Ketamine (CI-581): The new parentral general anaesthetic—The answer for one anaesthetie problem

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Introduction

KETAMINE HYDROCHLORIDE (trade name "Ketalar", Research Drug No. CI–581) is a non-barbiturate, short-acting, parenterally administered phencyclidine derivative. Its chemical structure is 2–(0–chlorophenyl)–2(methylamino)–Cyclohexanone-Hydrochloride (See fig. 1)..

Ketamine is the latest parenteral general anaesthetic. It is a cataleptic and anaesthetic agent with low toxicity and powerful analgesic activity of rapid onset and relatively short duration. When given intravenously or intramuscularly, it rapidly produces unconsciousness, a quiet patient and a degree of analgesia which permits surgical intervention.

The anaesthetic state as observed clinically is characterised by profound analgesia combined with a peculiar state of unconsciousness. The entrance into this state of disconnection from the surrounding (dissociation anaesthesia) is heralded by marked horizontal and vertical nystagmus which occurs while the patient's eyes abruptly open. Shortly thereafter the eyes become centred and appear in a fixed gaze. The pupils are moderately dilated and promptly react to light. Tearing is common, as is salivation, if not counteracted by antisialogogue drugs.

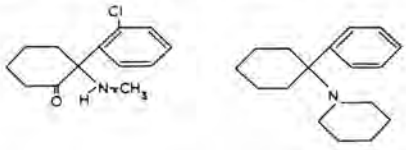

Fig. 1. The Chemical Structure of Ketamine compared to that of its parent drug (Phencyclidine).

The cardiovascular system is stimulated, resulting in a moderate to marked rise in heart rate and an increase in both systolic and diastolic blood pressure for several minutes. The pulse rate and blood pressure then gradually return to preinjection levels. Ketamine is said to have an anti-arrhythmic property (Corssen, Miyasaka, Domino, 1968).

Respiratory function is usually unimpaired; following rapid intravenous injection, it may be depressed briefly with return to normal respiratory exchange within 15 – 30 secs. One of the most striking and useful features of Ketamine induced anaesthesia appears to be the maintenance of an adequate airway regardless of the extremes of position. Since intra-oral musculature, especially the tongue, fails to relax, mechanical obstruction is virtually absent and there is no need for an oropharyngeal or endotracheal tube for artificially supporting the airway. The increase in muscle tone allows the patient to hold up his own jaw throughout the anaesthesia. In addition, the preservation of the protective laryngeal and pharyngeal reflexes throughout anaesthesia makes it unlikely for aspiration to occur. Evidence for this is found from the fact that of the eight cases out of a series of 116 cases in which vomiting did occur, during the procedure or post-anaesthetic recovery, the patients had no difficulty in clearing the airway (Corssen, Groves, Gomez and Allen, 1969).

Arterial blood gas studies by various groups of workers (Domino, Chodoff, Corrsen, 1965; Virtue, Alanis, Mashiro, Lafargue, Vogel and Metcalf 1967; King and Stephen, 1967; Vayden, Hunt, Willis and Stephen 1968) before, during, and after ketamine-induced anaesthesia have revealed no significant deviation from accepted physiological values.

Fig. 2. Data on Emergency Anaesthesia for Incision and Drainage of 4 cases of Submandibular Abscesses with Floor of Mouth Swelling ++ and Trismus

Case	Age (Yrs) & Sex	Wt. (Kgm)	Premed.	Duration (mins) — injection to dressings	Systolic B.P. (mm.Hg)	Recovery (min) Identity and place,	Dreams
1.	6, Male	22.5	I/V Atropine 0.6 mgm.	14 mins	↑ (44 mm. maxm. — back to normal in 10 mins. after injection).	40 mins	?
2.	9, Male	28.0	I/V Atropine 0.6 mgm.	17 mins	↑ (40 mm. maxm. — back to normal in 12 mins. after injection).	50 mins	+ (Pleasant)
3.	17, Male	36.0	I/V Atropine 0.6 mgm.	8 mins	↑ (60 mm. maxm. — back to normal in 8 mins. after injection)	40 mins	—
4.	30, Female	40.0	I/V Atropine 0.6 mgm.	11 mins	↑ (70 mm. maxm. — back to normal in 8 mins. after injection)	40 mins	+ (Pleasant)

I/V Ketamine (CI-581) Used for General Anaesthesia.
Dosage: 1.5 mgm/kgm (to next higher 10 mgm) initial dose.
Booster doses: (cases 1 and 2) ½ initial dose.

