

Ketamine

Introduction: Ketamine hydrochloride is a nonbarbiturate anesthetic chemically designated (\pm) -2-(*o*-Chlorophenyl)-2-(methylamino) cyclohexanone hydrochloride.

Mechanism of action: Ketamine has several clinically useful properties, including analgesia and less cardiorespiratory depressant effects than other anaesthetic agents; it also causes some stimulation of the cardiovascular system. Ketamine has been reported to produce general as well as local anaesthesia. It interacts with N-methyl-D-aspartate (NMDA) receptors, opioid receptors, monoaminergic receptors, muscarinic receptors and voltage sensitive Ca ion channels. Unlike other general anaesthetic agents, ketamine does not interact with GABA receptors.

Pharmacology: Ketamine is a rapid-acting general anesthetic producing an anesthetic state characterized by profound analgesia, normal pharyngeal-laryngeal reflexes, normal or slightly enhanced skeletal muscle tone, cardiovascular and respiratory stimulation, and occasionally a transient and minimal respiratory depression. Ketamine is indicated as the sole anesthetic agent for diagnostic and surgical procedures that do not require skeletal muscle relaxation. The anesthetic state produced by Ketamine has been termed "dissociative anesthesia"; in that it appears to selectively interrupt association pathways of the brain before producing somesthetic sensory blockade. It may selectively depress the thalamocortical system before significantly obtunding the more ancient cerebral centers and pathways (reticularactivating and limbic systems).

Indications: Ketamine hydrochloride injection is indicated as the sole anesthetic agent for diagnostic and surgical procedures that do not require skeletal muscle relaxation. Ketamine hydrochloride injection is best suited for short procedures but it can be used, with additional doses, for longer procedures. Ketamine hydrochloride injection is indicated for the induction of anesthesia prior to the administration of other general anesthetic agents.

Dosage: As with other general anesthetic agents, the individual response to ketamine is somewhat varied depending on the dose, route of administration, and age of patient, so that dosage recommendation cannot be absolutely fixed. The drug should be titrated against the patient's requirements.

Induction: Intravenous Route: The initial dose of ketamine administered intravenously may range from 1 mg/kg to 4.5 mg/kg (0.5 to 2 mg/lb). The average amount required to produce five to ten minutes of surgical anesthesia has been 2 mg/kg (1 mg/lb). Alternatively, in adult patients an induction dose of 1 mg to 2 mg/kg intravenous ketamine at a rate of 0.5 mg/kg/min may be used for induction of anesthesia. In addition, diazepam in 2 mg to 5 mg doses, administered in a separate syringe over 60 seconds, may be used. In most cases, 15 mg of intravenous diazepam *or less* will suffice. The incidence of psychological

manifestations during emergence, particularly dream-like observations and emergence delirium, may be reduced by this induction dosage program.

Rate of Administration: It is recommended that ketamine be administered slowly (over a period of 60 seconds). More rapid administration may result in respiratory depression and enhanced pressor response.

Intramuscular Route: The initial dose of ketamine administered intramuscularly may range from 6.5 to 13 mg/kg (3 to 6 mg/lb). A dose of 10 mg/kg (5 mg/lb) will usually produce 12 to 25 minutes of surgical anesthesia.

Maintenance of Anesthesia: The maintenance dose should be adjusted according to the patient's anesthetic needs and whether an additional anesthetic agent is employed.

Increments of one-half to the full induction dose may be repeated as needed for maintenance of anesthesia. However, it should be noted that purposeless and tonic-clonic movements of extremities may occur during the course of anesthesia. These movements do not imply a light plane and are not indicative of the need for additional doses of the anesthetic.

Dilution: To prepare a dilute solution containing 1 mg of ketamine per mL, aseptically transfer 10 mL (50 mg per mL vial) to 500 mL of Dextrose Injection, 5% or Sodium Chloride Injection, 0.9% and mix well. The resultant solution will contain 1 mg of ketamine per mL.

Supplementary Agents: Ketamine is clinically compatible with the commonly used general and local anesthetic agents when an adequate respiratory exchange is maintained.

The regimen of a reduced dose of ketamine supplemented with diazepam can be used to produce balanced anesthesia by combination with other agents such as nitrous oxide and oxygen.

Side effects:

Cardiovascular: Blood pressure and pulse rate are frequently elevated following administration of ketamine alone. However hypotension and bradycardia have been observed. Arrhythmia has also occurred.

Respiration: Although respiration is frequently stimulated, severe depression of respiration or apnea may occur following rapid intravenous administration of high doses of ketamine. Laryngospasms and other forms of airway obstruction have occurred during ketamine anesthesia.

Eye: Diplopia and nystagmus have been noted following ketamine administration. It also may cause a slight elevation in intraocular pressure measurement.

Neurological: In some patients, enhanced skeletal muscle tone may be manifested by tonic and clonic movements sometimes resembling seizures.

Gastrointestinal: Anorexia, nausea and vomiting have been observed; however, this is not usually severe and allows the great majority of patients to take liquids by mouth shortly after regaining consciousness.

General: Anaphylaxis. Local pain and exanthema at the injection site have infrequently been reported. Transient erythema and/or morbilliform rash have also been reported.

Drug Abuse and Dependence: Ketamine has been reported being used as a drug of abuse. Reports suggest that ketamine produces a variety of symptoms including, but not limited to, flashbacks, hallucinations, dysphoria, anxiety, insomnia, or disorientation. Ketamine dependence and tolerance may develop in individuals with a history of drug abuse or dependence. Therefore, ketamine should be prescribed and administered with caution.

PRECAUTIONS:

General: Ketamine should be used by or under the direction of physicians experienced in administering general anesthetics and in maintenance of an airway and in the control of respiration. Because pharyngeal and laryngeal reflexes are usually active, ketamine should not be used alone in surgery or diagnostic procedures of the pharynx, larynx, or bronchial tree. Mechanical stimulation of the pharynx should be avoided, whenever possible, if ketamine is used alone. Muscle relaxants, with proper attention to respiration, may be required in both of these instances. In surgical procedures involving visceral pain pathways, ketamine should be supplemented with an agent which obtunds visceral pain. Use with caution in the chronic alcoholic and the acutely alcohol-intoxicated patient. An increase in cerebrospinal fluid pressure has been reported following administration of ketamine hydrochloride. Use with extreme caution in patients with preanesthetic elevated cerebrospinal fluid pressure.

Usage in Pregnancy: Since the safe use in pregnancy, including obstetrics (either vaginal or abdominal delivery), has not been established, such use is not

Geriatric Use: dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

Contraindications: Ketamine is contraindicated in those in whom a significant elevation of blood pressure would constitute a serious hazard and in those who have shown hypersensitivity to the drug.

How supplied: Customized as per request.