

Ketamine: the introduction and clinical use in the Hospice and Palliative Care Center of Kiang Wu Hospital

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Ketamine as an adjuvant analgesic agent

Ketamine has been used as an anaesthetic agent for more than 30 years. With its N-methyl-D-aspartate (NMDA) receptor antagonist action, it has also been used, at low dosages, as an analgesic drug. In addition to the NMDA receptor, it also interacts with various other receptors, such as the opioid and muscarinic receptors. It also interacts with calcium and sodium channels and inhibits noradrenalin and serotonin re-uptake. Ketamine is used for pain that is unresponsive to standard therapies, not just for neuropathic pain, but also inflammatory, ischaemic, myofascial and procedure-related pain and its efficacy has been demonstrated in controlled trials.

Oral ketamine undergoes extensive first-pass hepatic metabolism to norketamine. Thus while the bioavailability of intramuscular ketamine is 93%, that of oral ketamine is only 20%. However, as norketamine is also an NMDA receptor antagonist, the parenteral to oral dose ratio has been demonstrated to be approximately 1:1, or even higher, despite first-pass metabolism. It has thus been suggested that lower dosages of ketamine are effective with the oral route.

The time to onset of action when ketamine is given intramuscularly, subcutaneously and orally is five minutes, 15 to 30 minutes and 30 minutes respectively. The plasma half-life of intramuscular and oral ketamine is one to three hours and three hours respectively, and that of norketamine 12 hours. The duration of action of oral morphine is usually four to six hours, but sometimes longer. Long-term use of ketamine may lead to hepatic enzyme induction and may affect its metabolism. Ketamine rapidly enters the central nervous system. Less than 10% of

ketamine is excreted unchanged, half in the faeces and the other half in the urine.

The usual recommended starting dose of subcutaneous ketamine is 1-2.5 mg/Kg/24 hours, which can be diluted with normal saline. If pain is not controlled, dosage could be increased by increments of 50-100 mg/day. The maximum reported dosage is 3.6 g/day. The starting dosage of oral ketamine is usually not more than 25 mg three to four times a day, increasing by increments of 10-25 mg if pain is not controlled. The maximum reported dosage is 200 mg four times a day. On switching from subcutaneous to oral ketamine, while some workers use a conversion ratio of 1:1, others recommended that the oral dosage should be less than 50% of the total parenteral dosage. In a syringe, ketamine is compatible with dexamethasone, diamorphine, haloperidol, levomepromazine, metoclopramide, midazolam and morphine.

Adverse effects include psychotomimetic phenomena, cardiovascular adverse effects and skin irritation, and occur in approximately 40% of patients when given as continuous subcutaneous infusion, but may be less frequent with oral administration. Psychotomimetic adverse effects might be prevented by haloperidol or benzodiazepines. Ketamine should be used with caution in patients taking diazepam, as plasma concentration of ketamine might be increased. Cardiovascular adverse effects are not uncommon with ketamine, and it should be used with caution in patients with hypertension, heart failure, ischaemic heart disease or a history of cerebrovascular accident. Ketamine might have an opioid sparing effect and the dosage of opioids should be reduced especially when the patient becomes drowsy.