Fig. 2a. This is a case of submandibular abscess with Trismus and swelling of the floor of the mouth.

CI-581 appears to be metabolised very rapidly in the body (Chen, Glazko and Kaump, 1965; work done on laboratory animals) with the appearance of several metabolic products in the urine. Very little unchanged drug was excreted, even in animals receiving massive doses of the drug by intravenous infusion over a period of hours. Two metabolic products have been isolated from monkey urine and identified chemically as the free amine produced by demethylation (metabolite I) and the cyclohexene derivative produced by oxidation of the amine (metabolite II).

The most commonly cited undesirable side-effects are elevation of blood pressure, vivid dreams during emergence from anaesthesia, purposeless muscular movements and possibly respiratory depression with usage of too high a dose.

Material, Methods and Results

Taking into account the advantageous features of ketamine, four cases of submandibular abscesses with marked floor of mouth swelling and trismus were given intravenous ketamine as general anaesthesia for emergency incision and drainage in the University Hospital, Petaling Jaya.

Material

There was no selection of patients. All four cases presented as emergencies when the author was on duty during the period July – December, 1969. Their ages, sex and weights are given in Fig. 2.

Method

All four cases were treated as emergencies, irrespective of the interval between the last drink or meal and the induction of anaesthesia; the intervals were 2½ hours, 3 hours, 5 hours and 4 hours respectively for cases 1 to 4. Premedication was the same in all cases – 0.6 mgm I/V Atropine just before induction, leaving the needle in-dwelling in the vein. No respiratory depressive narcotic-analgesics were used in premedication. The patients were anaesthetised on the operating table with the surgeon scrubbed up and in all readiness so as not to waste anaesthetic time. Intravenous 1% ketamine was administered for all cases as the sole anaesthetic with the patient breathing air in a dosage of 1.5 mgm/kgm body weight (to the nearest next highest 10 mgm). Booster doses (½ the initial dose) were given if indicated. The indication being facial grimacing or movement in response to surgical stimulus, anticipating the procedure to carry on for approximately a further 10 minutes.

The duration of the procedure was timed from injection of ketamine to the final dressings applied to the site of surgery.

The systolic blood pressure was noted at two minute intervals following injection of ketamine using a sphygmomanometer cuff using the palpation method.

Recovery time was measured from time of last injection of ketamine to time of orientation of the patient (in the recovery room) as to identity and place. The incidence of dreams (description and whether pleasant or frightening) was assessed by direct questioning, after the patient was assessed to be orientated.

Results

The results from the four cases are summarized in Fig. 2. Cases 1 and 2 required a second (booster) injection. The indication was movement and facial grimacing in response to surgical stimulus. This indication came on within one to two minutes following the return of the systolic blood pressure to pre-injection levels. Thus the return to pre-injection systolic blood pressure level can serve as a warning that the indication for a booster dose will follow within one to two minutes. In all four cases, the systolic blood pressure showed a rise within two minutes of the I/V injection. The maximum rise in systolic blood pressure was 44, 40, 60 and 70 mm.Hg. in cases 1 to 4, respectively (see Fig. 2). There was no incidence of vomiting, nausea or abnormal muscular movement in the four cases.

Discussion

(See Fig. 2A) Abscesses of the floor of the mouth with the possibility of associated oedema glottidis

pose a problem regarding anaesthesia for the required surgical incision and drainage. Maintenance of the airway during the procedure in such cases is the major problem.

In the presence of oropharyngeal oedema, a general anaesthetic is contraindicated under any circumstances unless the airway can be guaranteed. Prior to the advent of ketamine, the airway could never be guaranteed unless either preliminary laryngotomy or tracheostomy had been performed or an endotracheal tube had been passed under topical analgesia. Naturally the latter method was previously preferable and in most instances, it was performed with little or no discomfort to the patient. Once the tube was in situ, any form of anaesthesia could be used without danger of oedema of the glottis causing obstruction and death. (V. Goldman, 1965).

