KETAMINE

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Ketamine is frequently described as a "unique drug" because it has hypnotic (sleep producing), analgesic (pain relieving) and amnesic (short term memory loss) effects - no other drug used in clinical practice combines these three important features. It was first used clinically in 1970, and because of these combined effects it was thought that it might be the perfect anaesthetic agent. This is not quite the case, but its continued use in all parts of the world demonstrates that for certain situations, when used appropriately, it is a very valuable drug.

Ketamine is available in three different concentrations - 10mg/ml, 50 mg/ml and 100 mg/ml. The 10 mg/ml is for intravenous use; the 50 mg/ml and 100 mg/ml preparations are for intramuscular use. If only one strength is to be kept in a hospital, the 50 mg/ml ampoule is the best compromise as this may be diluted down to 10 mg/ml for intravenous injections.

Actions of Ketamine on the Body

Central nervous system (CNS).

After an intravenous (iv) injection the effects of ketamine on the CNS begin more slowly than after an iv injection of other anaesthetic induction agents (1-5 minutes for ketamine compared with 30-60 seconds for thiopentone). However, as already stated, it has quite different anaesthetic properties compared with these other drugs. The anaesthetic state produced is frequently called "dissociative anaesthesia" which implies that the patient is detached from their surroundings. Unlike other forms of general anaesthesia (ie. inhalational anaesthesia with ether or nitrous oxide, oxygen and halothane) the patient's eyes often remain open and constantly move from side to side (this is termed nystagmus).

The duration of action depends on the route of administration (see later), and in contrast to the smooth induction of anaesthesia, the patient may be agitated on recovery from ketamine. This is often called "emergence delirium", during which the patient may be disorientated, restless, and crying. Patients may continue to experience unpleasant dreams up to 24 hours after the drug has been given. The use of benzodiazepines (ie. diazepam) as premedication, as well as allowing the patient an undisturbed recovery helps to reduce these unpleasant side effects.

Ketamine causes a rise in intracranial pressure and should not be used in patients who have sustained a recent head injury.

Cardiovascular system (CVS).

Ketamine causes mild stimulation of the CVS. The blood pressure rises by about 25% (on average the systolic pressure rises by 20- 30 mmHg) and the heart rate is increased by about 20% - the overall effect is therefore to increase the workload of the heart.

In the majority of patients the blood pressure rises steadily over 3-5 minutes and then returns to normal 10-20 minutes after injection. There is wide individual variation in cardiovascular responses, and occasionally alarming increases in blood pressure can occur. These increases do not seem to be dose-related when more than 1 mg/kg is given and larger doses do not necessarily cause a greater increase in pressure. There is no evidence to suggest that patients with a high preoperative blood pressure are at greater risk of developing a rise in blood pressure following ketamine administration when compared with normotensive patients.

Premedication with diazepam reduces this rise in blood pressure. If the blood pressure rises excessively after induction, a further small intravenous dose of diazepam (2mg to the average 60-70 kg adult) may help to decrease the pressure. As the cardiovascular stimulation following ketamine is mediated through the sympathetic nervous system it would seem appropriate to give alpha or beta blockers to patients who develop excessively high blood pressures. However, the effects of these drugs are unpredictable, and they are probably best avoided in otherwise normal patients as there is no evidence of damage occurring from these short episodes of elevated blood pressure.

Respiratory system.

If ketamine is administered rapidly by intravenous injection it often causes the patient to stop breathing for a short time (up to one minute). After a slow intravenous induction, breathing is well maintained and may even increase slightly. The airway is usually well maintained during ketamine anaesthesia and

there is some preservation of pharyngeal and laryngeal reflexes in comparison with other intravenous agents. However this cannot be guaranteed, and normal airway care must be maintained to prevent obstruction or aspiration.

Recent research in Kenya using a pulse oximeter has shown that following an intravenous induction with ketamine (2 mg/kg) the oxygen saturation falls in a significant number of people (eight out of twenty three patients studied). Nevertheless, there were no untoward events even though this study took place at an elevation of 5000 feet where an increased incidence of hypoxia would be anticipated. The overall message is to observe the patient closely, and if oxygen is available give some during anaesthesia. A simple ward oxygen mask or nasal cannulae may be used.

