Proper Use of Ketamine and Innovar*

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KETAMINE. Success or failure with the use of ketamine depends largely on three factors:

1. Awareness that ketamine is *different* from traditional anesthetics. These differences include the following:

   Ketamine, unlike traditional anesthetics which cause *total* depression of the central nervous system, affects *selectively* pain conduction and perception systems, stimulating one area of the brain while simultaneously depressing another ("dissociation").

   Ketamine *stimulates the cardiovascular system* while traditional anesthetics depress cardiovascular function.

   Ketamine has *antiarrhythmic* properties while traditional anesthetics do not. They may even precipitate arrhythmias.

   Ketamine maintains or even exaggerates *protective reflexes* while traditional anesthetics suppress them.

   Ketamine *ensures airway patency*, provided no mechanical airway obstruction is present, while traditional anesthetics require additional tools and techniques.

   Ketamine does not produce the traditional "anesthetized" appearance in the patient, but rather a characteristic *"disconnected"* appearance.

2. Knowledge of the criteria used for selection of patients for ketamine anesthesia:

   Use of ketamine predominantly in *infants* and *children* up to 14 years of age.

   The use of ketamine in adult patients is confined to surgical conditions for which ketamine has proven to be particularly advantageous, safe, and superior to conventional anesthetic agents and methods (see under 3).

   Narcotic addicts and patients with a history of chronic alcohol abuse or suffering from acute alcohol intoxication are poor candidates for ketamine anesthesia because in these patients even excessive doses of ketamine may fail to control body movements.

3. Limiting the use of ketamine anesthesia to the following specific *surgical areas and conditions:*

   Surgical treatment of burns*

   Neurodiagnostic procedures such as pneumoencephalography, ventriculography, myelography, and carotid arteriography.

   Out-patient ophthalmology (tonometry, fundoscopy, gonioscopy).

   Out-patient oral surgery (tooth extraction, surgery on the gingiva).

   Out-patient otology (myringotomy, insertion of myringeal tubes, removal of foreign body from ear canal).

   Out-patient plastic surgery (removal of nevi, suturing of laceration, removal of scars).

* Patients of all ages may be included.

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Elective orthopedic surgery (reduction of congenital hip luxation, spicacast application).
Emergency orthopedic surgery (closed reduction of fractures).

Repeated manipulation under anesthesia (irradiation of inoperable intraocular or intracranial lesions).

Induction of anesthesia in high-risk patients, including asthmatics, prior to the use of the principle anesthetic. Ketamine-induced cardiovascular stimulation and its relaxant effect on bronchial musculature offer significant advantages over conventional anesthetic agents.*

Cardiac catheterization.

Open heart surgery, particularly involving patients with minimal or no cardiac reserve. Cardiovascular stimulation and antiarrhythmic affects of ketamine offer prime advantages over traditional anesthetics.*

Emergency surgery in patients suffering from hypovolemia or shock-like conditions. Ketamine may be used for induction or to enhance minimal conventional anesthesia. It offers the advantage of ensuring cardiovascular support until conventional measures to control hypovolemia and shock can be instituted and become effective.*

Contraindications. Ketamine is contraindicated with hypertension, history of cerebrovascular accident, upper respiratory infection, increased cerebrospinal fluid pressure, abdominal surgery, and other surgery involving visceral pain (unless supplemented with conventional anesthetics).

Technique of Administration of Ketamine.

Pre-anesthetic medication: Infants and children receive scopolamine 0.1 to 0.4 mg, depending on age and weight, given intramuscularly ½ to 1 hour prior to surgery to counteract ketamine-induced hypersalivation. Pentobarbital or secobarbital (0.5 to 1 mg per pound) may be given for additional sedation.

Adult patients receive a tranquilizer with antipsychotic properties, preferably droperidol (1 to 2 ml) or Innovar® (1 to 2 ml) combined with 0.4 mg of atropine administered intramuscularly ½ to 1 hour prior to surgery. Other combinations of narcotic analgesics, tranquilizers, and ataractics have proven less effective as compared with the above-mentioned medication.

Omitting narcotics or barbiturates in the pre-anesthetic medication will significantly shorten recovery time. No pre-anesthetic medication is given to patients undergoing ambulatory surgery provided that the surgical procedure is limited to 15 minutes.

Induction: With the intravenous route, the initial dose of ketamine ranges from 1 to 2 mg per kg depending on the physical state of the patient. It is recommended that ketamine be administered slowly, over a period of 30 to 60 seconds. More rapid administration may result in respiratory depression.

With the intramuscular route, the initial dose of ketamine ranges from 6 to 12 mg per kg.

Maintenance: Supplemental increments of ½ to ⅓ of the full induction dose may be administered intravenously every 8 to 10 minutes or intramuscularly every 20 to 30 minutes, or when movements of head or extremities indicate lightening of anesthesia.

