

## Ketamine anaesthesia for burns surgery

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### Summary

A study was set up to investigate whether the theoretical advantages ketamine offered as an anaesthetic in burns patients were real.

Patients under 35 kg body weight were anaesthetized by an intermittent intramuscular technique and patients over this weight with an intravenous technique.

The study showed that ketamine had distinct advantages, giving cardiovascular stability and avoiding intubation. It was especially useful in the very ill patients. There were few complications during the study which we are now trying to minimize.

### Introduction

Anaesthesia for burns surgery poses problems which are rarely encountered in other surgical procedures. The patient is, in effect, suffering from a chronic wound in a vital organ, the skin. This lesion is slow to heal, often infected and one in which red blood cells are constantly being destroyed, causing anaemia. Therefore, patients may come to surgery in a debilitated state.

The position of the patient may have to be changed several times during a skin grafting operation in order:

- (1) to prepare the burn for grafting;
- (2) to take a split skin graft;
- (3) to apply the graft, and finally
- (4) to apply the dressing to keep the grafted skin in place.

These changes in position may cause cardiovascular collapse.

It is rare for large arteries to be involved in a burn and the bleeding from this source is, of course, easily controlled. However, the ooze following curettage of a granulating burn, or following the taking of a graft from a recently healed donor site, can result in massive blood loss over a short period.

The face and neck are usually unclothed and are therefore often burnt. In order to allow surgery to these areas the patient must be intubated. Intubation is also necessary to maintain control of the airway as the patient is moved on the operating table.

Endotracheal intubation is not a simple procedure in burned patients. They are susceptible to post-intubation laryngeal oedema (Prendiville & Middleton, 1954), suxamethonium is contra-indicated in burned patients (Bush *et al.*, 1962) and introduction of the laryngoscope may cause bleeding from burned lips.

No change in anaesthetic technique should be made for its own sake, but ketamine appeared to have certain advantages as an anaesthetic agent for burns surgery. We therefore decided to set up a study to ascertain whether these apparent advantages were borne out in practice.

Ketamine is a rapid acting non-barbiturate drug for intravenous or intramuscular administration. It is a derivative of phencyclidine (C1-581) with a formula of a 2 chlorophenyl 2-methylamino cyclohexanone hydrochloride (Chen, Ensor & Bohner, 1968). 1; 10,000 benzethinium chloride is added as a preservative and the solution is made isotonic with sodium chloride.

Ketamine produces profound analgesia and a somnolent state of dissociation in which the patient is disconnected from his surroundings. It appears to depress the activity of the neocortex, that is the association area in the frontal cortex and the sub-cortical sensory areas.

Ketamine usually induces a 20% rise in blood pressure and pulse rate immediately after injection and this effect may persist throughout the period of anaesthesia. It does not depress the respiratory centre unless a gross overdose is used or the induction dose is administered very rapidly.

Muscle tone is maintained or increased during ketamine anaesthesia. The airway is therefore maintained regardless of the positioning of the patient on the operating table. As ketamine may act as a sialogogue it is necessary to include an anticholinergic drug in the premedication.

Ketamine appeared to offer advantages as an anaesthetic agent for burns surgery. Intubation is unnecessary and the surgeon has unhindered access to the head and neck. Ketamine does not depress the activity of the cardiovascular system. In fact, its mild

stimulant action may protect the patient from the hypotension which may ensue when altering the position of the patient during an operation.

There is no postanaesthetic anorexia when ketamine is employed and the patient's feeding on the day of operation is minimally disturbed. Adequate nutrition is essential for healing of burns to take place (Sutherland, 1955).

### Method

The patients had been resuscitated and the haemoglobin level had been checked before anaesthesia. Patients under 35 kg body weight were premedicated with trimeprazine 2 mg/kg and 0.6 mg atropine orally and were anaesthetized by intermittent intramuscular injections of ketamine.

Patients over 35 kg body weight were premedicated with a narcotic (usually pethidine) and atropine. Between the ages of 16 years and 65 years promethazine 25 mg was given in addition.

All patients were starved for 6 hr prior to operation. It was not always possible to weigh the patients. In many cases the weight was estimated and in these days of figure consciousness many patients knew their weight prior to admission.

