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Case Report

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The Use of Oral Ketamine for Wound Dressing in an Adult Patient

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Summary

Ketamine is a racemic mixture of two enantiomers, R- and S-ketamine [1]. The mixture is primarily used as anaesthestic agent. In low or sub anaesthetic doses, ketamine has potent analgesic properties, and it has been used effectively as either a primary analgesic or analgesic adjuvant in varieties of pain syndromes and burn dressings in children [2]. In this case report, we illustrate the effectiveness of oral ketamine in controlling pain during wound dressing in an adult patient with gluteal decubitus ulcer. Other advantages of this technique include few side effects of low dose oral ketamine, low cost, and its ready availability in developing countries.

Keywords

Ketamine, N-methyl-D-aspartate (NMDA) receptor, Pain management, Oral administration

Introduction

Ketamine is a derivative of phencyclidine (angel dust) with lesser tendencies to cause hallucination. It was first used as an intravenous anaesthetic in 1965 and it is presented in 10, 50 and 100 mg/ml solutions containing benzethonium chloride as preservative [2]. The analgesic effect of ketamine appears to be multifactorial as it interacts with varieties of pain mechanisms. These include N-methyl-D-aspartate receptors (the major pharmacological target), kappa opioid, monoaminergic receptors, and voltage gated calcium channels. In addition, ketamine has local anaesthetic effects comparable to lidocaine in high doses [3,4].

Acute pain which is commonly nociceptive is easily treated even by non-pain specialists. It is often treated with opioids such as morphine, pethidine, codeine, and tramadol. The opioids are used in moderate to severe pain conditions. Paracetamol, non-steroidal anti-inflammatory drugs (NSAIDS) for example, aspirin, ibuprofen, diclofenac are useful in mild pain conditions. In contrast, chronic pain which may be nociceptive, neuropathic, or mixed is challenging and difficult to treat effectively. Ketamine has been effective in neuropathic and mixed pain syndromes including postherpetic neuralgia, glossopharyngeal neuralgia, phantom limb pain, ischaemic pain, post operative pain, central pain syndrome, HIV and cancer pain [5,6].

Some of the major problems concerning ketamine acceptance for pain management relates to it neither been approved as an analgesic nor for oral use. It also has potential for addiction. The other limiting factor is its incidence of disturbing psychotomimetic side effects [7,8]. These include emergence phenomena, floating sensations, vivid dreams, delirium, and drowsiness. However, these side effects are dose dependent and can be minimized by using ketamine in low doses with concurrent administration of a benzodiazepine [9]. Clear vigilance for cognitive and psychotropic disturbance is required, particularly during initiation of ketamine therapy. The importance of systemic effects of chronic use is not known, therefore patients on prolonged use of ketamine should be monitored frequently.

We report the analgesic effectiveness and tolerability of oral ketamine during wound dressing in an obese 57-year-old woman with Pott's disease complicated with paraplegia and

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a large gluteal decubitus ulcer. The results of the case study suggest feasibility of use of oral ketamine with advantages of easy accessibility, especially in developing countries; less technicalities with oral administration; and wide safety margin.

Case Report

A 57-year-old woman was admitted into the medical ward with previous history of pulmonary tuberculosis, two years before presentation. She now presents with three months history of upper back pain, eight days of inability to move her legs, pain over the buttocks, urinary incontinence, and constipation. She was 1.52 m tall and weighed 70 kg with a body mass index (BMI) of 30.3 kg/m^2.

There were coarse crepitations on the lung middle zones bilaterally. She also had spastic paraplegia and the sensory level was at T10 with positive spinal tenderness and hyperaemic skin over the gluteus bilaterally. The tone was increased, power was one and reflexes were exaggerated in both lower limbs but were within normal limits in the upper limbs. X-ray of the spine showed T6 vertebra wedge collapse and spondylotic changes at T11 and T12 vertebrae. There was no significant radiological finding in the chest radiograph. Screening for acid fast bacilli, carcinoembryonic antigen and Bence Jones protein were all negative. Erythrocyte sedimentation rate was elevated at 70 mm/hour, while the full blood count and electrolyte and urea were within normal limits. An assessment of compressive myelopathy secondary to Pott's disease was made and the patient was commenced on anti-tuberculous therapy consisting of isoniazid, ethambutol, rifampicin, pyrazinamide, and pyridoxine.

Other medications given are oral co-proxamol, bisacodyl suppositories, amitriptyline, ferrous sulphate, folic acid, and subcutaneous unfractionated heparin 5000 IU 12 hourly. Nursing care was provided by regular turning on the bed every two hours and the hyperaemic skin over the buttocks was painted daily with gentian violet. In addition, patient was on continuous urinary catheter drainage and received daily physiotherapy.

Despite the medications and nursing care, the patient developed extensive blisters and decubitus ulcer over the gluteus fourteen days following hospital admission. The ulcer bed measured about 20 × 30 cm. Aggressive wound care was instituted with wound debridement, daily wound dressing with honey, tetanus prophylaxis and a waterbed was substituted for the regular hospital bed. Daily wound care was marked with spells of painful distress, which the patient described as deep burning sensations in the wound area. She was seen crying after wound dressing. Using the Visual Analogue Scale, the pain score was assessed and rated 9/10 by the patient and she could no longer tolerate daily wound care. Oral ibuprofen 400mg 8-hourly and oral carbamazepine 200 mg 12-hourly were introduced with little effect and the pain score only dropped to 8/10.

