Anaesthesia, 1981, Volume 36, pages 183–187

Adverse reactions to ketamine anaesthesia

Abolition by a psychological technique

GARRY S. SKLAR, STEPHEN R. ZUKIN AND THOMAS A. REILLY

Summary

Ketamine, a phencyclidine derivative, has been used as a general anaesthetic since 1965. Numerous reports of adverse psychological reactions have caused diminished use of this drug. Many investigators have tried by pharmacological means to modify these reactions with limited success. In this study, a psychological strategy has resulted in the absence of any adverse psychological reactions and acceptance of ketamine anaesthesia by all patients. Additionally, all surgeons were satisfied with operating conditions.

Key words

Anaesthesia, intravenous; ketamine, phencyclidine.
Complications; adverse reactions.

Ketamine, a derivative of phencyclidine, has been used to produce general anaesthesia in humans since 1965. Initial enthusiasm for its safety and efficacy gave way to controversy and rejection by physicians and patients as it became clear that 12–36% of patients anaesthetised with this agent suffered from distressing emergence reactions characterised by agitation, vivid dreams, hallucinations and bizarre, impulsive behaviour.[1–4]

Various attempts to ameliorate these reactions by utilisation of pre- or intra-operative medications have been reported.[5–9] Pre-operative medication has been shown not to change the proportion of patients having dreams except when the period between administration of the sedative-hypnotic drug and the termination of anaesthesia was short.[10] These reports have shown a reduction of the dreaming rate from about 50–60% to 10–15%. The rate of bad dreams and hallucinations was reduced proportionately.

Egbert *et al.*[11] demonstrated the effectiveness of the pre-operative visit by the anaesthetist in reducing the incidence of anxiety as perceived by patients from 63 to 47% without the use of pre-operative medication. In dealing with ketamine emergence reactions, one confronts not only patient anxiety but a drug-induced psychosis.[12]

Demonstration of an effective technique to prevent these reactions would yield the possible benefits of renewed acceptance of ketamine as a safe and effective anaesthetic, and utilisation of similar techniques in attempts to modify psycho-

Garry S. Sklar, MD, Assistant Professor of Clinical Anesthesiology, Mount Sinai School of Medicine, Director of Anaesthesia, City Hospital Center at Elmhurst E5-26, 79-01 Broadway, Elmhurst, New York 11373 USA. Stephen R. Zukin, MD, Assistant Professor of Clinical Psychiatry, Mount Sinai School of Medicine, 100th Street and 5th Avenue, New York, New York 10029 USA. Thomas A. Reilly, MD, Assistant Professor of Community Medicine, Mount Sinai School of Medicine, Mount Sinai Services, City Hospital Center at Elmhurst, 79-01 Broadway, Elmhurst, New York 11373 USA.

0003-2409/81/0200-0183$02.00

tic reactions to other drugs, especially phencyclidine and other abused cyclohexylamines.

In this study the authors have chosen to modify the patient response to ketamine psychologically rather than pharmacologically.

Methods

Ninety patients who underwent surgery between January 1977 and June 1978 were entered into the study. The patients were divided into four groups depending upon whether they had received pre-operative medication and whether the initial dose of ketamine was 1 or 2 mg/kg (Table 1). The operations performed included dilatation and curettage, drainage of cysts and abscesses, circumcision, excision of lipomas and skin grafts.

The expected duration of surgery and the total expected dose of ketamine were not considerations in the conduct of anaesthesia once the technique had been decided upon. Patients with a history of psychosis and those with untreated hypertension were excluded from the study. Informed consent was obtained from all patients.

All patients undergoing elective procedures underwent routine pre-anaesthetic visits the evening prior to surgery. The pre-operative medications given to patients in Groups III and IV included a wide variety of narcotics, barbiturates and tranquillisers prescribed by physicians who were not participating in the study. The drugs included pethidine, pentobarbitone, droperidol, fentanyl, diphenhydramine, diazepam and hyoscine. On the day of surgery each patient received an intensive 10 to 20-minute interview by one of the authors (GSS). Careful medical, surgical, anaesthetic and psychiatric histories were taken. It was explained to all patients that a general anaesthetic would be administered which would render them unconscious and free of operative pain. Patients were encouraged to share their ideas and feelings about surgery and anaesthesia with the interviewer. It was explained that the anaesthetic agent to be used would permit the patient to dream about a topic of his or her choice. Patients were asked to choose pleasant topics and communicate them to the interviewer. They were again advised that they would be unconscious and have no pain and were asked to concentrate on the previously enunciated pleasant thought. They were also told that they would be questioned postoperatively about dream content, satisfactoriness of the dream, satisfactoriness of the anaesthetic and willingness to receive the same anaesthetic again.

Operating room environment and conditions were strictly controlled. Traffic into and out of the operating room was minimised. Surgeons, nurses and anaesthetists spoke in whispers and the patients were shielded from other stimuli, especially lights, which were not allowed to shine on their faces.

