

Ketamine: an Old Drug Commonly Used in Clinical Practice

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Ketamine, an old intravenous anesthetic, is a non-narcotic and non-barbiturate drug. It has been there in clinical anesthesia practice for more than sixty years. Importantly, it plays an invaluable role in the developing countries including Thailand. Ketamine mainly works by non-competitive antagonist at the N-methyl-D-aspartate (NMDA) receptors. It has several properties of the ideal anesthetic agent. Ketamine was formerly used as a sole agent for anesthesia, inducing analgesia, amnesia, loss of consciousness and immobility. Therefore, its properties are interesting in various clinical settings, although it can produce the psychological adverse effects.^{1,2}

Pharmacology

Ketamine is a non-narcotic and non-barbiturate drug. It exists as a racemic compound containing equimolar amounts of S (+) ketamine and R (-) ketamine. S (+) ketamine has greater potency and fewer side effects. In subanesthetic dose, it was initiated to display analgesic properties because it binds to the mu and kappa opioid receptors.^{1,2} Ketamine preserves the cardiovascular function and has the least harmful effect on the hypoxic tissues when compared to the other anesthetic drugs.³ Its cardiovascular effects are usually associated with tachycardia, hypertension and increased cardiac output. In addition, ketamine has minimal effect on central respiratory

drive, although a transient decrease in ventilation can occur after bolus administration. The response to carbon dioxide is unaltered except the administration of a large dose. The airway reflexes and airway muscle tone are still preserved. Moreover, ketamine is also a bronchial smooth muscle relaxant. However, ketamine induces saliva and mucous secretions which can produce some problems.

Ketamine creates the dissociative anesthetic state that has been described as dissociative anesthesia. The unique clinical state produced by ketamine is characteristically as a cataleptic-like state of unresponsiveness with occasional coordinated but seemingly purposeless movements of head, arms, legs and trunk and head. Additionally, ketamine increases cerebral blood flow, intracranial pressure with little effect on overall cerebral metabolic rate.^{1,2} Emergence reactions have occurred in about 5-30%. However, the psychological manifestations after ketamine may vary in severity and could be alterations in mood state and body image, floating sensations, dramatic dreams or illusions, occasional frank delirium, confusion, excitement and unreasonable behavior.

Clinical use

Ketamine is not popular anymore because of its undesired psychomimetic effects.

The renewed interest has focused on the use of subanesthetic dose of ketamine for treatment of acute and chronic pain. Low dose ketamine (0.1-0.2 mg/kg i.v.) exhibits few of the adverse side effects. Consequently, low dose ketamine could be utilized for sedation and analgesia during monitored anesthesia care or in the intensive care unit (ICU).⁴ One of the reasons for the use of ketamine in the ICU patients is the lower undesirable influence on bowel motility than opioids. Several previous studies demonstrated that the preemptive effect from the administration of ketamine prior to surgical incision could lead to decrease in wound hyperalgesia for several days after the surgical procedure.⁵

Ketamine has demonstrated a wide margin of safety, with little risk of serious adverse effects. It has been shown to have beneficial cardiovascular effects when administered as maintenance sedation via continuous infusion.⁶ Additionally, it offers a favorable hemodynamic profile and does not promote respiratory depression. Ketamine is appropriate for children undergoing procedures in isolated situations. It can be used in procedures outside the operating room such as radiological investigations, radiotherapy, cardiac catheterization, and burns dressings. In general, the subanesthetic dose is required for minor procedures. Ketamine is often combined with premedication to reduce the dose requirement and emergence reactions. It can also be used as a supplement during regional anesthesia. The use of ketamine as a general anesthetic is not popular because of its unfavorable psychomimetic effects. However, it remains the mainstay of anesthetic practice in the patients with cardiorespiratory system disorders such as severe

hypovolemia or reactive airway disease.^{1,2}

Ketamine has been used widely for analgesia and anesthesia in many situations, including disaster surgery where appropriate monitoring is not available. There are many features of ketamine that seem to make it an ideal drug for prehospital use.⁷ It inhibits central sensitization, thus potentiating the analgesic effect of epidural morphine. The adding small-dose ketamine to a multimodal patient-controlled epidural analgesia regimen provides better postoperative analgesia and reduces morphine consumption. Furthermore, ketamine has been used as an adjuvant analgesic for the treatment of cancer-related pain. It has also been used in chronic noncancer pain.⁸ The combination use of ketamine, opioid and anti-inflammatory drug is safe and effective in the inpatient palliative care population during episodes of poorly controlled pain.⁹ Interestingly, ketamine is also an effective agent for treating postoperative shivering. Ketamine 0.5-0.75 mg/kg is more rapid than meperidine (25 mg) for the reduction of postoperative shivering.¹⁰

Ketofol is a combination of ketamine and propofol in various concentrations. The combination of propofol and ketamine has several benefits because of hemodynamic stability, lack of respiratory depression, good recovery and potent post-procedural analgesia. This combination can be mixed in the same syringe or administered independently in the two separate syringes. It can be administered as a bolus or as a continuous infusion for longer procedures. The safety and efficacy of ketofol as a sedoanalgesic agent are depended on the dose and the ratio of the mixture. Therefore, ketofol should be an ideal combination drug for

procedural sedation.^{11,12}

Ketodex is a combination of ketamine and dexmedetomidine. It is a sedoanalgesic agent for procedural sedation and analgesia. This combination also has several benefits in terms of hemodynamic stability, absence of respiratory depression, post-operative analgesia and recovery. The most effective regimen seems to be the use of a bolus dose of a 1 mcg/kg of dexmedetomidine and a 1-2 mg/kg of ketamine. This could be followed by 1-2 mcg/kg/h of dexmedetomidine infusion with supplemental bolus doses of 0.5-1 mg/kg of ketamine as needed. Several previous studies have been demonstrated the therapeutic utility of the combination of ketamine and dexmedetomidine.¹³

Dosage and routes of administration

Ketamine could be administered through several different routes such as intravenous, intramuscular, oral, nasal, rectal, transmucosal and epidural routes. The dose depends on the route of administration and the preferred therapeutic effect.¹⁴ The dose for induction of anesthesia is 0.5-2.0 mg/kg intravenous or 5-10 mg/kg intramuscular. In subanesthetic dose, 0.5-1.0 mg/kg intravenous or 0.5-5.0 mg/kg intramuscular is suitable for sedation and analgesia. The maintenance dose of anesthesia is 10-30 mg/kg/min intravenous infusion.

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