Ketamine produces some bronchodilation making it a useful anaesthetic drug for patients with asthma.

Gastrointestinal tract.
Salivation is increased.

Skeletal muscle.
Muscle tone is often increased. Spontaneous movements may occur during anaesthesia but reflex response to surgery is uncommon if the patient is adequately anaesthetised.

Uterus and Placenta.
Ketamine crosses the placenta easily and concentrations in the fetus are approximately the same as those in the mother.

The eyes.
The pressure within the eyeball (intra-ocular pressure) rises for a short time following administration. Eye movements may continue throughout surgery. It is not suitable for use in patients with a perforated eye injury or for ophthalmic surgery where a still eye is required.

Routes of Administration

Ketamine can be given by either the intravenous or intramuscular routes to provide surgical anaesthesia. Excellent analgesia and sedation can be obtained with smaller intravenous doses. (It has also been used orally or rectally as a form of premedication. However, this only produces sedation, not surgical anaesthesia and is unpredictable in its effect).

Indications for Use

Ketamine may be used as the sole anaesthetic agent for a large number of superficial operations and procedures in both adults and children. Common procedures undertaken with ketamine anaesthesia include minor to intermediate orthopaedic surgery (especially distal arm or lower leg surgery including manipulation of fractures), gynaecological surgery (eg. dilatation and curettage and other minor surgical procedures), drainage of abscesses, debridement of burns, change of dressings and minor dental procedures, as well as a variety of examinations under anaesthesia.

Administering a Ketamine Anaesthetic (See Table)

Premedication.
As ketamine increases salivation it is best to give atropine at a dose of 10-20 mcg/kg (to a maximum dose of 600mcg) intramuscularly 30 minutes before the ketamine (or alternatively it can be given intravenously at the time of ketamine administration). Some workers now suggest that atropine is not necessary in adults as salivation is not a major problem. However, it has been this author's practice to administer atropine routinely before ketamine anaesthesia. Diazepam 0.15mg/kg orally in adults, or promethazine 0.5mg/kg orally in children may also be given one hour prior to administration of ketamine. Alternatively, diazepam 0.1mg/kg may be given intravenously on induction. Both these drugs will reduce the amount of ketamine required for superficial surgery.

Intramuscular Ketamine.
The traditional dose quoted to produce surgical anaesthesia is 8- 10 mg/kg. Surgery can start approximately 5 minutes after the injection and anaesthesia will last for 20-30 minutes. If the surgery is to last longer, a further intramuscular dose may be given, as half the original intramuscular dose used to produce anaesthesia. Further intramuscular increments may be given as required if surgery is prolonged. Alternatively, following the initial intramuscular dose a smaller intravenous top up dose may be given to maintain anaesthesia - this is especially useful in children (see case history).

In practice the author has found that for many minor surgical procedures (eg. change of burns dressing, setting of minor fractures) an initial dose of 5-7 mg/kg provides adequate anaesthesia especially when combined with diazepam (for adults) or promethazine (for children) premedication. In these instances, if further doses are required, half the original intramuscular dose should again be used. Care must be taken when ketamine is used in children especially if they are malnourished, and in these instances it is always better to start with a smaller dose (ie. 5-7 mg/kg).

Intravenous Ketamine.

If intravenous access is available this route is often preferred. A dose of 1-2 mg/kg is required for induction of anaesthesia and as noted earlier should be given slowly. Surgery can start about 2 minutes after injection with anaesthesia lasting 10-15 minutes. If the duration of anaesthetia needs to be lengthened further doses of 0.5 mg/kg may be given when the depth of anaesthesia lightens. During longer procedures, the anaesthetist should note the time interval between induction and the first top up. He is then able to slowly inject further increments at the appropriate time to reduce patient movement.

Alternatively, a continuous infusion of ketamine may be administered once anaesthesia has been induced. Ketamine is added to a bag of saline or dextrose to make a dilution of 1mg/ml and the infusion administered at a rate of 1-2mls per minute (that is 1-2 mg of ketamine per minute). This is an average adult dose and the rate of infusion should be adjusted as necessary. Some patients may need as much as 4mg/min - this is judged according to the depth of anaesthesia and the size of the patient, care being taken to avoid an overdose.