Children were originally induced with an intramuscular injection of 10 mg/kg body weight, but it was later found that an initial dose of 4 mg/kg was sufficient. This dose produced sufficient anaesthesia for preparation of the patient and the setting up of a blood transfusion. After the patient had been prepared a supplementary injection of 2 mg/kg was usually necessary before surgery commenced and the effect lasted 15–20 min. If the operation had not finished further supplements of 2 mg/kg were given.

Patients over 35 kg were originally anaesthetized by intermittent intravenous injections using 2 mg/kg body weight as an induction dose supplemented by doses of 1 mg/kg as required. Later these patients were anaesthetized by using an intravenous infusion of 0.1% solution of ketamine (500 mg in 500 ml of 5% dextrose). A cannula was inserted in a superficial vein using 1% lignocaine as a local anaesthetic. Anaesthesia was induced by running the infusion until 2 mg/kg body weight had been administered over a period of 30–60 sec. The rate of the infusion was then regulated according to the reaction of the patient. With experience it was possible to regulate the administration of ketamine both intravenously and intramuscularly so that the patient started to emerge within 5 min of the cessation of the operation.

The pulse rate, blood pressure and respiration were monitored before anaesthesia was induced and during the operation. Postoperative analgesia was rarely necessary but where required was achieved with papaveretum according to body weight.

### Results

There were sixty-two patients in the study and a total of 102 administrations of ketamine.

Twenty-five patients in the study weighed 35 kg or less and were anaesthetized by intermittent intramuscular injections. There was a total of forty-two administrations by this method. The youngest patient was aged 11 months and the oldest 10 years. The average age was 3 years 6 months.

Only five of these patients were given an initial dose of 10 mg/kg body weight and the doses are summarized in Table 1. All the operations were complete in under 45 min.

TABLE 1. Amount of ketamine given using induction dose of 10 mg/kg body weight intramuscularly

Times used	Minimum		Maximum		Average (mg/kg/hr)
	(mg/kg/hr)	(mg/kg)	(mg/kg/hr)	(mg/kg)	
5	21	12	39.5	15	31.5

Twenty patients were given an initial dose intramuscularly of 4 mg/kg body weight. Twelve of these patients had one ketamine anaesthetic and eight had multiple administrations, the maximum in one patient being eight ketamine anaesthetics. The doses are summarized in Table 2.

TABLE 2. Amount of ketamine given using induction dose of 4 mg/kg body weight intramuscularly

Times used	Minimum		Maximum		Average (mg/kg/hr)
	(mg/kg/hr)	(mg/kg)	(mg/kg/hr)	(mg/kg)	
37	4	4	21.6	12	11.3

There was a marked individual response to the drug but consistent response was observed in patients who had multiple ketamine anaesthetics. Less ketamine was required expressed as mg/kg hour of anaesthesia for longer operations than for shorter procedures. For operations complete in under 44 min the average dose was 13.6 mg/kg/hr. In operations lasting more than 45 min the average dose was 9.3 mg/kg/hr.

### Intermittent intravenous administration

Eight patients early in the series were given ketamine by the intermittent intravenous route. The results are summarized in Table 3. Again there was a marked difference in individual responses to the drug.

### Intravenous infusion

Skin grafting operations may be prolonged and as we were monitoring the pulse rate, blood pressure and respiration rate, frequently it was found more

TABLE 3. Amount of ketamine given using intermittent intravenous injections

Times used	Minimum		Maximum		Average (mg/kg/hr)
	(mg/kg/hr)	(mg/kg)	(mg/kg/hr)	(mg/kg)	
8	2.6	2	9.5	14	7.3

convenient to employ an intravenous infusion of 0.1% ketamine in 5% dextrose.

Twenty-three patients were anaesthetized by this method, including five patients who had had the drug by the intermittent intravenous route. There was a total of fifty-two administrations by this method, summarized in Table 4. These patients showed a marked difference in individual response to the drug. Less ketamine was required for longer operations. For operations complete in under 44 min the average dose was 12.4 mg/kg/hr and for those which lasted 45 min or more the average dose was 6.4 mg/kg/hr.

