Effects of Droperidol and Nitrazepam on Emergence Reactions Following Ketamine Anesthesia

J. C. ABAJIAN, M.D.
P. PAGE, F.F.A.R.C.S.
M. MORGAN, F.F.A.R.C.S.
London, England*

For years, anesthesiologists have been seeking a compound that could be given parenterally and that would provide profound analgesia while sparing cardiovascular and respiratory functions; the advantages of such a drug would obviously be enormous. The first drug of this type, phencyclidine, was withdrawn from clinical practice because of the high incidence of resulting psychoses. Further research led to the introduction, into anesthetic practice, of the phencyclidine derivative, ketamine.[1]

Ketamine has been shown to produce profound somatic analgesia, transient cardiovascular stimulation, minimal respiratory depression, and usually an increase in muscle tone. Nevertheless, its use is still associated with "emergence reactions," which may be defined as a state of vivid dreaming, or any vocalization or movement by the patient that might indicate a phase of vivid dreaming. These dreams range from pleasant to frankly terrifying, and the reported incidence varies from virtually zero to over 30 percent in adults. Hence, many anesthesiologists, particularly in the United Kingdom, have been reluctant to use the drug widely despite its many advantages.

If it were possible by some simple pharmacologic means to abolish or even markedly reduce these emergence reactions, ketamine would almost certainly gain wider acceptance. Several attempts to achieve this desirable end have been made.[2-7] Recently, Johnstone[8] reported that premedication with oral droperidol and nitrazepam prior to ketamine anesthesia for relatively minor surgery had completely abolished any dreams or mental agitation during recovery.

We report here our experiences with this drug combination on the incidence of emergence reactions following ketamine as the sole anesthetic agent in adult patients undergoing minor surgical procedures.

*Department of Anaesthetics, Royal Postgraduate Medical School and Hammersmith Hospital, London, England.

METHODS

Sixty patients, 22 male and 38 female, ranging in age from 16 to 69 years (mean 38) and in weight from 38 to 118 kg. (mean 63) were studied. Each received as premedication 20 mg. of droperidol and 10 mg. of nitrazepam given orally, and 0.6 mg. of atropine intramuscularly, 1 to 1½ hours preoperatively. Any patient with hypertension, cardiac or cerebrovascular disease, or a history of mental illness was excluded from the trial. No patient had had a previous ketamine anesthesia.

Induction was with 2 to 2.2 mg./kg. of ketamine intravenously given over a period of 45 to 60 seconds, supplementary doses, when required, being half the induction dose. Pulse rates and blood pressures were recorded prior to induction, and the maximum levels reached during anesthesia were noted. The anesthesia was assessed by the anesthesiologist as excellent, good, fair, or poor. At the termination of operation, patients were transferred to the recovery room, where they were not stimulated in any way. They were returned to the ward when they were fully conscious and orientated. Each patient was visited by one of us on the day following operation.

RESULTS

Of the 60 patients, the effects of the premedication were judged as being totally satisfactory in 58. The surgical procedures were completed with ketamine as the sole agent in all but one patient.

In all, 27 patients (45 percent) reported dreaming; 11 (18 percent) reported their dreams as being pleasant, 10 (17 percent), as unpleasant, and 6 (10 percent), as frankly terrifying. The incidence of dreaming of all types was greater in male than female patients, but the numbers are too small to draw any significant statistical inference. Table 1 shows the incidence of dreams and dream-related factors.

Forty-nine patients found ketamine anesthesia to be acceptable, but 11 (18 percent) stated that they would prefer not to have the drug again. Interestingly enough, 5 patients who reported their experiences as unpleasant stated that they would be prepared to have another ketamine anesthesia.

TABLE 1

Incidence of Dreams and Dream-Related Factors

	Number of patients	Percent incidence of dreaming			
		None	Pleasant	Unpleasant	Terrifying
Total number	60	55	18	17	10
Male	22	41	27	18	14
Female	38	63	13	16	8
Surgical procedure					
Gynecologic	13	77	8	15	0
General	28	61	18	11	11
Orthopedic	3	0	66	33	0
Genitourinary	16	38	25	19	19
Assessment of anesthesia					
Excellent	30	57	10	23	10
Good	20	45	35	10	10
Fair	8	75	13	0	13
Poor	2	50	0	50	0
Number of doses					
One	8	75	13	13	0
Two	18	61	22	6	12
Three	19	63	0	26	11
Four or more	15	33	40	13	13
Purposeless movement					
Present	10	50	10	20	20
Absent	50	56	20	16	8
Vocalization					
Present	17	47	35	6	12
Absent	43	58	12	21	9

TABLE 2
Mean Preinduction Pulse Rates and Blood Pressure (±1 Standard Deviation) and Maximum Level Reached