Intravenous infusions were started on all patients. Those undergoing surgery in the lithotomy position were positioned, with their consent, before induction of anaesthesia. Patients for surgery in the supine position had skin preparation and draping before induction, with their consent. During induction of anaesthesia, the patients were reminded of the previously selected dream content.

Groups I and III received intravenous ketamine in a dose of approximately 2 mg/kg. Groups II and IV received up to 1 mg/kg, the end point of dosage in all patients of Groups II and IV being the anaesthetist's evaluation as to when the patient stopped responding to being spoken to softly.

Table 1. Description of study groups

Group	I	II	III	IV
Number of patients	25	20	22	23
Type of operation	Emergency and elective	Emergency and elective	Elective	Elective
Pre-operative medication	No	No	Yes	Yes
Initial dose of ketamine	2·0 mg/kg	1·0 mg/kg	2·0 mg/kg	1·0 mg/kg
Duration of operation (minutes)	10–75	15–70	15–130	15–75

Pulse rate, arterial blood pressure and electrocardiogram were monitored throughout anaesthesia in each case. Supplementary ketamine in doses of about 10–20 mg intravenously was administered as blood pressure returned towards the pre-induction dose level or when the anaesthetist observed facial grimaces by the patient.

Postoperatively, all patients were taken to the recovery room where the nursing staff was advised that the patient had received ketamine. Vital signs were monitored as in non-ketamine patients. No special care was requested except that the patient receive minimal sensory stimulation.

Patients were interviewed by the anaesthetist (GSS) in the recovery room just after they became able to identify and communicate correctly the number of fingers held before their eyes. After orientation to place and person had been ascertained, they were asked what operation they had had, whether they had any pain, whether they had felt, seen or heard anything during surgery and whether they remembered the pre-operative interview. They were asked whether they had dreamed during surgery; those who replied affirmatively were asked to describe dream content and satisfactoriness. All patients were asked whether they would accept the same anaesthetic agent again if they should need future surgery.

All surgeons were questioned postoperatively as to the acceptability of the anaesthetic technique and satisfactoriness of operating conditions.

Statistical analysis was carried out by the use of the Chi-square test and Fisher's exact test.

Results

The mean age of the patients in this study was $31{\cdot}7 \pm 2{\cdot}2$ years. Eighty percent of the patients were women. There was no statistically significant differences in age or sex of the patients in the four study groups.

The rates of dreaming of the four groups are shown in Table 2. The dreaming rate of the premedicated patients, Groups III and IV, was 24% less than the rate of the unpremedicated patients in Groups I and II, but this was not statistically significant ($p > 0{\cdot}05$).

The dreaming rate for the patients receiving 2 mg/kg of ketamine, Groups I and III was 40·4% (range 26·4 to 55·7—95% confidence limits) compared to 37·2% (23·0 to 53·2) of those who received 1 mg/kg of ketamine, Groups II and IV ($p = 0{\cdot}7$).

All patients remembered the pre-operative interview. None of the patients in any group experienced any unsatisfactory dream or hallucination and all would be willing to receive ketamine again. Operating conditions were acceptable to all surgeons.

Discussion

In this study, ketamine has proven to be an effective general anaesthetic devoid of acute adverse psychological sequelae and very well accepted by patients. All ketamine 'dreams' reported by our patients were pleasant, and no signs of postoperative psychosis were noted. This was the case whether or not any adjunctive medications were used, and whether initial doses of 2·0 or 1·0 mg/kg were utilised. In contrast, other investigators have reported 34–41·5% of patients would not accept this drug again, and that up to 36% reported unpleasant dreams.[3, 4]

The authors believe that a key factor in the results was the use of the pre-operative interview in which patients received from the empathic interviewer a confident suggestion that the drug experience would be a pleasant one under the patient's control. It was felt that a patient informed in advance of the likelihood of vivid visual

Table 2. Dream responses to ketamine with psychological intervention (parentheses represent 95% confidence limits)

Group	I	II	III	IV
Number of patients	25	20	22	23
Dream rate %	44·0 (24·0–65·1)	45·0 (23·1–68·5)	36·3 (17·2–59·3)	30·4 (13·2–52·9)
Unsatisfactory dream %	0 (0–13·7)	0 (0–16·8)	0 (0–15·4)	0 (0–20·6)
% Unwilling to have ketamine again	0 (0–13·7)	0 (0–16·8)	0 (0–15·4)	0 (0–20·6)

imagery during the anaesthetic experience would be less likely to become frightened than one in whom the hallucinations were unexpected. In our discussions with the patients the term 'dreams' rather than 'hallucinations' was used in order to avoid the unpleasant connotations of the latter word.