Trismus is often an added problem in anaesthesia for cases of abscesses around the floor of the mouth and the application of the topical analgesic can thus meet with difficulty. As previously advocated, intubation was a must for ensuring the airway maintenance during general anaesthesia. The problems associated with intubation in such cases are, first, mechanical difficulties because of trismus, floor of mouth swelling and oedema glottidis; on extubation, the oedema might be made worse with consequent airway problems.

When general anaesthesia is required, an inhalational method with spontaneous respiration was advocated as the safest choice but Thiopentone was not recommended as an induction agent. Thiopentone alone is never justified since it increases reflex activity in the glottis area (Wylie and Churchill-Davidson, 1966). If a laryngeal spasm should thus occur, one can imagine the problems that can arise. The problem with inhalational anaesthesia (cyclopropane and oxygen is a good choice) in the presence of floor of mouth swelling is the technical difficulty of holding up the jaw with a mask over the mouth and nose, to ensure an unobstructed upper respiratory passage.

A simple abscess or Ludwig-type angina of the neck can be safely incised under inhalational anaesthesia without a tube provided there is no preoperative upper respiratory obstruction present, the surgeon is speedy and unconsciousness is fleeting (Wylie and Churchill-Davidson, 1966). This is obviously not without risk.

CI-581 or Ketamine, the new intravenous general anaesthetic, seems to be one way out of the problems associated with anaesthetic techniques previously advocated for floor of the mouth abscesses requiring incision and drainage. It is indeed an addition to the anaesthetists repertoire and armamentarium. This new intravenously or intramuscularly administered anaesthetic has distinct advantages, e.g. adequate, unobstructed airway can be maintained during ketamine-induced anaesthesia without the need of an oropharyngeal or endotracheal tube or manual jaw-support; also the protective reflexes, such as cough, gag and swallowing, are maintained throughout anaesthesia. It has been found to be useful in eye surgery (Falls, Hay, Corssen, 1966) oral surgery (Corssen, Hayward, Gunter, Groves, 1969), severely burnt patients (Bjarnesen, Corssen, 1967), neuroradiological diagnostic procedures in children (Corssen, Groves, Gomez, Allen, 1969). The advantages, disadvantages and contraindication of ketamine have been set out in Fig. 3.

As with most intravenous anaesthetics, there is always one added danger. Those not trained in the care or resuscitation of an anaesthetised or unconscious patient might be tempted to administer the drug, thinking that the ability to perform a venepuncture is the only requisite. As with the administration of all general anaesthetics, cardio-respiratory equipment and drugs must be at hand and the administrator of the anaesthetic drug must be trained in the use of such equipment for cardio-respiratory resuscitation. It should thus be clear that only the anaesthetist should use this drug.

Summary

A description of the pharmacology and clinical effects of the new parenteral, non-barbiturate, general anaesthetic, ketamine (CI-581) is outlined. Its clinical use in the anaesthetic management of four cases of submandibular abscesses with trismus and floor of mouth swelling is described. Discussion of such cases as an anaesthetic problem follows. Ketamine is advocated as the answer to this problem. The advantages, disadvantages and contraindications of ketamine are tabulated.

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Figure 3.

Advantages, Disadvantages and Contraindications of Ketamine (Vayden, Hunt, Willis, Stephen, 1968)

Advantages	Disadvantages	Contraindications
1. Profound analgesia without significant impairment of respiratory function.	1. Vasopressor activity resulting in rise in blood pressure.	1. Hypertension I 160 mm.Hg)
2. Stimulation of cardiovascular system thereby avoiding hypotension, instead, producing a rise in blood pressure.	2. Salivation in absence of antisialogogues.	2. History of cerebro-vascular accident.
3. Preservation of protective reflexes.	3. Occasional extra-pyramidal activity.	3. Marked cardiac decompensation.
4. Maintenance of unobstructed airway regardless of extremes of position.	4. Dreams (usually pleasant sometimes frightening).	4. Abdominal surgery and other procedures involving visceral pain.
5. Absence of organ toxicity despite multiple administration.		5. Patients with a known history of psychiatric problems.
6. Excellent tissue compatibility.		
7. Virtual absence of post-anaesthetic nausea and vomiting.		
8. Wide margin of safety (ratio of toxic to anaesthetic dose 16 : 1)'		
9. Ease of administration: I/V or I/M.		
10. Anti-arrhythmic property.		
11. Amnesia.		

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