	Preinduction	Maximum
Pulse rate, beats/min.	85.6 ± 15.2	108.4 ± 21.5
Systolic, mm. Hg	115.4 ± 15.6	152.5 ± 21.2
Diastolic, mm. Hg	71.7 ± 10.8	90.1 ± 10.0

Thirteen patients showed an increase in muscle tone, but this did not interfere with the operative procedure. Purposeless movements occurred in 10 patients, these being severe enough in 1 patient to require administration of a conventional general anesthetic to complete the operation. Vocalization during the operation occurred in 17 patients, which the surgeons found rather distressing. Respiratory obstruction necessitating intervention on the part of the anesthesiologist occurred in 7 patients (12 percent).

Table 2 shows the mean preinduction pulse rates and blood pressures, and the maximum levels reached during anesthesia. The inclusion of droperidol in the premedication did not prevent the hypertensive response to ketamine. There were no cases of bradycardia or hypotension in this series. Only 1 patient vomited postoperatively.

DISCUSSION

Such is the potential of ketamine that, as mentioned earlier, attempts have been made to derive some simple pharmacologic means of reducing the unpleasant sequelae of ketamine anesthesia, with varying degrees of success.[2-7] Only 60 patients are included in the present series; although originally we had intended to investigate a larger number, initial examination of the results showed the incidence of unpleasant dreams to be virtually the same as in our two previous series.[7,9]

The effects of the premedication were judged to be excellent in all but 2 patients, confirming the initial report by Johnstone.[10] Using this drug combination prior to ketamine anesthesia in 100 patients, he reported complete suppression of dreams and mental agitation in the recovery period, even though no special precautions were taken to maintain silence and avoid patient disturbance.[8] Corssen and coworkers[11] reported that after avoiding stimulation of the patient in any way during recovery, emergence reactions were virtually eliminated in their patients. This rule has been strictly observed in all our patients given ketamine, but the incidence of frightening dreams has remained high.

It must be pointed out that the mean induction dose of ketamine in Johnstone's series[8] was 250 mg. intravenously, with supplementary doses of 100 mg. at approximately 10-minute intervals. Both these doses would appear to be much in excess of the usually recommended induction dose of 2 mg./kg. and supplementary doses of half this amount. Knox and associates,[12] using atropine premedication before ketamine anesthesia supplemented with nitrous oxide, showed that the incidence of undesirable sequelae, including unpleasant dreams, was dose related. However, Loh and colleagues[7] recently questioned the efficacy of using nitrous oxide as a supplement to ketamine anesthesia for minor procedures.

★ JOHN CHRISTIAN ABAJIAN, M.D., a graduate of the University of Vermont College of Medicine in Burlington, completed his internship at Montreal General Hospital, Montreal, Canada, and his Residency in Anesthesiology at Hammersmith Hospital, Royal Postgraduate Medical School, London, England, where he currently holds the position of Registrar.

Bovill and his coworkers[2] reported that opiate and opiate-hyoscine mixtures were the most effective premedicant drugs in reducing emergence sequelae, but that tranquilizers, hypnotic drugs, and droperidol-containing mixtures were least effective in this respect. Galloon,[3] however, reported that the best premedicant for reducing postoperative dreams was diazepam with hyoscine or atropine. The former workers[2] also showed that 5 mg. of droperidol intravenously at the end of operation had little effect on the number of dreams, but that 5 mg. of diazepam reduced the incidence of unpleasant dreams to 15 percent. Similarly, Collier[6] has shown that routine postoperative administration of diazepam causes a reduction in recovery complications. In contrast, Loh's group[7] was unable to reduce the incidence of unpleasant dreams with diazepam, although the incidence was still lower than that reported by Bovill and associates.[2]

Sadove and coworkers[4] reduced the number of dreams after ketamine anesthesia by giving intravenous droperidol just before induction, but the incidence of bad dreams was still high (20 percent) and appeared unaffected by the droperidol. In a further study,[5] they showed that intravenous droperidol was superior to intramuscular droperidol or pentobarbital in reducing the incidence of unpleasant dreams during recovery.

Because of the side effects known to occur after ketamine administration, we have not given the drug to patients known to have, or to have suffered from, mental illness. It is therefore interesting to note that Brewer and his associates[13] have given ketamine as the anesthetic agent for electroconvulsive therapy to depressed and psychotic patients, without the occurrence of hallucinations or other emergence phenomena. They point out that this may possibly be due to the effect of the electroconvulsive therapy or to the one or more psychotropic drugs their patients were receiving.

