
Oral ketamine for phantom limb pain: An option for challenging cases

INTRODUCTION

Phantom limb pain (PLP) is a referred neuropathic pain perceived to arise from an amputated part of the body. It occurs in up to 80% of limb amputees and affects the patient's quality of life and rehabilitation.^[1,2] The mechanisms of PLP remain unknown but involve both peripheral and central neural factors including activation of N-methyl-D-aspartate (NMDA) receptors.^[2] Although ketamine, an NMDA receptor blocker, has been successfully used in many neuropathic pain conditions, its role in treating PLP is unclear.^[3,4] We describe a challenging case of PLP where treatment with oral ketamine provided adequate relief.

CASE REPORT

A 55-year-old man underwent right above-elbow amputation due to synovial sarcoma. After the amputation, he suffered short-lasting stump pain. He underwent forequarter amputation of his right upper limb for recurrent sarcoma after 4 months. Two weeks later, he began complaining of phantom pain in the amputated limb, which he described as feeling 'ice-cold' and 'cramping'. Six months later, he developed severe continuous pain in the lower back. Magnetic resonance imaging and bone scan showed multiple metastases in L₃₋₅ and S₁ vertebrae. He was prescribed oral tramadol- paracetamol combination, to which he initially responded, but after a month the pain became excruciating.

In the pain clinic, he complained of severe pain in the back and legs, which he rated as 9 of 10 on the verbal categorical pain score.^[5] He also reported burning,

cramping intermittent PLP and rated it as 7/10. He said that 'I know that I am dying of cancer. But please treat the pain, but I do not want any injections.'

His medical treatment of pain consisted of oral opioids 4 hourly followed by paracetamol, sustained-release morphine, sustained-release amitriptyline 50 mg and sustained-release pregabalin 150 mg twice daily, along with immediate-release morphine for his breakthrough pain. After 2 weeks of treatment, his pain in the back decreased to 2/10. However, he still rated his PLP as 7/10. The patient refused any invasive procedure as he was extremely anxious and had undergone multiple surgeries. After explaining the pros and cons and obtaining verbal consent from the patient and his wife, he was started on oral ketamine in liquid form (mixed with cola drink to mask its bitter taste) 50 mg 3 times a day. After 2 days, he reported pain relief. Over a period of 2 weeks, his phantom pain reduced to 3/10 without any side effects.

He was also continued on other medications along with 270 mg of oral sustained release morphine. Ketamine was stopped after about 4 months, considering its off-label use. However, 2 weeks later his phantom pain recurred, and oral ketamine was restarted. His general condition deteriorated further, and 2 weeks later he died at home while free from PLP on oral ketamine.

DISCUSSION

PLP can be a devastating consequence of an amputation. Patients found to be at risk for PLP are those who have pre-amputation pain, traumatic amputation, residual pain in remaining limb and upper extremity amputation.^[1,2]

Once established, it can pose a therapeutic challenge in some patients. Suggested therapies include administration of pharmacological agents (e.g., anti-epileptic drugs, anti-depressant drugs, opioids and calcitonin), behavioural interventions, transcutaneous electrical nerve stimulation, various invasive techniques (e.g., epidural blockade, sympathectomy, dorsal root entry zone lesion, spinal cord stimulation, motor cortex stimulation) and even electroconvulsive therapy.^[2]

Early therapy with NMDA receptor antagonists can prevent central sensitisation in neuropathic pain. Ketamine is a phencyclidine anaesthetic agent that has analgesic properties at subanaesthetic doses.^[6] Besides

acting on the NMDA receptor, it also acts on nicotinic, muscarinic and opioid receptors. Ketamine has proven to be effective in the treatment of opioid-resistant pain syndromes due to its opiate-sparing effects, where it can either be used as a primary analgesic or analgesic adjuvant.^[3,4] Oral administration is preferred for long-term use, starting with a single dose of 0.25–0.5 mg/kg with an average dosing frequency of 3–4 times daily. Doses can be increased in steps of 0.25 mg/kg daily until adequate analgesia is achieved, or side effects are seen.^[6]

