Use of ketamine in uncontrolled acute and procedural pain


Summary
This article explores the role of ketamine in pain management. Ketamine is an analgesic used to treat uncontrolled acute and procedural pain. It has protective properties and can prevent patients from developing persistent pain. In sub-anaesthetic analgesic doses, ketamine is a safe drug and produces minimal side effects.

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Keywords
Drug therapy, ketamine, pain transmission, procedural pain

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WARD NURSES MAY NOT be familiar with the use of ketamine, which is commonly used in operating theatres as an anaesthetic agent. However, it is an effective analgesic that when used appropriately can prevent patients from developing persistent pain (McCartney et al 2004, Schug 2004, Hocking et al 2007). Ketamine was first used as an anaesthetic in the Vietnam War. It increases heart rate and blood pressure by stimulating the sympathetic nervous system, which is useful in emergency situations. Ketamine also allows patients to maintain control of their breathing. Pain-relieving effects of ketamine are observed even in sub-anaesthetic doses. Ketamine is a safe drug to use for pain relief as small doses produce no anaesthetic or sympathomimetic effects (Bell et al 2006).

Chronic pain after surgery
Ketamine can prevent patients from developing chronic pain after a surgical procedure (McCartney et al 2004, Schug 2004, Hocking et al 2007). Chronic post-surgical pain is a subject that has been investigated only recently (Crombie et al 1998, Macrae 2001, Kehlet et al 2006). An audit found that 23% of patients attending chronic pain clinics did so as a direct result of a surgical procedure (Crombie et al 1998). Many of these patients had continuous pain, scored as moderate or severe, for more than two years.

Action of ketamine
In normal pain transmission, a primary afferent nerve carries impulses from the site of pain, initially to the dorsal horn in the spinal cord. At the dorsal horn, this nerve synapses with a spinal nerve and impulses travel to the brain, where they are then recognised as a painful sensation (Figure 1).

For the impulses to cross the synapse, a chemical transmitter called glutamate is required to cross the gap and attach to the alpha-amino-3-hydroxy-5-methyl-4-isoxasolepropionic acid receptor on the spinal nerve. When pain becomes persistent, the N-methyl-D-aspartate (NMDA) receptor, which is normally dormant, becomes active and increases the intensity of the pain impulses or signals (Figure 2). To prevent pain from becoming persistent, it is important to block this NMDA receptor quickly. Ketamine works by blocking the NMDA receptor, thereby making it inactive.

Ketamine only works when the NMDA receptor is active, and it is therefore not given...
routinely to all patients. The NMDA receptor is thought to be active when pain is difficult to manage and does not respond to morphine-type medication. Criteria can be used to identify suitable patients (Box 1).

Signs and symptoms of neuropathic pain

Neuropathic pain occurs as a result of nerve damage. Pain can become worse irrespective of movement; patients may experience paroxysms of pain that occur without warning. Patients often describe pain as a burning, shooting or electrical sensation. Occasionally, pain may be likened to ants crawling under the skin.

Patients who have active NMDA receptors may also experience allodynia or hyperalgesia. Allodynia occurs when a stimulus that does not normally result in pain, such as light touch, becomes painful. Patients with allodynia may dislike clothes or sheets touching the skin. They may object to the window being open or a fan in the room, as even a slight breeze can produce pain. Hyperalgesia is an increased sensitivity to pain.

If a patient fulfils one or more of the criteria in Box 1, then uncontrolled pain might be the result of an active NMDA receptor. In these circumstances, an intravenous trial of ketamine can be commenced, to see if the patient responds to the drug. Ketamine is routinely administered by specialist pain teams, palliative care teams or by anaesthetists. It should not be prescribed unless the patient is under the care of a specialist team.

In a recent audit involving 45 patients – selected using the criteria in Box 1 – all but three responded to the drug (Chumbley et al 2008).

Intravenous trial of ketamine

Administering an intravenous trial of ketamine is relatively straightforward. Before the trial, a pain score at rest and when moving should be obtained from the patient. Ketamine is then administered intravenously in 2.5mg aliquots, every five minutes, to a maximum of 10mg. If the patient has an active NMDA receptor, then the pain will diminish rapidly – usually from severe to mild – in five to ten minutes. If the NMDA receptor is not active, ketamine will have no effect (Chumbley 2010).

In the author’s NHS trust, patients receiving a trial of intravenous ketamine do not have to be monitored, provided they are stable. The rationale for this policy is that the drug produces no effect on vital signs at sub-anaesthetic doses (Schug 2004). Patients may occasionally feel lightheaded when undergoing a ketamine trial. Patient safety is key and other organisations may recommend monitoring of vital signs during any such trial. Local guidelines or protocols should always be followed.

Maintenance doses of ketamine

Patients who respond to ketamine can continue taking the drug orally or as an intravenous or subcutaneous infusion. Oral administration of ketamine suspension starts at 2.5mg, four times daily. It can be titrated to a maximum of 100mg, four times daily, depending on the patient’s response. Occasionally, patients may experience breakthrough pain when ketamine is administered six-hourly. Ketamine can be
prescribed four-hourly for these patients, but at a maximum dose of 75mg (Chumbley 2010). Ketamine can be given in conjunction with opioid analgesics, such as morphine. There is evidence to suggest that the patient may require less opioid (Subramaniam et al 2004).

Intravenous or subcutaneous administration of ketamine is prescribed according to the patient’s body weight. An infusion of 0.1mg/kg/hour is given. For example, if the patient weighs 70kg, then he or she would receive 7mg/hour, as an infusion. The rate can be titrated to 0.2mg/kg/hour or 14mg/hour (Chumbley 2010). Higher concentrations of ketamine may cause hallucinations. Therefore concentrations higher than 0.2mg/kg/hour are usually avoided.

Ketamine patient-controlled analgesia

Higher doses of ketamine can be administered for procedural pain using patient-controlled analgesia, for example, during burns dressings. When patients activate the machine they receive 10mg of intravenous ketamine plus 0.5mg of midazolam. This combination can be requested at five-minute intervals for the duration of the procedure. As this is a higher dose of ketamine, midazolam is required to prevent any unwanted side effects such as dysphoria (Schug 2004, Visser and Schug 2006, Hocking et al 2007). Midazolam is a sedative that is usually administered only in a critical care environment.

Discontinuing ketamine

Ketamine and strong opioids are usually discontinued before patients are discharged. Patients do not need to be weaned off ketamine, but in practice a slow reduction is helpful; if painful symptoms recur, then the patient is not ready to stop taking the drug. Occasionally, a patient may need to start other neuropathic pain medication, such as gabapentin or nortriptyline.

Gabapentin was the drug of choice before ketamine began to be used for the treatment of uncontrolled acute neuropathic pain. Gabapentin takes approximately five days of titration to reach therapeutic levels, but this used to mean five days of uncontrolled pain for the patient (Chumbley 2010). Ketamine has allowed pain services to control this type of pain in 15 minutes, reducing the levels of stress and discomfort experienced by patients.

Conclusion

Low-dose ketamine is a safe and effective method for treating uncontrolled pain. It should not be used routinely, but reserved for patients with active NMDA receptors. Ketamine should be administered by specialist pain services and given in conjunction with other medications to manage pain. If ketamine is used effectively, it can prevent patients from developing persistent pain NS.

Acknowledgement

Each of the articles in this series have been written by a member of the Royal College of Nursing London Pain Interest Group. Nursing Standard would like to thank Felicia Cox, senior nurse in pain management, Royal Brompton and Harefield NHS Foundation Trust and chair of the Royal College of Nursing London Pain Interest Group, for co-ordinating and developing this series.

References