It must of course be borne in mind that dreaming occurs after other forms of anesthesia. A 44 percent incidence of dreaming has been reported[14] after thiopental-d-tubocurarine-nitrous oxide anesthesia, these dreams being unpleasant in 12 percent of patients. Using a similar technic,[15] the addition of morphine as premedication or 0.1 to 0.3 percent methoxyflurane reduced the incidence of dreaming to 23 percent, while dreams were completely abolished by the addition of 0.3 to 0.5 percent halothane.

In our hands, despite not stimulating the patients in any way during recovery, we have been unable to reduce the incidence of unpleasant sequelae to acceptable levels by pharmacologic means. Neither have we been able to detect any factors that might indicate a particularly susceptible group of patients. Were this possible, ketamine could be exhibited with greater confidence after patient screening. In the light of our results with ketamine anesthesia, it is now our policy to reserve the use of this drug for situations in which its advantages outweigh its disadvantages.

SUMMARY

Droperidol and nitrazepam were given orally to 60 patients as premedication prior to ketamine anesthesia for minor surgery, to evaluate the usefulness of this combination in reducing the incidence of unpleasant emergence reactions to acceptable levels. Results overall were considered unsatisfactory. Ketamine is now used only when the advantages it offers outweigh the disadvantages.

ACKNOWLEDGMENT

We should like to thank Dr. J. A. L. Gorringe, Parke-Davis & Company, for the supply of ketamine, and Miss J. Green for secretarial assistance.

Generic and Trade Names of Drugs

Droperidol—Droleptan
Nitrazepam—Mogadon
Ketamine—Ketalar, Ketaject
Phencyclidine—Sernyl
Hyoscine—Scopolamine
Diazepam—Valium
Pentobarbital—Nembutal
Sodium thiopental—Pentothal® Sodium
d-Tubocurarine—Tubarine
Methoxyflurane—Penthrane
Halothane—Fluothane

REFERENCES

1. Corssen G, Domino EF: Dissociative anesthesia: further pharmacologic studies and first clinical experience with the phencyclidine derivative CI-581. Anesth & Analg 45:29-40, 1966

2. Bovill JG, Clarke RSJ, Dundee JW, et al: Clinical studies of induction agents. XXXVIII: Effect of premedicants and supplements on ketamine anaesthesia. Brit J Anaesth 43:600-608, 1971

3. Galloon S: Ketamine for dilatation and curettage. Canad Anaesth Soc J 18:600-613, 1971

4. Sadove MS, Hatano S, Zahed B, et al: Clinical study of droperidol in the prevention of the side effects of ketamine anesthesia: a preliminary report. Anesth & Analg 50:388-393, 1971

5. Sadove MS, Hatano S, Redlin T, et al: Clinical study of droperidol in the prevention of the side-effects of ketamine anesthesia: a progress report. Anesth & Analg 50:526-532, 1971

6. Collier BB: Ketamine and the conscious mind. Anaesthesia 27:120-134, 1972

7. Loh L, Singer L, Morgan M, et al: Influence of diazepam on the emergence reactions following ketamine anaesthesia. Canad Anaesth Soc J 19:421-425, 1972

8. Johnstone M: Psychoses and ketamine. Brit Med J 1:442, 1972

9. Morgan M, Loh L, Singer L, et al: Ketamine as the sole anaesthetic agent for minor surgical procedures. Anaesthesia 26:158-165, 1971

10. Johnstone M: The effects of oral sedatives on the vasoconstrictive reaction to fear. Brit J Anaesth 43:380-384, 1971

11. Corssen G, Miyasaka M, Domino EF: Changing concepts in pain control during surgery: dissociative anesthesia with CI-581. A progress report. Anesth & Analg 47:746-759, 1968

12. Knox JWD, Bovill JG, Clarke RSJ, et al: Clinical studies of induction agents: XXXVI: Ketamine. Brit J Anaesth 42:875-885, 1970

13. Brewer CL, Davidson JRT, Hereward S: Ketamine ("Ketalar"): a safer anaesthetic for ECT. Brit J Psychiat 120:679-680, 1972

14. Brice DD, Hetherington RR, Utting JE: A simple study of awareness and dreaming during anaesthesia. Brit J Anaesth 42:535-542, 1970

15. Harris TJB, Brice DD, Hetherington RR, et al: Dreaming associated with anaesthesia: the influence of morphine and two volatile adjuvants. Brit J Anaesth 43:172-178, 1971

WILD GEESE

By John F. McDonnell

I leaned upon my elbow when
The old familiar cry,
Resounding through my window,
Told of wild geese in the sky.
I raised the blind and tried to see
Through clouds that dark'd the night:
Through clouds that gave protection
To the wild geese in their flight.

Their flight from placid northern lakes
Where they had raised their young;
Their flight that nature lovers trace
And poets long have sung.
For there are pathways through the air
And roads within the sky.
If you would know the milestones there
Watch where the wild geese fly.