The amount of ketamine required is again determined by the nature of the surgery (minor procedures requiring a smaller dose) and whether or not the patient has received a premedication. A smaller dose of intravenous ketamine (ie. 1mg/kg) may be used in conjunction with intravenous diazepam (0.1mg/kg) or, in combination with intravenous thiopentone (1-2mg/kg), and both these drugs will help reduce the hypertensive responses occasionally seen when ketamine alone is administered. Care has to be taken when using combinations of drugs and close monitoring of the respiratory system is required to ensure that respiratory obstruction does not occur.

Ketamine administered intramuscularly or intravenously as described will provide adequate operating conditions for a wide variety of superficial minor or intermediate surgical procedures which do not require muscle relaxation. It is not unusual for patients to move spontaneously during this type of anaesthesia and this may be disconcerting to both surgeon and anaesthetist. However, given ketamine's unique properties, excellent anaesthesia for the patient is provided and these movements should not deter surgery. Experience with the drug will ensure that the surgeon and anaesthetist are able to differentiate between spontaneous ketamine movements occurring during full ketamine anaesthesia and spontaneous movements as a result of "lightening" of anaesthesia.

Intravenous infusions of ketamine may be used in conjunction with muscle relaxants and intermittent positive pressure ventilation to produce good conditions for intra-abdominal surgery. In this instance a non-depolarising muscle relaxant such as tubocurarine or alcuronium is used. It is best to avoid pancuronium as the combination of pancuronium and ketamine has been shown to produce marked increases in blood pressure. The patient should be intubated and ventilated with air or oxygen enriched air.

Although general anaesthesia can be provided for abdominal surgery using the techniques described above it is this author's opinion that the EMO system provides cheaper and easier general anesthesia for this type of surgery.

Finally, a case history is included to demonstrate how ketamine can provide adequate surgical conditions for a complex case in less than ideal circumstances.

Case History

A three month old child weighing approximately 7 kg was admitted to a district hospital for possible removal of a large tumour of the buttock which weighed a further 3 kg. An initial biopsy was performed under intramuscular ketamine, surgery lasting approximately 15 minutes.

Histology reported a benign tumour and the surgeons decided a full excision was required. Two choices of anaesthesia were available, either ketamine anaesthesia or ether via a Schimmelbusch mask - the author opted for the use of ketamine. Following an atropine premedication intramuscular ketamine at a dose of 50 mg (7 mg/kg) was used to obtain anaesthesia

to allow intravenous access to be gained. This proved to be difficult and eventually two further doses of 3 mg/kg intramuscular ketamine were used to maintain anaesthesia). Once intravenous access was obtained the operation for removal of the tumour took two hours. This was performed using intermittent intravenous ketamine with iv top up doses of 3 mg (approximately 0.5 mg/kg), resulting in doses of 15 mg of ketamine being given in both the first and second hour. The tumour was successfully removed with minimal blood loss and although spontaneous movement of the legs occurred throughout surgery, the surgeon stated that the conditions were satisfactory. There were no cardiovascular or respiratory complications and a full recovery was made. This demonstrates the value of ketamine anaesthesia when used in less than ideal circumstances.

Table 1. Simple guide to ketamine anaesthesia

1. Intramuscular Administration

Premedication	Atropine 20 mcg/kg IM 30 mins pre-op
	Diazepam 0.15 mg/kg orally 1 hr pre-op in adults
	Promethazine 0.5 mg/kg orally 1 hr pre-op in children
Induction	5-10 mg/kg
Maintenance	3-5 mg/kg IM or 0.5 mg/kg IV as bolus dose

2. Intravenous Administration

Premedication either as for intramuscular administration or, no premedication and administer atropine 10-20mcg/kg iv prior to ketamine

Induction	1-2 mg/kg
Maintenance	IV boluses 0.5 mg/kg

The addition of IV diazepam (0.1 mg/kg) or IV thiopentone (1-2 mg/kg) on induction allows a reduction in the initial dose of ketamine (to 1 mg/kg). These combinations should only be used if no oral diazepam premedication has been given.

3. Infusion techniques

(See text for full description)