Complications. The following complications may be encountered:

Temporary *augmentation of pulse rate and blood pressure* beginning shortly after injection of the drug. This cardiovascular-stimulating effect of ketamine may prove beneficial in certain circumstances, for example, in the presence of hypotension or shock-like states. In hypertensive individuals, however, stimulation may be considered undesirable or unsafe.

Transient *depression of respiration* in response to rapid intravenous injection or in connection with an overdose of ketamine.

Paroxysmal coughing in the presence of upper respiratory infection, occurring immediately following the initial injection of ketamine and recurring with supplemental increments.

Vivid dreaming, with or without *psychomotor activity,* confusion, and irrational behavior occurring during emergence from anesthesia. This complication is more often observed in adults than in children and infants.

Tonic and clonic muscle movements resembling convulsive seizures occurring in certain patients without electroencephalographic evidence of seizure activity.

Erythema or morbilliform rash occurring subsequent to the initial injection of ketamine. The skin eruption is transient and usually confined to face, neck, and upper chest.

Treatment of Complications. Proper pre-anesthetic medication as outlined above may signficantly suppress or even eliminate most adverse reactions. This holds particularly true with regard to post-anesthetic emergence delirium reactions. The incidence and degree of these psychic disturbances can be further minimized by avoiding premature verbal or tactile stimulation of the patient ("sensory deprivation").

Post-anesthetic emergence delirium reactions, should they occur in spite of proper pre-anesthetic medication, may be successfully treated with intravenous droperidol—1 to 2 ml. Also recommended are ultra short-acting barbiturates such as pentothal or surital administered intravenously at doses of 75 to 100 mg.

Tonic and clonic movements during anesthesia may be effectively treated with small intravenous doses (2 to 5 mg) of diazepam (Valium®).

Ketamine does not provide adequate control of pain originating from the viscera. Therefore, the drug is not recommended for use as a sole anesthetic in abdominal or thoracic surgery or where visceral pain is expected to occur. In order to control visceral pain, ketamine may be supplemented with other general anesthetic agents.

In summary, ketamine, a phencyclidine derivative, is a unique and unusually safe, effective anesthetic agent. It is short-acting; it can be given either intravenously or intramuscularly; it is relatively easy to control, requiring little in the way of adjunctive or supportive drugs or devices. It differs markedly from previously established general anesthetics because of its selectivity with respect to the central nervous system. Ketamine is capable of simultaneously depressing cortico-thalamic pathways and activating limbic areas, referred to as "dissociation," and the resulting state is, therefore, termed "dissociative" anesthesia.

Profound analgesia is produced without concomitant respiratory depression and without inhibiting reflexes that protect the air passages. The cardiovascular system is slightly stimulated.

Ketamine has proved to be of unique value in the anesthetic management of patients, particularly infants and children, undergoing a variety of surgical and diagnostic procedures involving the head, neck, and extremities and those necessitating frequent position changes such as are encountered in neurosurgical diagnostic procedures and in the treatment of severely burned patients of any age.

Properly administered and with due regard for its specific advantages as well as its possible disadvantages, ketamine may prove superior to conventional anesthetic agents and methods in a variety of specific surgical procedures.

INNOVAR. Innovar is a mixture of two drugs: *droperidol,* a butyrophenone derivative, with strong tranquilizing, antiemetic, and adrenergic-blocking properties; and *fentanyl,* a powerful narcotic analgesic related to meperidine which differs from conventional narcotics by its high potency and its fast onset and short duration of action. The two drugs are mixed in a ratio of 50 to 1. When administered intravenously in appropriate doses, a state of neurolept*analgesia* is produced in which the patient is rendered immobile and insensitive to pain. His face being expressionless, the patient appears detached from his surroundings, yet he remains alert and cooperative. Respiratory function is depressed and it may be necessary to assist or control the respiration via a face mask or endotracheal tube. If nitrous oxide-oxygen mixtures are added to produce sleep and memory deficit, the state of neurolept*anesthesia* is established.

Innovar or its separate component drugs, droperidol and fentanyl, can and will provide optimal conditions for the patient and surgeon provided that *certain basic principles and rules are observed* along with the use of the drugs which may be listed as follows:

1. Adherence to minute details with regard to the *technique* of administering the neuroleptanalgesic drugs.
2. Employing neuroleptanalgesia and anesthesia preferably in *poor-risk, debilitated, or geriatric patients* undergoing *major, traumatic, and prolonged surgery,* and avoiding their use in pediatric surgery and in short-lasting, uncomplicated, and minor surgery.

Technique of Administration of Innovar or Its Separate Components, Droperidol and Fentanyl, to Produce Neuroleptanalgesia.