TABLE 4. Amount of ketamine given using an intravenous infusion

Times used	Minimum		Maximum		Average (mg/kg/hr)
	(mg/kg/hr)	(mg/kg)	(mg/kg/hr)	(mg/kg)	
52	19	2.1	15	14.3	7.7

### Complications

There were few complications due to ketamine during the study. Dreams or emergence phenomena were experienced by five patients. Details are summarized in Table 5.

TABLE 5. Summary of emergence phenomena

Age	Sex	Description
47	♂	Confused Distortion of vision Refused repeat ketamine
49	♀	Disorientated in time and space Refused repeat ketamine
57	♀	Space fantasy Science fiction fan Not unpleasant
47	♀	Confused
45	♀	Confused

It is perhaps significant that all these patients were in the fourth or fifth decades of life. Emergence phenomena are plotted against the ages of the patients in the study as a whole in the histogram (Fig. 1).

Hypotension occurred in two patients. In one case, the hypotension was due to inadequate replacement of blood loss, and this would suggest that ket-

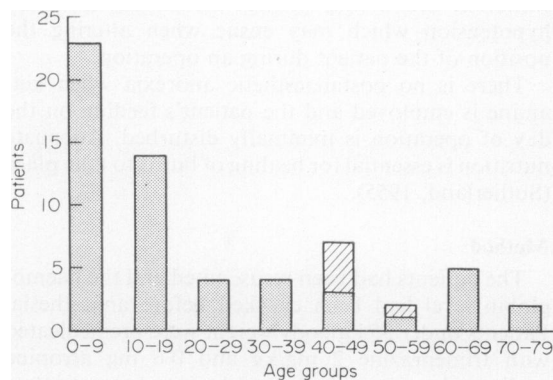


FIG. 1. Histogram showing age of patients in the study and age of those who experienced emergence phenomena (diagonal hatching).

amine's cardiovascular stimulant action does not support the circulation when excessive blood loss occurs.

The other patient in whom hypotension occurred was a very sick child. In her case there was no response to blood replacement and she recovered when given 100 mg hydrocortisone sodium succinate intravenously.

Hypotensive episodes complicated subsequent ketamine anaesthetics in this child. On each occasion she recovered when given cortisone, in spite of having a plasma cortisol level of 19–23 mg/100 ml at the time of the collapse. Ketamine raises the plasma cortisol level (Oyama *et al.*, 1970).

In our opinion, shared by the surgeons, this child would not have survived eight conventional anaesthetics. She has now left hospital and returned to school. In no patient did hypotension follow alteration of position on the operating table.

One female patient aged 72 years developed left-sided cardiac failure when anaesthetized with ketamine. Her pulse rate had risen to 120 from a resting rate of 80 beats/min, although her blood pressure did not rise proportionately. Her cardiac failure was manifested by pulmonary oedema and peripheral cyanosis and she responded rapidly to 0.25 mg digoxin intravenously. She was not given a diuretic.

Patients admitting to a high alcohol intake were more resistant to ketamine. Random movements were present in a number of patients. These movements are movements of the limbs unrelated to surgical stimulation and were especially marked in epileptic patients. We now control these movements by administration of 50% nitrous oxide and oxygen.

Vomiting only complicated one case and since this did not occur until 16 hr postoperatively, it is unlikely that ketamine can be implicated.

## Discussion

Our expectations that ketamine should be a good anaesthetic for burns surgery were confirmed. The problem of emergence phenomena in certain adult patients remains. Two of our patients who experienced postoperative confusion requested that they never be given ketamine again. Dreaming under anaesthesia is well known to occur but the dreams and hallucinations that may occur when ketamine is used are bizarre.

We are at present trying a number of drugs postoperatively in an attempt to abolish this complication and we find that chlorpromazine in doses of 1 mg/kg body weight is showing greatest promise. It is of interest that chlorpromazine is used to terminate the hallucinations caused by lysergic acid, although it should be stated that ketamine is not a member of the LSD group.

One factor has impressed and it is one that is

difficult if not impossible to evaluate scientifically. Patients who have had major surgery under ketamine anaesthesia are extremely fit immediately post-operatively, and indeed look and feel as though they have not had an operation.

