CLINICAL USE OF KETAMINE (CI-581)

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INTRODUCTION

Ketamine Hydrochloride is a derivative of phencyclidine nucleus. It is chemically known as 2-(o-chlorophenyl)-2-(methyl amino cyclohexanone) hydrochloride. Domino, E. F. and Corssen, G. were the first to use the drug as an anaesthetic agent in Ann Arbour, Michigan, experimentally on animals and clinically on human volunteers (prisoners) and patients. The drug when injected intravenously acts within thirty seconds and it causes a state of "dissociative anaesthesia". The patient looks as if he is in a state of "pharmacological sensory isolation".

Ketamine acts on the Central Nervous System affecting the thalamo-neocortical system more selectively than the conventional anaesthetic agents. The Reticular Activating System and the Limbic System are less affected by Ketamine than by the Thiobarbiturates or ether. It abolishes the normal alpha waves and induces the theta waves, during the anaesthetic state. Dr. G. Corssen says that "the anaesthetic state produced by Ketamine is characterised by profound analgesia combined with a peculiar state of unconsciousness". The patient is disconnected rather than asleep. When entering anaesthesia, the eye lids open, nystagmus is prominent and after a few seconds the eyeballs become centered and appear in a fixed gaze. The airway is unobstructed. Respiration is not depressed. Cardiovascular system seems to be stimulated. There is complete amnesia for the surgical intervention. It apparently does not exert any toxic effects on the vital organs. Local tissue compatability of the intravenously or intramuscularly administered drug is excellent.

The biological half life is two hours. Small amounts are excreted unchanged in the urine. Major metabolites are:—

(*a*) N-dealkylated amine.

(*b*) 3 oxidation products involving the cyclohexanone ring and the introduction of a double bond in the ring.

OBJECT OF OUR PRESENT STUDY

The object of our study is to evaluate the usefulness of this drug and to compare its complications on our Malaysian patients with that of American patients quoted by the American writers.

MATERIAL, METHOD AND RESULTS

Material

One hundred and seventy-four unselected patients were anaesthetised with Ketamine between November 1969 and August 1970. There were 126 males and 48 females. Their age distribution can be seen in Table I. The youngest patient was eight months old, the oldest being 46. The average weight was 44 lbs. (range from 10 lbs. to 148 lbs.). Table II shows the types of cases on which Ketamine was used. The total dose depends on the weight of the patient and the duration of the operative procedure. As little as 10 mgm. was used on a wound inspection lasting 10 minutes in a child eight months old whose weight was only 15 lbs. The highest dose used was on a male Chinese boy aged 12 years weighing 44 lbs. He had a plastic operation of his face which was grossly deformed and a deformed hand which he sustained after an acid burn. The duration of the operation was two and a half hours. 100 mgm. of Ketamine were used on this child.

TABLE I

Age in Years	No. of Cases
Below 1	7
1 - 2	19
3 - 5	59
6 - 10	60
11 - 20	19
21 - 30	3
31 - 40	3
Above 40	1
TOTAL	174

TABLE II

Nature of Operations	No. of Cases
Orthopaedic	56
Neurosurgical diagnostic	43
Ear, nose and throat	15
Genito-urinary	18
Plastic-reconstructive	7
General surgical	35
TOTAL	174

No premedication was given to 134 cases; 19 had only Injection Atropine and the rest (21) had Injection Atropine and a Narcotic (usually Injection Pethidine Hydrochloride).

Method

The recommended dose of the American authors is 1-2 mgm./kilo body weight or 1 mgm./1 lb. body weight. We use 0·25 mgm. to 0·5 mgm./lb. body weight as our initial dose. This is given intravenously over a period of twenty to thirty seconds. The patient was judged ready for operation when the eyelids were opened and the pupils were in the central position. In infants and small children, scalp vein needles of 23 to 21 gauges were used. The duration of analgesia and anaesthesia lasted from eight to ten minutes. If the operation was not completed by that time and the patient started to move, supplementary dose of one-fifth to one quarter of the initial dose was given. Most of our cases had the drugs intravenously but should the needle come out accidently, then twice the calculated dose was given intramuscularly.

The systolic blood pressure was taken preoperatively, at regular intervals during the operation and also during the post-operative period.

Similarly the pulse rate was monitored constantly.

In the first twenty cases, the respiration was monitored for its adequacy by means of a face mask with an attached Wright's Respirometer. The minute volume was found to be adequate. Subsequently only the chest movement and the colour of the patients' mucosa or the blood, if there was an open wound, were watched.

In adult patients or children who had reached the age of reasoning, auto-suggestion of pleasant dreams were made while the injection was given.

The patients were allowed to wake on their own without tactile or unnecessary audible stimuli.

The recovery time is the interval between the last dose of Ketamine given and the full return to consciousness.

Results

Table III shows the recovery time.

TABLE III

RECOVERY TIME

Minutes	No. of Cases
Below 10	50
10 - 20	117
21 - 30	7
Above 30	0
TOTAL	174

Table IV shows the incidence of complications. Here our figures are compared with that of Corssen and his colleagues.

DISCUSSION

It can be seen from the rather small dose we used (0·25 mgm. to 0·5 mgm./lb. body weight for the initial dose) that the recovery time of our patients was shorter than that of Corssen *et alia*.

