 8/10. The symptom had persisted for over six months despite optimised dialysis

and conventional therapies, with routine biochemical evaluation- including serum urea, creatinine, calcium, and phosphate- failing to identify a reversible metabolic cause.

He had received multiple prior treatments, including non-sedating antihistamines, topical emollients, and low-dose naltrexone, with little to no benefit. The use of sedating antihistamines and opioids was avoided due to daytime drowsiness and risk of respiratory depression. Given the limited therapeutic options, gabapentin was considered as an off-label alternative, supported by emerging evidence in uraemic pruritus.

Gabapentin was initiated at 100 mg after each haemodialysis session (three doses per week) to minimise drug accumulation and neurotoxicity, and was gradually titrated to 300 mg post-dialysis. Within two weeks, the patient reported a marked reduction in pruritus intensity, with the VAS score improving from 8/10 to 3/10, along with significant improvement in sleep quality, achieving uninterrupted sleep of 5-6 hours per night. Gabapentin was continued at 300 mg after each dialysis session for a total duration of four weeks, with sustained symptomatic benefit and stable renal parameters.

Adverse effects were minimal. He reported mild dizziness on the first day of treatment, which subsided spontaneously. No confusion, ataxia, or gastrointestinal intolerance was noted. Renal parameters were monitored, and gabapentin was continued at the same post-dialysis dosing schedule.

### Case 4: Hot Flashes in a Breast Cancer Survivor

A 52-year-old woman with hormone receptor-positive breast cancer, status post mastectomy and adjuvant chemotherapy, was on long-term tamoxifen therapy for recurrence prevention. She presented to the palliative care clinic with severe vasomotor symptoms, primarily frequent hot flashes and night sweats. She reported 10-12 hot flash episodes daily, often accompanied by palpitations, flushing, and disrupted sleep. On the ESAS, she rated the symptom burden as 8/10.

Conventional management strategies had been attempted. Life-style modifications such as yoga, paced breathing, and caffeine restriction were ineffective. Pharmacological trials with clonidine and Selective Serotonin Reuptake Inhibitors (SSRIs) produced minimal relief and caused intolerable adverse effects, including dizziness and gastrointestinal discomfort. Hormonal replacement therapy was contraindicated due to her breast cancer history. With worsening sleep quality and impaired daily functioning, an alternative approach was sought.

Gabapentin was initiated at 300 mg at bedtime to address both hot flashes and nocturnal symptoms. Over two weeks, the dose was titrated to 900 mg/day in three divided doses. By the end of the first month, hot flash frequency decreased to 4-5 episodes daily, with reduced intensity and improved sleep duration. ESAS score declined to 3/10, reflecting significant symptomatic benefit. The patient also reported improved mood and energy levels.

Gabapentin was well tolerated, with only transient somnolence during the first week of therapy. No neurocognitive or gastrointestinal adverse effects were observed.

### Case 5: Restless Legs Syndrome (RLS) in Advanced Pancreatic Cancer

A 61-year-old man with metastatic pancreatic carcinoma was referred to the palliative care service for management of severe restlessness in the lower limbs, most pronounced at night. He described an uncontrollable urge to move his legs accompanied by tingling and discomfort, which improved temporarily with movement but recurred within minutes. These symptoms were consistent with RLS and had been present for several weeks, significantly disrupting sleep and contributing to fatigue and irritability. His symptom distress score on the ESAS was 7/10.

The patient was receiving opioid-based analgesia for cancer pain, which may have exacerbated his RLS symptoms. Non-pharmacological measures such as massage, leg elevation, and sleep hygiene strategies were trialed without meaningful benefit. Benzodiazepines induced excessive sedation with little improvement in leg restlessness. Given the persistence of symptoms and impact on quality of life, gabapentin was considered as a therapeutic option due to its central neuromodulatory properties.

Gabapentin was initiated at 300 mg at bedtime. Within five days, the patient reported a noticeable reduction in RLS symptoms and improved nocturnal rest. The dose was increased to 600 mg nightly after one week, resulting in sustained symptom control, with ESAS distress scores reducing to 3/10. Sleep duration increased from 2-3 fragmented hours to 5-6 hours per night.

Gabapentin was well tolerated, with only mild dizziness reported during dose escalation, which resolved spontaneously.

## DISCUSSION

Effective symptom control in palliative care requires therapeutic flexibility, as patients frequently experience distressing and refractory symptoms that respond poorly to conventional, symptom-specific treatments. Gabapentin, a structural analogue of γ-aminobutyric acid (GABA), is traditionally used for neuropathic pain through modulation of the α2δ subunit of voltage-gated calcium channels, resulting in reduced excitatory neurotransmitter release. Increasing evidence, however, suggests that this neuromodulatory mechanism may be exploited to manage a broader spectrum of non-neuropathic symptoms commonly encountered in advanced illness [1].