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## Discussion

DR A. W. EDRIDGE (East Grinstead): I should like to know whether Dr Sage has ever had ketamine himself, for 'kicks' or for any other reason.

DR SAGE: No.

DR ENDERBY: If, as appears from what Dr Sage says, this is treated as a major anaesthetic performance, does he starve the patient beforehand? There must be a period of time, and in my limited experience this period of time must be fairly prolonged. I wonder how much interference you get with your feeding.

DR SAGE: At Chepstow we usually do the burns surgery in the morning, so they miss their breakfast, and usually by mid-day they have fluids, and some of the meal that has been served at mid-day, or slightly later, is kept for them till later. So there is minimal disturbance. In fact, in some patients ketamine seems to stimulate the appetite, and the patient eats quite heartily a little later than mid-day, and so the nutrition of the patient is minimally disturbed.

DR LAIRD (Chepstow): We have used ketamine for burns dressings on children, as opposed to surgery, where we have not starved the patient pre-operatively, and they have actually taken fluid within  $\frac{1}{2}$  hr of their return to the ward after dressing.

DR ENDERBY: I should like to comment on that, if I may. In my large series of one case, the child to whom I gave ketamine in the recommended dosage spent all day here in this hospital and was intended to go back in the evening, but ultimately had to wait the night and go home the next day. A day was spent in looking after this child. He spent most of the day screaming. We so felt that this was a totally unacceptable performance with a child that I have not dared stick my neck out since.

DR SAGE: What dose?

DR ENDERBY: The recommended dose. I think it must have been 10 mg.

DR SAGE: We use 4 mg. If you want to do just a burns dressing you can get away adequately with less. But if

you give 4 mg/kg body weight, you can take off the burns dressing, set up your blood transfusion, and you will need a 2 mg/kg body weight additional if you are going to start taking split skin grafts and that sort of thing. This reduces the dosage quite considerably.

MR KIRK (Perth): May I speak briefly as a mere surgeon and stimulate my anaesthetist also to get up on his feet. We have used ketamine to quite an extent in children's burn dressings, both as an initial dressing and as interval dressing procedures, and even in taking split skin grafts. We have not needed to starve them. In the morning dressing procedure, certainly by lunch time they would be taking fluids, if not light food. We have used it also on out-patients, but there has not been this experience that Dr Enderby referred to.

DR BUSH: May I ask a few questions? Dr Sage, there have been a number of reports in the literature of patients who have vomited under this drug and have inhaled and have died. There have also been reports indicating that laryngeal reflexes are not as potent as one had originally thought. There are also rather alarming reports on the incidence of laryngeal spasm which occurs with this drug. My experience with it is extremely limited but the incidence of vomiting in my small series was very much greater than the 5% that I was quoted by the manufacturers.

Another point, concerning dreams: I had one burn patient, aged 15, whom I tried it on and, like the case quoted by Dr Enderby, this patient had to be sedated for the whole day, and next day he said to me 'Never give me that drug again'. If this is said to me once, I feel that I am not in a position to give this drug to any other patient lest I cause in that patient dreams of a very unpleasant nature, which these dreams often are. Therefore, I have ceased to use it.

One other point. It is reputed to be an extremely short-acting drug. It has not been my experience that it is as short-acting as one would like.

DR SAGE: If I may refer to the point about the laryngeal reflexes, we had only one incident of vomiting, so vomiting has not been our problem. Secondly, as to the report that came out about laryngeal reflexes, these showed that these reflexes were not competent, and we accept this. We therefore do not feed our adult patients for 6 hr before the operation. But we thought that we were giving such a small dose in children that the laryngeal reflexes probably were competent. I had one child whom we decided to try it out on, and we put 2 ml dionosil down into the pharynx during the operation. We took a chest X-ray and we found that all of it went down into the oesophagus and looked like an oesophageal swallow. None of that went into the lungs. However, so far this is encouraging, and we shall have to continue doing this to find out what happens to children with small doses.

DR LAIRD: I think if the patients have not been given atropine they are liable to get laryngeal spasm.

DR W. N. ROLLASON (Aberdeen): May I ask Dr Sage what other drugs he has tried in addition to chlorpromazine to prevent these hallucinatory phenomena in the postoperative period?