TABLE IV

COMPLICATIONS—TYPES AND NO. OF CASES

Types	Law and Gunn (174)		Corssen *et alia* (1508)	
	No.	Percent	No.	Percent
Rise in B.P. above 10 mm. HG. systolic	11	6·32%	128 (above 25% of resting B.P.)	8·1%
Tachycardia	1	0·57%	66	4·3%
Apnoea	—	—	93	6·2%
Increased salivation	2	1·14%	—	—
Purposeless movement of the limbs	7	4·02%	22	1·5%
Dreams:				
Good	18	10·34%	—	—
Bad	1	0·57%	—	—
Prolonged sleep	1	0·57%	6	0·4%
Vomiting	2	1·14%	28	1·8%

In point of fact all our cases recovered within thirty minutes from the last dose (Table III). In the series of Corssen *et alia* 537 out of 1291 patients recovered within thirty minutes. The rest took a longer time to recover. Some even more than two hours. This is a great disadvantage as the patients could not be treated as out-patients.

In the first few cases when we used the dose of 1 mgm./lb. body weight as recommended by the Americans, we recorded rise in systolic blood pressure of up to 40 mgm. Hg. Subsequently we amended the initial dose. Since then the rise in systolic blood pressure was only in the region of 10 mm. Hg. Podlesch and Zindler have recorded very high rise in the blood pressure. Only 11 cases (6·32%) in our series had rise in systolic blood pressure of between 10 mm. Hg. to 40 mm. Hg. This is more satisfactory than the 8·1% of Corssen's figures.

The Upper Respiratory Airway was always well maintained throughout the whole operation in whatever posture the patient was placed. This is a great advantage in Neurosurgical Diagnostic Procedures (e.g. air-encephalographic studies) where the patient is put in the sitting position, the head is tilted from side to side to get the air into the ventricles, and in the prone position. Since we started using Ketamine, we have never recorded any fall in blood pressure. Apart from this complication there was a tendency for the endotracheal tubes to get kinked or to slip out when conventional anaesthesia was used. Now all neurodiagnostic procedures in children are done under Ketamine anaesthesia.

Although the literature warns that Ketamine should not be given to patients who just had food or drinks, we have used it on patients who had ingested food recently. There were only two cases of post-operative vomiting in children who were prepared for their operations. They had been starved for the appropriate period of time. The vomiting was probably due to the narcotic given in the pre-operative period.

The majority of our cases were confined to the younger age group (Table I). This was partly due to the fact that in the beginning we had a limited supply of Ketamine (we used the experimental drug Cl-581) and partly due to the fact that Ketamine being a derivative of Phencyclidine we were afraid that if we had used it extensively in the elderly the incidence of bad dreams, hallucinations, etc., might be higher. This is discussed later on.

We have not encountered any case of apnoea. Although the apnoeic period is transient, one should know how to treat it. Overdose and fast administration are the causes of apnoea.

Corssen *et alia* have reported incidence of persistent rise in blood pressure in the post-operative period. Respiratory inadequacy, rash, increased muscular tone have also been noted. We have only seen two cases of purposeless movements in our series.

Ketamine has very good tissue compatability as there was not a single case of erythema nor pain at the site of injection even when accidental extravenous injection was made.

We have used this drug in children who had upper or lower respiratory tract infection. We would have been very hesitant to give conventional anaesthesia to these children.

Ketamine has been used by others in obstetrical and gynaecological cases (Chodoff, P. and Stella, J. G.); in ophthalmology (Falls, H. F., Hoy, J. E. and Corssen, G.). It is particularly useful in the changing of dressings in burnt patients (Bjarnesen, W. and Corssen, G.). We have used the drug in a few cases of wound debridement. In view of the fact that these patients release a lot of potassium into their blood stream if succinyl scoline is used and this may lead to cardiac arrthymias or even ventricular fibrillation and arrest, Ketamine would seem to be the drug of choice.

From the patients' point of view, none have so far objected to the use or re-use of this drug. Most of the Surgeons have expressed that operating conditions were very good or excellent.

Emergence syndrome was encountered on one occasion only. This happened to a male adult patient who dreamt that "he went to hell". Others report that the patients go through a phase of vivid dreaming with or without psychomotor activity, manifested by confusion and irrational behaviour. These reactions appear similar to those observed with other general anaesthesia. The incidence is reduced if verbal or tactile stimulation of the patient is avoided during the recovery period. It has been suggested that the giving of barbiturates concurrently may reduce its incidence.

We have used this drug in inducing patients considered poor risk because of poor cardiovascular status.

Ketamine should not be used indiscriminately. There are certain contra indications against its use and there are definite precautions to be taken when the drug is being used. Patients with high blood pressure (systolic above 160 mm. Hg. and diastolic above 110 mm. Hg.); with a past history of cardiovascular accident; or are in congestive cardiac failure the use of Ketamine is to be avoided.

Because overdosage can cause apnoea and severe hypertension, only doctors trained in cardio-pulmonary resuscitation are allowed to use Ketamine. There must also be facilities available for the treatment of these two hazardous complications.

Ketamine is not the answer of the "ideal anaesthetic" agent but it is useful to have it in our armamentarium of anaesthetic drugs.

SUMMARY

We have used Ketamine on 174 patients. It gives very good analgesia, satisfactory amnesia and anaesthesia. We have found it to be extremely useful in neurosurgical diagnostic procedures, certain short orthopaedic and general surgical and genito-urinary cases. The complications in our series are less than those quoted by Corssen *et alia*.

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