Intractable hiccups remain an underappreciated yet debilitating complication in patients with advanced cancer, significantly impairing nutrition, sleep, and psychological well-being. Standard agents such as chlorpromazine, baclofen, and metoclopramide are often ineffective or poorly tolerated in frail patients. Recent case-based reviews and observational studies have reaffirmed the utility of gabapentin in malignancy-associated hiccups, demonstrating rapid symptom resolution with minimal adverse effects [2,3]. Case 1 in our series supports these observations, highlighting gabapentin as a well-tolerated and effective option when conventional therapies fail.

Refractory cough is another symptom with profound impact on quality of life in patients with advanced thoracic malignancies. While opioids remain a cornerstone of management, their use is frequently limited by sedation, constipation, and delirium. Contemporary clinical guidelines and recent systematic reviews continue to endorse gabapentin as a centrally acting antitussive, particularly in refractory chronic cough, through modulation of cough reflex hypersensitivity [4,5]. The improvement observed in Case 2 aligns with emerging evidence supporting gabapentin as a valuable adjunct or alternative when standard antitussives are inadequate.

Pruritus, especially uraemic pruritus in ESRD, presents a persistent therapeutic challenge in palliative care. Its pathophysiology involves both peripheral and central sensitisation pathways. Recent randomised trials and meta-analyses have confirmed that gabapentin significantly reduces itch intensity, improves sleep quality, and enhances overall well-being compared to placebo, with acceptable tolerability when appropriate renal dose adjustments are applied [6,7]. Case 3 further reinforces gabapentin's role in alleviating refractory pruritus in palliative renal care, emphasising the importance of cautious dosing.

Vasomotor symptoms such as hot flashes are highly prevalent among breast cancer survivors receiving endocrine therapy, where hormonal treatments are contraindicated. Updated clinical reviews and network meta-analyses published in the last three years support gabapentin as an effective non-hormonal therapy, demonstrating

meaningful reductions in hot flash frequency and severity, along with improved sleep parameters [8,9]. The clinical response seen in Case 4 mirrors these findings and underscores gabapentin's utility as a safe, non-hormonal option in this population.

RLS is frequently under-recognised in palliative care despite its substantial impact on sleep, fatigue, and psychological distress. Recent consensus statements and controlled trials support the use of gabapentinoids as first-line or alternative therapy, particularly when dopaminergic agents are unsuitable due to augmentation risk or drug interactions [10,11]. Case 5 highlights gabapentin's effectiveness in managing refractory RLS in a palliative patient, offering symptomatic relief and improved sleep without exacerbating opioid-related adverse effects.

Beyond individual symptom relief, the broader relevance of gabapentin in palliative care lies in its capacity to address multiple symptom domains simultaneously. Patients with advanced illness often experience symptom clusters involving pain, insomnia, anxiety, and sensory disturbances. Recent observational studies suggest that gabapentin may improve sleep architecture and overall symptom burden, thereby reducing the need for multiple pharmacologic agents [12]. Such a polypharmacy-sparing effect is particularly advantageous in palliative populations vulnerable to drug-drug interactions and cumulative adverse effects.

Nevertheless, limitations must be acknowledged. Much of the evidence supporting off-label use of gabapentin in palliative care is derived from small trials, observational studies, and case series. While our findings add to this growing body of literature, larger prospective studies are needed to define optimal dosing strategies, duration of therapy, and patient selection. Adverse effects such as somnolence, dizziness, and ataxia remain clinically relevant, particularly in elderly and renally impaired patients, necessitating careful monitoring [13]. Additionally, recent literature has raised concerns regarding gabapentin misuse in non-palliative populations; although the risk appears low in advanced illness, clinician awareness remains important [14].

## CONCLUSION(S)

This case series demonstrates that gabapentin, though traditionally prescribed for neuropathic pain, holds promise in the management of several refractory symptoms frequently encountered in palliative care. Intractable hiccups, persistent cough, uraemic pruritus, vasomotor hot flashes, and RLS each responded favourably when conventional measures had failed or were poorly tolerated. The consistent clinical improvements observed across diverse symptom domains highlight gabapentin's neuromodulatory versatility and its potential to reduce the need for multiple pharmacological agents in complex palliative regimens.

Importantly, gabapentin was well tolerated in our patients, with only minor and transient adverse effects reported. Its relatively favourable safety profile, lack of major drug-drug interactions, and capacity to improve symptom clusters make it a particularly attractive option in frail patients burdened by polypharmacy. Nevertheless, the current evidence remains limited to small randomised trials, observational studies, and case reports, underscoring the need for larger, well-designed clinical investigations to confirm efficacy, define optimal dosing strategies, and monitor long-term safety.

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