DR SAGE: When we started we decided that in some patients ketamine would be contra-indicated—in hypertensives and patients who had had mental illnesses. We were so impressed with the drug that we started using it on patients who had had mental illnesses, but we had to take precautions to prevent them having hallucinations and to avoid exciting their mental state. We tried chlorpromazine and diazepam. We found with diazepam they were worse and had hallucinations. We are using narcotics in our pre-med, and this is said to be the better way of reducing hallucinations, to have the narcotics in the pre-med rather than given drugs postoperatively.

DR ROLLASON: Which narcotics are you using?

DR SAGE: Usually pethidine.

DR LUXMOORE (Portsmouth): Could you explain the last slide which you showed, please? It showed the histograms of emergence phenomena; the age group 6–9 was 23%, and as the ages of the patients increased, so the incidence of the emergence phenomena decreased.

DR SAGE: No. The histogram showed the number of patients in each age group, and there was only an incidence of emergence phenomena in the 40–50 age group. There were no emergence phenomena in the others.

DR LUXMOORE: Thank you very much. Would you care to comment, then, on the disparity between this set of results and the work done by Professor Dundee and others on the high incidence of emergence phenomena in other cases?

DR SAGE: Professor Dundee was using ketamine for different operations from us. He was also waking his patients up at intervals after the operation. This may have led to his different results. When we started our study we were using the Parke-Davis treatment where they wanted us to provide data immediately postoperatively and within 24 hr. Now that we leave the patients and do not enquire whether they have had any dreams immediately postoperatively the hallucinations have dropped virtually to nil. I think it is a question of the postoperative care of the patient, that you leave them to come round gradually

and do not, as in the case of conventional anaesthetics, wake them up as soon as possible. If you let the patient recover quietly you will not have this high incidence. I think this is the difference between our survey and the other one.

DR LAIRD: If you ask questions about unpleasant experiences, you may elicit recalls.

DR DONNELL (Bristol): I think we agree with you entirely on rather a short series of cases. The more you leave these patients alone afterwards, the better results you seem to get. We have used the intramuscular and the intravenous route, and where intravenous anaesthesia would have been extremely difficult this has been a very useful drug. I think we all feel that we do not know quite where the patient is anaesthetically while the process is on. They open their eyes at you. They do all sorts of exciting things. But speaking to them 24 hr afterwards, if you ask them the question directly 'Did you know anything about it?' they say 'No, it was absolutely marvellous.' I think this is the answer. Leave them. Do not slap their faces and wake them up.

DR J. MURRAY: I should like to know whether or not we confuse the issue by using supplementary drugs, in particular diazepam. We have found that the duration of anaesthesia is much longer. I wonder whether Dr Sage has had this experience.

DR SAGE: We have had very little experience. We have found that we do not need to give supplementary drugs very often, so my experience of that is very limited.

DR BASKETT: I think your good results are probably largely enhanced by giving an opiate premedication beforehand, thus enabling you to keep the dosage low. The suggestion that this keeps the incidence of unpleasant after effects down is interesting. The same applies, I think, to the use of neuroleptics, the droperidol group. If you give droperidol alone you get unpleasant dreams undoubtedly, but if you cover it well with an opiate this incidence tends to be reduced.

DR ANTIC: Our experience is based on about 1000 cases of ketamine with children. In only one case did we have vomiting. We are very satisfied with this.

DR PURSER (Derby): On this business of ketamine maintaining the airway when the patient has got contractures under the neck, do you not consider that the advantage of keeping the airway outweighs the disadvantage of subhypnotic dreams?

DR BUSH: I would say that the danger of regurgitation and inhalation in these patients, where you cannot possibly release them, would be much more hazardous after the use of ketamine than giving them a conventional anaesthetic and asking the surgeon to cut their throat before intubating. Because of this risk of losing the airway and vomiting, where you can do nothing about it, I would rather give them a conventional anaesthetic.

DR R. S. NEILL (Glasgow): I chose on one occasion to give ketamine to a man who had a massive resection of his face and jaw and had contractures and ulcerations afterwards. I felt that the use of the conventional anaesthetic was precluded. I have never been so frightened in all my life when I gave him ketamine. Having got respiratory obstruction, I could not intubate and I could not do anything about it. It really was a frightening experience. He had space fantasies. He said to me afterwards, 'I don't

care if you never do anything to me again. Do not give me that stuff again.'