Our patient had severe PLP, which proved to be refractory to multiple pharmacological agents including opioids. Our second plan was stellate ganglion block, which the patient refused; hence we could not perform an invasive procedure. Recently, a number of studies have reported the successful use of ketamine as an analgesic in patients with chronic non-malignant pain.^[5] It has been used as infusion^[7] but rarely through the oral route.^[6,8] Considering the long-term administration and patient refusal to invasive route, we decided to start oral ketamine in the dose of 50 mg thrice a day. A wide range of doses for oral ketamine has been reported in the literature, which includes 150 mg/day.^[6,8] With this dose, our patient had rapid and satisfactory pain relief without any adverse effects. He did not experience the side effects such as sedation/insomnia, dizziness, diarrhoea, trouble sitting still and psychiatric side effects such as agitation and hallucinations. Interestingly, one recent case report described an exacerbation of PLP with ketamine, but the authors clarified that this was because of hallucination with flashback phenomenon in their patient.^[9]

Ketamine is poorly absorbed after oral administration and undergoes extensive first-pass metabolism. Oral bioavailability is 16%, which is about one-fifth of the availability after intravenous injection. Due to high first-pass hepatic metabolism, serum nor-ketamine levels after oral ketamine are 2–3 times greater than those after parenteral ketamine.^[6] Nor-ketamine is one-third to one-fifth as potent as ketamine and has been demonstrated to have analgesic properties.^[3,4] After oral administration, peak plasma concentrations are achieved in approximately 30 min. The elimination half-life is 2–3 h for ketamine and approximately 4 h for nor-ketamine. Oral ketamine has been suggested to produce fewer and less severe adverse effects than parenterally administered ketamine. Common adverse effects are nightmares, anxiety, hallucinations, nystagmus, diplopia, nausea, vomiting, loss of appetite and abdominal pain.^[10]

CONCLUSION

Oral ketamine was effective in reducing the intensity of PLP in our patient. Pending confirmation in larger series, this case report suggests that individual or adjunct treatment with oral ketamine remains a tangible alternative where invasive treatments fail, are not possible, or refused by the patient.

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REFERENCES

- Nikolajsen L, Jensen TS. Phantom limb pain. *Br J Anaesth* 2001;87:107-16.
- Angarita MA, Villab SC, Riberoc OF, Garcíad RG, Siegerf FA. Pathophysiology and treatment of phantom limb pain. *Rev Colomb Anesthesiol* 2014;42:40-6.
- Hocking G, Cousins MJ. Ketamine in chronic pain management: An evidence-based review. *Anesth Analg* 2003;97:1730-9.
- Knox DJ, McLeod BJ, Goucke CR. Acute phantom limb pain controlled by ketamine. *Anaesth Intensive Care* 1995;23:620-2.
- Fitzgibbon EJ, Hall P, Schroder C, Seely J, Viola R. Low dose ketamine as an analgesic adjuvant in difficult pain syndromes: A strategy for conversion from parenteral to oral ketamine. *J Pain Symptom Manage* 2002;23:165-70.
- Blonk MI, Koder BC, van den Bemt PM, Huygen FJ. Use of oral ketamine in chronic pain management: A review. *Eur J Pain* 2010;14:466-72.
- Shanthanna H, Huilgol M, Manivackam VK. Early and effective use of ketamine for treatment of phantom limb pain. *Indian J Anaesth* 2010;54:157-9.
- Enarson MC, Hays H, Woodroffe MA. Clinical experience with oral ketamine. *J Pain Symptom Manage* 1999;17:384-6.
- Sakai T, Sumikawa K. Phantom limb pain exacerbated by intravenous ketamine. *J Anesth* 2014;28:643.
- Dworkin RH, Turk DC, Farrar JT, Haythornthwaite JA, Jensen MP, Katz NP, *et al.* Core outcome measures for chronic pain clinical trials: IMMPACT recommendations. *Pain* 2005;113:9-19.

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