Case Report | Symptom Management in Palliative Medicine and Palliative Care

Tapentadol helps in trigeminal neuralgia: a case report

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Background: Trigeminal neuralgia (TN) usually affects people over 50 years old. TN-related pains are short-lived, and the disease course is characterized by exacerbations and remissions. Sometimes chronic pain develops due to central sensitization. This is the first case report on the effectiveness of tapentadol in pain control in TN.

Case Description: It is an instructive case history demonstrating the high effectiveness of tapentadol in a 55-year-old Caucasian male with severe [Visual Analogue Scale (VAS) 9/10] TN-related pain and a history of ineffective treatment with antiepileptic drugs. The neuralgia had occurred twice a year for the three preceding years, and typically the TN periods lasted 2–3 weeks with complete remissions between. Previously the patient had been treated with antiepileptic drugs (e.g., carbamazepine, phenytoin, clonazepam, gabapentin, and lamotrigine). However, he found all treatments to be ineffective and accompanied by unacceptable somnolence. Thus, a prolonged-release oral tapentadol was proposed at the beginning of the next relapse. After application of tapentadol, the patient reported a significant improvement. The severity of pain declined to VAS 6/10 (2nd day) and 4/10 (3rd day), and the attacks resolved entirely on the fourth day of treatment. He reported no side effects. The drug was discontinued after 14 days.

Conclusions: Despite pain chronification, tapentadol was efficient and well tolerated in TN. Further research is needed to reveal tapentadol's efficacy in neuralgias.

Keywords: Neuralgia; pain; tapentadol; neuropathy; case report

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Introduction

Trigeminal neuralgia (TN) is the most common form of cranial neuralgia, with a yearly prevalence of 12/100,000, usually affecting people over 50 years old (1). Contrary to typical chronic neuropathic pains of various etiologies (e.g., cancerous, diabetic), TN-related pains are usually short-lived (up to two minutes). Pain episodes may be numerous, and the disease runs with exacerbations and remissions (spontaneous or therapy-related). Most patients with typical TN possess a neurovascular conflict. However, in 12% of cases, no conflict exists (2). In 10–15%, a transformation from paroxysmal to chronic pain is observed due to central sensitization (3).

The pharmacological treatment of TN is based on antiepileptic drugs. They are often poorly tolerated and reduce the quality of life. If they fail, treatment options are limited. In 10–15% of TN cases, a transformation from paroxysmal to chronic pain is observed due to central sensitization. We present this case in accordance with the CARE reporting checklist (available at https://apm.amegroups.com/article/view/10.21037/apm-23-439/rc).

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Case presentation

A neurologist referred a 55-year-old Caucasian male to a pain clinic due to severe refractory pain during TN. The patient reported numerous episodes of recurrent, severe, piercing pain localized within the sensory division of the second and third branches of the left trigeminal nerve. The TN had occurred twice a year for the three preceding years. The TN periods lasted 2–3 weeks with complete remissions between. He reported no shingles, depression, or epilepsy in his medical history. The pain attacks lasted up to 2 minutes and were always severe [Visual Analogue Scale (VAS) 8–9/10], described as an electrical discharge, and accompanied by lachrymation. The episodes were numerous (~15/day), spontaneous, or due to touching the trigger zones. However, he reported gradual transformation into persistent pain with overlapping breakthrough pains during the last two relapses [classical TN with concomitant continuous pain according to the International Classification of Orofacial Pain (ICOP)] (4). Head MRI did not reveal any abnormalities. Previously the patient was treated with antiepileptic drugs (e.g., carbamazepine, phenytoin, clonazepam, gabapentin, and lamotrigine). A list of previously used drugs with their dosage and patient tolerability is presented in *Table 1*. However, he found all treatments to be ineffective and accompanied by unacceptable side effects. The patient was against invasive treatments, including minimally invasive, e.g., nerve blocks. Despite discussing all options, he accepted only pharmacological treatment, and after another relapse started, he requested urgent help.

Looking for a better-tolerated strategy, I proposed prolonged-release oral tapentadol 50 mg twice daily at the beginning of the next relapse. No other drugs were prescribed due to their negligible efficacy before.

All procedures performed in this study were in accordance with the ethical standards of the institution and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the editorial office of this journal.