DR A. W. EDRIDGE (East Grinstead): Possibly as a result of the last 20 or 30 years experience of hallucinogenic drugs, which were explored by Huxley and other people, and in interesting cultures which rely upon hallucinogens for religious experiences, we all of us are very much more sensitized to the enormous area of mental experience—call it the subconscious or whatever you like—which can be potentially terrifying. In using these dissociative drugs we are treading, I believe, on various aspects of a person's mentality which may be extremely dangerous to them as personalities. I could instance a number of people to whom I have given droperidol who have not been happy afterwards. Many of them appear to feel that these are rather unmanly reactions, and, unless questioned, will not proffer them. Some of them exhibit unease when they came back for further surgery, maybe 2 or 3 months later, and they say to the ward sister or to somebody who examines them pre-anaesthetically 'I hope I do not have the stuff I had last time.' I do not know how much we are damaged by the possible terror dreams and the nightmares we have; many of us go through these experiences nightly for all I know, and forget them later when we wake up. So maybe we are doing the patient no harm. I do know, in terms of LSD taken for fun or sometimes therapeutically that patients have been unhinged, to use an old-fashioned term, by these experiences.

Some South Africans took twelve patients to the second or third plane with ether anaesthesia, and to a pre-arranged scheme. They stopped the anaesthetic. The anaesthetist said 'Will you please stop the surgery? I am worried about this patient.' After an interval of 30 sec he said 'I have now given more oxygen. Everything is all right. You may carry on.' These twelve patients were hypnotized the next day. This was a pre-arranged set-up, although the patients did not know about it. I think it was three or four of the twelve who remembered what had been said. Two went through a terror reaction, and the others could produce nothing. Even during ordinary anaesthesia perhaps we tread upon these minefields of the mind.

I think this is terribly dangerous territory. If you leave one patient in a hundred with a deeply disturbed mental background, you have done a very bad thing. I view these drugs with great suspicion. They should all be covered with an opiate or barbiturate or some other agent which we are told helps to obviate these fantasies.

DR F. STOCKINGS (Portsmouth): Following on what the last speaker said, most people say that when ketamine is given to children it does not have any effects. Are we sure about this? How do we know? When children are 6 or younger, if they cry or become very distressed, obviously they are having ill-effects. Are not children of this age quite incapable of telling whether they have suffered mental distress or anything of the sort? It is difficult to get anything like this out of children. If a child is ordinarily frightened it is difficult to get out of him what he is frightened of. He has not got the capability of expressing himself. Is not this the point when one is assessing the results of this drug?

DR SAGE: This is an argument which has been put forward before. This may be the reason why children seem to have no recollection. After the age of 6 a lot of children are quite capable of expressing themselves about dreams or telling you that they have had dreams. So the argument, I think, is a proper one for children below 6, but above 6 I have my doubts. I think that below 6, your argument may well be the reason why children do not seem to have emergence phenomena.

DR LAIRD: Certainly children live in a fantasy world of their own at times, and they are much more capable of describing a fantasy than an adult.

DR ROLLASON: Over a period of a year I think one would have had comments from the nursing staff or ward sisters if they had found anything significantly different in the postoperative recovery of these children. I do not know whether Dr Laird can confirm this, but I have had no complaints from the nursing staff about children who have had ketamine during the past 12 months.

DR LAIRD: We have used it not only in the burns unit but also in the main part of the hospital for such things as the removal of sutures and the change of plasters and minor orthopaedic procedures without any trouble at all with children. The nursing staff have made no comment about the children appearing to be disturbed. I think it is a question of dosage. If one keeps the dosage down to the absolute minimum, one will not get emergence phenomena in children.

DR BENNETT (Maidstone): I just want to say that in the hospital in which I work one of my colleagues is keen on ketamine, and the nurses are considerably disturbed by this.

*The meeting closed with a vote of thanks to the organizer, Dr Russell Davies, and to Messrs Abbott Laboratories, Parke-Davis and Janssen Pharmaceuticals for their support.*