Pre-anesthetic medication: Droperidol alone (2.5 to 10 mg, depending on age and physical state) or Innovar (1 to 2 ml) is given intramuscularly 30 to 60 minutes prior to surgery. Atropine or scopolamine (0.4 to 0.6 mg i.m.) may be added to control secretions.

Induction using Innovar: The recommended dose of Innovar is 1.0 ml per 25 pounds of body weight. This may be reduced to 0.5 ml per 25 pounds

of body weight in extremely poor-risk and debilitated patients. Individuals in good physical state may receive 1.5 to 2.0 ml per 25 pounds of body weight. In a patient of average weight the total calculated dose of Innovar ranges from 6 to 8 ml. Debilitated and reduced patients may receive 5, 4, or 3 ml, while patients in a satisfactory physical state may receive 9 or 10 ml. The total dose of Innovar will rarely exceed 10 ml.

A *test dose of 1 to 2 ml* of Innovar injected intravenously over a period of 1 minute is *always* used prior to the administration of the full calculated dose. One to two minutes following the injection of the test dose, the blood pressure is recorded, and if unchanged, the remainder of the dose is administered. A *blood pressure drop* of more than 25 mm Hg in response to the intravenous test dose usually indicates inadequate circulatory volume requiring *rapid intravenous infusion* of 500 to 1,000 mm of fluids before proceeding with further administration of Innovar.

The compounded total dose of Innovar may be administered as follows:

a. *Intravenous drip:* The solution to be infused should contain 10 ml of Innovar added to 250 ml of 5% dextrose in water or saline. This mixture is administered by the microdrip technique at the rate of 150 to 200 drops per minute. When increased somnolence and psychic detachment are noticeable —usually within 3 to 5 minutes after start of the infusion—a local anesthetic (cocaine 5%, lidocaine 4%) is topically applied either by intralaryngeal spray or by injection through the crico-thyroid membrane. When the patient's respiratory rate has slowed to 10 per minute, the intravenous drip is slowed to 100 drops per minute. At this point, psychic indifference is further enhanced, and analgesia has usually reached the optimal level. The intravenous drip is then discontinued and the patient is ready for the surgical procedure while still responding to commands such as "take a deep breath" or "open your mouth."

b. *Intravenous injection:* The calculated dose of Innovar is injected intravenously in increments of 1.0 to 2.0 ml over a period of two to three minutes.

Maintenance: In order to hold the level of surgical analgesia, *fentanyl* in doses of 0.05 to 0.1 mg (1 to 2 ml) is administered intravenously when changes in vital signs such as increased heart rate, elevated blood pressure, increased respiratory rate, or irregular breathing indicate lowering of the pain threshold. It is *not* recommended that *Innovar* be administered for maintenance of surgical analgesia because of possible cumulative effects of the longer-acting droperidol which may result in over-tranquilization postoperatively.

Postoperative period: Usually, analgesia extends well into the postoperative period. Therefore, patients rarely require narcotic analgesics for pain relief. If narcotic analgesics are administered, their dose should be reduced to ¼ or ⅓ of the usually recommended dose.

Induction using droperidol and fentanyl as separate drugs: Induction is started with the intravenous administration of droperidol (0.15 mg per kg). The patient's vital signs are observed for 5 to 6 minutes and if no change is noted, an initial dose of 20 to 60 mcg of fentanyl is administered intravenously followed by 20 to 40 mcg doses of fentanyl, given at about two-minute intervals at which time the patient is considered ready for the operative procedure.

Indications. Neuroleptanalgesia should be limited to patients in whom *retention of consciousness* and *cooperation* during the surgical procedure is desired. Such procedures include: bronchoscopy, laryngoscopy, and esophagoscopy; neurodiagnostic procedures such as pneumoencephalography and carotid arteriography; cardiac catheterization; stereotactic procedures including cryothalamotomy; resection of epileptogenic focus; ophthalmic surgery (in conjunction with regional anesthesia); middle and inner ear surgery (in conjunction with local anesthesia); and oral surgery including tooth extraction and other intraoral surgical procedures involving the gingiva and the tongue.

Contraindications. Neuroleptanalgesia is contraindicated for ambulatory surgery, surgery in infants and children, acute alcohol delirium or history of alcoholism, and narcotic addicts.

Technique of Administration of Innovar or Its Separate Components, Droperidol and Fentanyl, to Produce Neuroleptanesthesia.

Pre-anesthetic medication: This is the same as that described under neuroleptanalgesia as is the composition of the total dose to be administered for producing the neuroleptanesthetic state.