Highlight box

Key findings

- Despite pain chronification, tapentadol proved effective and well tolerated in a trigeminal neuralgia patient previously unsuccessfully treated with antiepileptic drugs.

What is known and what is new?

- The pharmacological treatment of trigeminal neuralgia is based on antiepileptic drugs. They are often poorly tolerated and reduce the quality of life. In 10–15% of cases, a transformation from paroxysmal to chronic pain is observed due to central sensitization.
- This is the first case report on tapentadol efficacy in trigeminal neuralgia. Norepinephrine reuptake inhibition (NRI) likely explains tapentadol's activity in neuralgic pain.

What is the implication, and what should change now?

- As in the better understood neuropathic pain, NRI likely explains tapentadol's activity in neuralgic pain. The drug may also prevent or resolve pain chronification. Further research is recommended.

Results

After the first two doses of tapentadol, the patient reported a significant improvement. The pain severity declined to VAS 6/10 (2nd day) and 4/10 (3rd day), and the attacks resolved entirely on the fourth day of treatment. He was taking the drug regularly and reported no side effects. We discontinued the drug after 14 days. The pain did not recur during the following twelve months.

Discussion

Strengths and limitations

To date, this is the first report on tapentadol efficacy in TN. Tapentadol's application led to a rapid improvement with negligible side effects. Treatment time was short. Its financial cost was low, and patient satisfaction was high.

The patient had a history of multiple but ineffective pharmacological treatments, with severe complaints. Although he had a less typical TN course with complete remissions, the pain features did not match other headaches according to the ICOP criteria. Many patients with TN with concomitant continuous pain experience improvement in 1–2 weeks. However, the pain usually returns after drug discontinuation. In this case, despite the patient's negative opinion of the previous treatments, their efficacy could not be assessed due to the limited therapy periods, treatment discontinuations, and less typical course of the disease with complete remissions between the episodes.

Another question is, however, what led to such a rapid improvement on tapentadol. It can most likely be attributed to a hyperadditive synergism of opioid and norepinephrine reuptake inhibitor activities and neuron plasticity.

Table 1 Previously used drugs with their dosage and patient tolerability

Drug	Dosage	Treatment period	Why perceived as unsatisfactory
Carbamazepine	3×100 mg	12 days	Somnolence, confusion, dizziness, ataxia, limited efficacy, discontinued by the patient
Phenytoin	100–100–200 mg (400 mg/day)	9 days	Drowsiness, confusion, limited efficacy, discontinued by the patient
Gabapentin	3×300 mg up to 3×600 mg	2 weeks	Minimal relief, discontinued by the neurologist due to somnolence and at the patient's request
Clonazepam	3×0.5 mg	Single days, unable to determine	Unacceptable somnolence, minimal relief, discontinued by the patient
Lamotrigine	25 mg–>50 mg	10 days	Blurred vision, discontinued by the patient

Spontaneous remission, in this case, also cannot be ruled out. However, the previous pattern of pain, its dynamics, and pain chronification argue against this possibility.

As with all case reports, no definitive conclusions should be drawn. The effectiveness of an intervention in a single patient may not be confirmed in clinical trials.

Similarly to all opioids, tapentadol is associated with the risk of side effects, which may limit its use. The most common (≥1/10 patients) are dizziness and somnolence (usually transient), nausea, and vomiting. Anxiety, sleep disorders, abnormal dreams, constipation, diarrhea, dyspepsia, muscle cramps, excessive sweating, pruritus, and asthenia have also been reported. Many side effects are similar to those of antiepileptic drugs, but no comparative studies exist.

Data concerning tapentadol's long-term effectiveness and safety remain scarce. However, they were recently confirmed by Mateos *et al.* in an observational study of up to 72 weeks of observation time concerning people with knee and low back pain. In line with their findings, tapentadol could also prove valuable in TN patients with a more typical course of the disease requiring longer therapy (5). Also, according to Baron *et al.*, the incidence of the composite of dizziness and somnolence was significantly lower with tapentadol alone (16.9%; 500 mg a day) than tapentadol 300 mg combined with pregabalin 300 mg/day (27.0%; P=0.0302), as demonstrated in people with severe, chronic low back pain with a neuropathic component (6).

