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# Beneficial effect of ketamine hydrochloride in phantom limb pain: report of a case

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## Introduction

Amputees often develop pathological pain processes, such as phantom limb pain, that persist for several days or even years after all possible tissue healing has occurred [1]. We present a case in which intravenous ketamine hydrochloride, an antagonist of *N*-methyl-D-aspartate (NMDA) receptors [2], was effective in controlling severe phantom limb pain. In this case, a short-term intermittent therapy involving a low dose of ketamine resulted in adequate pain relief without undesirable side effects.

## Case report

A 61-year-old man who, although suffering from diabetes for the previous 10 years, was otherwise healthy, fell from a roof and bruised his left leg. Three days after the accident, he was referred to our hospital because of uncontrollable severe pain in his left leg. A physical examination revealed gas gangrene. An emergency tension-relief incision and hyperbaric oxygen therapy were tried, but the procedure was unsuccessful, the stump remaining swollen, infected, and painful. An amputation of his left leg was performed under general anesthesia with nitrous oxide and sevoflurane in oxygen. Although the postoperative course was satisfactory and the gas gangrene showed complete remission within 2 months, he experienced severe pain continuously in the affected leg during these 2 months. In addition, 1 week after the operation, he developed phantom limb pain; this increased daily in severity. After a consultation with surgeons, he was transferred to our pain clinic for the control of his pain.

At first, diclofenac by suppository or pentazocine by intramuscular injection was effective for the stump pain, but ineffective for the phantom sensation. Although we administered morphine orally in combination with oral imipramine as the next stage in his treatment, the relief of both stump and phantom pain was transient, and he soon complained of both pains again. Accordingly, we inserted an epidural catheter at the L2–3 interspace and administered 1.0% mepivacaine $4\,ml \cdot h^{-1}$ with buprenorphine 0.2 mg per day epidurally; this achieved adequate relief of the stump pain relief. However, he was still experiencing the phantom sensation. For this symptom, several psychotropic agents (haloperidol, chlorpromazine hydrochloride, or etizolam) were given orally, but with little effect. Oral dextromethorphan was also ineffective. Then, a bolus injection of ketamine hydrochloride $0.2\,mg \cdot kg^{-1}$ was given intravenously. Immediately after the injection, he had mild hallucination, and complete relief of his phantom pain was achieved. When the phantom pain returned after 12 h, a further intravenous injection of the same dose of ketamine again provided pain relief; this time, the relief lasted 24 h. After a further ketamine injection, on the third day, complete relief of phantom pain was achieved. After that, all the symptoms disappeared over a further 5-month period with additional physiotherapy and rehabilitation, and he was subsequently discharged.

## Discussion

The present patient suffered severe phantom limb pain following amputation, but a dramatic decrease in his

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pain was achieved on the intravenous injection of a low dose of ketamine hydrochloride. Our patient experienced complete relief of the phantom pain with only three intravenous ketamine injections given over 3 days. Although the reason behind such a dramatic effect is not clear, we speculate that ketamine acted as an antagonist of NMDA receptors and induced a rapid normalization of some abnormality in the central nervous system (CNS).

The exact mechanism underlying phantom limb pain is uncertain [3], but it has been suggested that a central sensitization, such as windup or long-term potentiation [4] of supraspinal structures may contribute to the genesis of phantom sensation [1]. Moreover, amputees are more likely to develop phantom limb pain if they have been suffering from pain in the limb prior to amputation [5]; this suggests that the presence of neuropathic pain can increase the potential for central sensitization [6]. Our patient suffered from severe pain in his left leg, originally due to a gas gangrene before and after amputation, in agreement with the above findings. However, postural phantom sensations do not usually persist beyond a few days, and in most cases are at least temporarily reversed by competing visual inputs which reveal a dissociation between the real and the perceived limb [6]. In the present case, however, phantom limb pain persisted for about 4 months, so the possibility exists that prolonged continuous deafferentation pain from the stump region caused the phantom limb pain to persist.

Some years ago, it was said that once phantom limb pain was established, no palliative then available provided suitable treatment [7]. Although we made several attempts to alleviate our patient's phantom limb pain, by trying medications such as analgesics, antidepressants, opiates, and psychotropic agents, none of these trials resulted in a favorable result. Epidural administration of local anesthetics produced an analgesic effect on the stump pain, but not on the phantom limb pain or sensation. These results may indicate that the neural mechanism in the CNS via which peripheral noxious stimulation leads to the development of phantom sensation needs to involve a specific type of nociceptor (one not blocked by the above treatments) if phantom pain is to occur. Recently, some clinical case reports have been published in which ketamine hydrochloride was tried therapeutically for cases of phantom limb pain, with beneficial results [3,8,9]. Our present report may also support these earlier findings and put forward, in addition, the idea that NMDA receptor-mediated transmission of noxious stimulation may play a major role in the development of phantom limb pain.

In summary, we successfully managed a patient with severe phantom limb pain by giving a low dose of ketamine intravenously. This may suggest that NMDA receptors play an important role in the genesis of phantom limb pain.

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