Induction: Innovar may be administered as follows:

a. *Intravenous drip:* Preparation of the solution to be infused and induction are identical with the method described under neurolept*analgesia*. At the time the patient shows signs of somnolence and obtundation in response to the infusion, the intravenous drip is slowed to 100 drops per minute and continued at this rate throughout the anesthesia course. Administration of nitrous oxide-oxygen (4:2) by face mask is begun, and the patient is encouraged to take deep breaths. Within one minute the patient usually lapses into unconsciousness without excitement. An intravenous dose of short-acting muscle relaxant is administered to facilitate endotracheal intubation and to counteract muscle rigidity which may develop during this phase. As a rule, the patient resumes spontaneous breathing within five to eight minutes. D-tubocurarine is administered intravenously at conventional dosages if muscle relaxation is needed for surgery. When changes in vital signs indicate lightening of anesthesia, the drip rate is increased until vital signs return to normal.

b. *Intravenous injection:* Similar to the method of neuroleptanalgesia, a test dose of 1 to 2 ml of Innovar is administered intravenously over a period of 1 minute. Blood pressure is recorded subsequent to this injection and, if found essentially unchanged, further increments of 1 to 2 ml of Innovar are administered intravenously at 1- to 2-minute intervals. By the time the total calculated dose has been administered, the patient shows signs of drowsiness and increasing tranquilization. While the patient still is able to respond to questioning, the breathing mask is applied and nitrous oxide-oxygen, at the flow of 4 liters of nitrous oxide and 2 liters of oxygen per minute, is administered. While spontaneous breathing is increasingly more depressed, positive pressure ventilation via the face mask is begun with the patient responding to the command to take deep breaths. As a rule, after 5 to 8 breaths the patient lapses into unconsciousness without excitement. Immediately prior to the loss of consciousness, an intravenous dose of a short-acting muscle relaxant is administered to facilitate endotracheal intubation and avoid the development of fentanyl-induced muscle rigidity.

Maintenance: For maintenance of the neuroleptanesthetic state, administration of nitrous oxide-oxygen (4:2) is continued. Fentanyl is administered intravenously at doses to 1 to 2 ml (0.05 to 0.1 mg) when changes in vital signs (increased heart rate, elevated blood pressure, increased respiratory rate, or irregular breathing) indicate lowering of the pain threshold. The response to the administration of fentanyl is usually prompt, and signs of inadequate pain threshold elevation disappear within 45 to 60 seconds. If the vital signs continue to indicate insufficient analgesia, another increment of 1 to 2 ml of fentanyl is administered intravenously. In an average patient, administration of supplemental intravenous fentanyl doses is required at 45 to 60 minute intervals. Fentanyl for maintenance of anesthesia may also be given intramuscularly at the same dose as mentioned above. Adequate pain threshold elevation usually is accomplished with this route of administration within 7 to 8 minutes and may last up to 2 hours.

In abdominal surgery or other procedures requiring muscle relaxation, d-tubocurarine may be administered at conventional intravenous doses.

Emergence: Return to consciousness is rapid, as soon as the administration of nitrous oxide-oxygen is discontinued. Within 3 to 5 minutes the patient is usually in contact and can answer questions. If respiratory exchange is inadequate, the endotracheal tube may be left in place in order to mechanically support ventilation until satisfactory respiratory function is reestablished, at which time the endotracheal tube is removed. Levallorphan (Lorfan®) may also be given at intravenous doses of 1 mg to counteract fentanyl-induced respiratory depression. If Lorfan fails to restore adequate respiratory function, other factors causing respiratory depression should be examined.

Complete analgesia usually is maintained for 4 to 6 hours. Nausea and vomiting are rarely encountered.

Indications. Neuroleptanesthesia is indicated for the following: biliary surgery for which halogenated anesthetics may be contraindicated; major, traumatic, prolonged surgery involving poor-risk patients; neurosurgery; cardiovascular surgery including open heart procedures; surgery for organ transplantation, particularly kidney transplants; middle and inner ear surgery; and emergency surgery involving elderly, debilitated, and reduced patients; and patients in shock-like states.

Contraindications. The contraindications for neuroleptanesthesia are the same as those under neuroleptanalgesia. In addition, the use of Innovar may be contraindicated in asthmatic patients since it may precipitate an attack.

Complications. *Hypotension* is most commonly

encountered during induction of neuroleptanesthesia, indicating inadequate circulatory volume and inability of the patient to compensate for peripheral vasodilatation caused by droperidol-induced alpha-adrenergic blockade. Treatment should consist of rapid infusion of 500 to 1,000 ml of lactated Ringer's solution or 5% dextrose in water solution in preference of the use of vasopressors.

Excessive blood pressure elevation, the etiology of which is undetermined, has occurred in rare instances. Intermittent administration of halothane at conventional concentrations or small intravenous doses of chlorpromazine (7.5 to 15 mg i.v.) have proved to be effective in restoring acceptable blood pressure levels.

Droperidol may induce *extrapyramidal muscle activity* which may be controlled with anti-Parkinson agents such as Cogentin®.

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