Comparison with similar research

Tapentadol is the first agent of a new opioid class [μ opioid receptor (MOR)-norepinephrine reuptake inhibition (NRI)]. It combines MOR agonism and NRI. Its favorable safety profile can be attributed to markedly lower μ receptor activation when compared to classical opioids. Tapentadol has no active metabolites. The major metabolic pathway for elimination is phase II glucuronidation. It affects pain chronification—a phenomenon attributed to the plasticity of neurons and pain spreading on physical, psychological, or even social levels.

Since its approval by the United States Food and Drug Administration in 2008, over 70 clinical trials on tapentadol have been announced and 600 publications have appeared. Several studies have demonstrated a beneficial effect of tapentadol on chronic neuropathic pains of various etiologies (5-7). Still, there are no dedicated reports on tapentadol efficacy in neuralgia. Also, neuralgic pain has distinct characteristics from more common chronic neuropathic pains.

Explanations of findings

The evidence on the effectiveness of tapentadol in neuropathic pain is limited and concerns low-back pain, cancer-related pains, and diabetic neuropathy. It is worth noting, however, that tapentadol efficacy was compared to oxycodone by Baron *et al.* (8). In a randomized controlled study, they found that in severe neuropathic chronic low back pain, tapentadol was associated with more significant improvements and a better global health status than oxycodone/naloxone. Also, according to Imanaka *et al.*, tapentadol's gastrointestinal tolerability profile is superior to that of oxycodone/naloxone (9).

Although the pathogenesis of neuralgic pain is not fully elucidated, some vital clues should be considered. The classical opioid morphine is a much more potent μ agonist than tapentadol (and, similarly to tapentadol, a weaker κ

and δ receptor agonist). However, its efficacy in neuropathic pain appears to be limited. According to a recent Cochrane review, the evidence that morphine is more effective than a placebo is doubtful in neuropathic pain, and no reliable data exist regarding neuralgia (10). Thus, if tapentadol proved efficacious in neuralgic pains in clinical trials, it could provide further support for NRI's importance in treating neuralgic pains. It seems that the hyperadditive synergism of opioid and NRI activities is crucial, while both pharmacodynamic actions analyzed separately possess a limited potential.

Implications and actions needed

TN is a severe disease, significantly affecting the quality of life, relapsing, and frequently incurable. Although this condition usually remains at the periphery of palliative medicine, TN may develop as a paraneoplastic syndrome, as a result of a cancerous infiltration, as a symptom of multiple sclerosis, etc. TN is a problem to face by pain treatment specialists if others cannot cope. Thus, a presented topic should not raise any controversy in light of the growing field of palliative medicine and the journal's scope (11).

Treatment options are limited when antiepileptic drugs fail in patients without a detectable and treatable cause of neuralgia or who are ineligible or unwilling to accept invasive treatment. Extending the indications for using a known agent with a favorable safety profile would expand the available therapeutic options and benefit many patients. If efficacy is confirmed in clinical trials, comparative studies on the effectiveness and safety of tapentadol versus antiepileptic drugs would also be beneficial.

Conclusions

Despite pain chronification, tapentadol proved effective and well tolerated in a TN patient previously unsuccessfully treated with antiepileptic drugs. Tapentadol may prove helpful in TN and other neuralgias, including cases with pain chronification. Further research is recommended.

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Footnote

Reporting Checklist: The author has completed the CARE reporting checklist. Available at https://apm.amegroups.com/article/view/10.21037/apm-23-439/rc

Peer Review File: Available at https://apm.amegroups.com/article/view/10.21037/apm-23-439/prf

Conflicts of Interest: The author has completed the ICMJE uniform disclosure form (available at https://apm.amegroups.com/article/view/10.21037/apm-23-439/coif). K.M. reports speaker bureaus (G.L. Pharma, PLN 2000, 06.2023) for giving a lecture for primary care physicians on pain management. The author has no other conflicts of interest to declare.

Ethical Statement: The author is accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in this study were in accordance with the ethical standards of the institution and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the editorial office of this journal. The applied treatment was not experimental, as it was based on the general principles of pain management, and the drug used was registered as a painkiller.

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