It might seem surprising that in an unselected group of patients, simple suggestions could so strongly modify a presumably powerful drug effect. There is some evidence that ketamine and other 'dissociative anaesthetics' may promote state dependent learning.[13] If so, the fact that the interview continued during induction may have enhanced suggestibility. Careful minimisation of sensory stimulation during the drug experience could also be of significance for the results obtained.[14] It should be mentioned that all patients in the study were interviewed pre-operatively as it would not have been ethical to study a group who had not been interviewed and received no medication as the possibility of adverse reactions is well established.

Reduction of unpleasant psychological effects could be approached either by attempts to reduce the dream rate or attempts to decrease the proportion of unacceptable to acceptable dreams. The dream rate in several studies[3–10, 13] varied from 36% to 61% with a median of 40%. Coppel, *et al.*[10] were able to reduce the dream rate to 8% by using diazepam at the end of surgery. Hervey & Hustead[3] showed that the incidence of dreaming and the refusal of further ketamine anaesthesia were quite low when the duration of anesthesia was short. Both of these studies suggest that the dreaming rate can be reduced by the use of sedative hypnotics if the effect of the drug is present at the end of anaesthesia.

The highest proportion of acceptable dreams reported previously was 60%; this figure is similar whether ketamine is used alone or with adjunctive medication. The authors feel that differences between the expectations of the experimenters and the subjects and in the experimental surroundings may account for these variations. In emphasising pharmacological suppression of ketamine dreams and hallucinations, previous studies may have been self-defeating in that under the influence of a drug which may render patients more highly suggestible, the assumption by the investigator that any hallucinatory experience will be adverse is more likely to be adopted by the patients.

In conclusion, it seems that the role of ketamine in anaesthesia merits re-evaluation. Pharmacological techniques have failed to eliminate ketamine emergence reactions or to make ketamine anaesthesia more widely acceptable. This study suggests the merit of psychological strategies in the prevention and treatment of adverse psychological reactions of ketamine and other cyclohexylamines, including phencyclidine and cyclohexamine.

References

1. Fine J, Finestone SC. Sensory disturbances following ketamine anaesthesia. Recurrent hallucinations. *Anesthesia and Analgesia; Current Researches* 1977; **52:** 428–30.
2. Johnstone RE. A ketamine trip. *Anesthesiology* 1973; **39:** 460–1.
3. Hervey WH, Hustead RF. Ketamine for dilatation and curettage procedures: Patient acceptance. *Anesthesia and Analgesia; Current Researches* 1972; **51:** 647–55.
4. Krestow M. The effects of post-anesthetic dreaming on patient acceptance of ketamine anesthesia: A comparison with thiopentone-nitrous oxide anesthesia. *Canadian Anaesthetists' Society Journal* 1974; **21:** 385–9.
5. Erbguth PH, Reiman B, Klein RL. The influence of chlorpromazine, diazepam, and droperidol on emergence from ketamine. *Anesthesia and Analgesia; Current Researches* 1972; **51:** 693–700.
6. O'Neil AA, Winnie AP, Zadigian ME, Collins VJ. Premedication for ketamine anesthesia: Phase I: The 'classic' drugs. *Anesthesia and Analgesia; Current Researches* 1972; **51:** 475–82.
7. Sadove MS, Hatano S, Zahed B, Redlin I, Arastounejad P, Roman V. Clinical study of droperidol in the prevention of the side effects of ketamine anesthesia: A preliminary report. *Anesthesia and Analgesia; Current Researches* 1971; **50:** 388–93.
8. Sadove MS, Hatano S, Redlin T, Thomason R, Arastounejad P, Roman V. Clinical study of droperidol in the prevention of the side effects of ketamine anesthesia: A progress report. *Anesthesia and Analgesia; Current Researches* 1971; **50:** 526–32.
9. Abajian JC, Page P, Morgan M. Effects of droperidol and nitrazepam on emergence reactions following ketamine anesthesia. *Anesthesia and Analgesia; Current Researches* 1973; **52:** 385–9.
10. Coppel DL, Bovill JG, Dundee JW. The taming of ketamine. *Anaesthesia* 1973; **28:** 293–6.
11. Egbert LD, Battit GE, Turndorf H, Beecher HK. The value of the pre-operative visit by an anesthetist. *Journal of the American Medical Association* 1963; **185:** 553–5.
12. Siegel RK, Jarvik ME. Drug induced hallucinations in animals and man. *Hallucinations: behavior, experience and theory* in: Siegel RK, West LJ. New York: John Wiley & Sons, 1975: 81–161.

13. OVERTON DA. A comparison of the discriminable CNS effects of ketamine, phencyclidine and pentobarbital. *Archives Internationales de Pharmacodynamie et Therapie* 1975; **215:** 180–9.

14. SHAPIRO RA, BERLAND T. Noise in the operating room. *New England Journal of Medicine* 1972; **287:** 1236–8.