As opioid analgesics were not readily available at the time of this case report, a decision was made to use oral ketamine. Ketamine hydrochloride injection USP by Rotex Medica 50 mg/ml at oral doses of 5 mg/kg/day (350 mg/day) was administered 10 minutes before routine wound dressing. Ketamine solution is bitter to taste, and its taste was modified by adding sugar to make it acceptable to the patient. Vital signs (respiratory rate, pulse rate and blood pressure) were recorded before and after ketamine administration. Pain control was satisfactory as reflected by pain score of 2/10 using the numeric rating scale of 0-10 and the patient recorded a sense of feeling comfortable with the wound dressing. Ketamine was maintained at 350 mg/day while the patient continued to express satisfaction. A total of thirty-five doses of oral ketamine were administered. Ibuprofen and amitriptyline were discontinued, and the patient was maintained on other medications including co-proxamol, simvastatin, bisacodyl suppositories, ferrous sulphate, folic acid, and the anti-tuberculous therapy.

Two weeks into the commencement of oral ketamine, the patient showed signs of depression. Psychiatrist evaluation revealed mild depression secondary to the general medical condition and only suggested further observation for symptoms of depression. There were no signs of any psychotomimetic side effects or ketamine tolerance. Essentially, episodes of painful wound dressing stopped following the initiation of oral ketamine. The wound healing progressed optimally, with bright red surfaces and healing wound edges and the patient was discharged home after 78 days of hospitalization. Subsequently, patient commenced alternate day wound dressing on out-patient basis without the need for oral ketamine.

Discussion

The use of ketamine as an analgesic agent in sub anaesthetic doses is not a new discovery [10]. The drug has often been used off-label for wound dressing for burn victims [11,12] Ketamine is commonly licensed as anaesthetic induction agent which may have reduced its popularity as an analgesic. Nevertheless, ketamine is the only anaesthetic induction agent with analgesic properties. Study on the use of ketamine as an analgesic adjuvant early in chronic cancer pain management suggested that ketamine can be opioid sparing and effective as a co-analgesic and reduce the development of opioid tolerance [13]. Also, the need to reduce opioid doses when starting patients on ketamine for pain management has been suggested by many authors [14]. Ketamine has also been used effectively in varieties of pain syndromes such as somatic pain, visceral pain and mixed pain conditions [15]. In the event that opioids, anticonvulsants or antidepressants have proved ineffective in chronic pain management, ketamine as the third line may provide a suitable choice. This report identifies the role of oral ketamine as an analgesic in the management of acute nociceptive wound pain.

Parenteral administration, intravenous (IV) and intramuscular (IM) are the commonest routes of ketamine administration in our center. Other possible routes are subcutaneous, rectal, nasal, or transdermal [16], and oral route have been explored. Epidural administration of ketamine in complex regional pain syndrome with a dose of 20-30 mg/day has also been tried [17]. Patients on prolonged

hospital admission may be better off on oral ketamine for their pain management as this route avoids parenteral routes which may be painful and be source of infections. The dosing regimen varies with different routes. Oral doses reported among adult patients in the literature vary between 25-50 mg, 8-hourly to maximum of 1000 mg per day [18]. In this report, we used 5 mg/kg body weight per day, equivalent of 350 mg. These values showed that ketamine has a wide therapeutic index.

The NMDA receptor is an ionotropic receptor for glutamate and possibly for aspartate which does stimulate NMDA receptor weakly. Ketamine and other drugs like tramadol, nitrous oxide, ethanol, methadone, and amantadine are classical NMDA receptor antagonists. The NMDA receptors found in humans are important for sensory perception, memory function, cognition, and consciousness [19]. If these higher functions are blocked, then psychotomimetic side effects may develop. It has been noted that the psychotomimetic side effects of ketamine are reduced with pre-administration of benzodiazepines. This may be an indication for co-administration of benzodiazepine at each session during repeated and prolonged administration of oral ketamine. Benzodiazepine was not used in this case report as sub anaesthetic doses were administered perhaps that could have prevented the psychotomimetic side effects. The patient in this report had thirty-five sessions of oral administration of ketamine, maybe it takes longer to develop psychotomimetic side effects. We have to keep vigilance for any other side effect. In case the dose of ketamine is increased, psychotomimetic side effects may become problems to contend.

Ketamine may transiently increase blood pressure and heart rate. Blood pressure variation in this report ranged between 125-155 mmHg systolic and 80-98 mmHg diastolic with heart rate variation of 78-124 beats per minute. The increase in blood pressure may be up to 50% over the pre-anesthesia values when given in standard anaesthetic doses, but usually decreases to pre-anesthesia values within 15 minutes of initial administration. Despite its tendency to augment blood pressure, ketamine has been associated with cardiovascular depression with repeat dosing to the initial dose of ketamine [20] and among patients with cardiac disease [21].

Compared with morphine, which is a potent analgesic, administration of standard ketamine dosage does not usually cause hypotension. The histamine released with morphine administration may contribute to vasodilatory effects and subsequently lead to hypotension [22,23]. Among patients with chronic pain and who cannot tolerate hypotension; and patients with chronic pain conditions which are resistant to strong opioids-oral ketamine administrations may yield good alternative results. Furthermore, in developing countries where opioids are not readily available, ketamine may provide a good substitute for adequate pain management.

Essentially, oral administration of racemic ketamine may be a useful and effective analgesic for repeated wound dressing in adult patients. This finding is important and might be applicable among hospitalized patients with similar chronic pain. The use of oral ketamine in combination with low dose opioid might reduce opioid dependency and addiction. In addition, the findings of this report underscored the significance of the value of future clinical study of oral ketamine for other pain conditions.

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