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Uneventful total intravenous anaesthesia with ketamine for schizophrenic surgical patients

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Summary

Ketamine has been considered to be contraindicated for schizophrenic patients because it may induce psychologial emergence reactions and psychiatric deterioration. Total intravenous anaesthesia (TIVA) with ketamine combined with droperidol and fentanyl (DFK) has been used in 14 schizophrenic patients undergoing various surgical procedures. Two patients died postoperatively of concomitant severe disease rather than from schizophrenia related pathophysiology or anaesthetic complication. One patient showed transient mild anxiety in the early post-operative period soon relieved by the patient's routine medication. However, no patient developed exacerbations of psychosis or psychological emergence reactions during the first post-operative month. The cardiovascular state during and after DFK remained stable in all cases. It is concluded that ketamine when combined with droperidol and fentanyl is a satisfactory anaesthetic for patients with schizophrenia.

Keywords: SCHIZOPHRENIA; ANAESTHETIC AGENTS; KETAMINE; TOTAL INTRAVENOUS ANAESTHESIA.

Introduction

Ketamine has been considered unsuitable for patients with schizophrenia, because the drug might induce psychological emergence reactions with a deterioration in the psychic state of such patients [1]. However, the true picture remains unclear in such patients, because there is only one clinical report which describes a deterioration in psychosis following ketamine anaesthesia [2]. Other reports suggest that ketamine may be used safely in clinical practice for schizophrenic patients and even in mentally handicapped patients [3–6].

More than 150 schizophrenic patients who needed various surgical treatments under either general or local anaesthesia during the past 20 years have been managed. Inhalational anaesthetics may produce profound hypotension when antipsychotic drugs are chronically administered [7], ketamine is therefore frequently chosen for major anaesthesia in these patients, because as it has minimal adverse effects on respiratory, cardiovascular, hepatic and renal function [8] rather than for its psychic action. Intravenous anaesthesia (TIVA) with ketamine and with droperidol and fentanyl (DFK) has been used in this department in more than 3000 non-psychotic patients and in 14 schizophrenic patients and there have been no major anaesthetic complications [8], the psychiatric follow up was made during the 1 month post-operative period. None of these patients experienced any psychological deterioration during the post-operative period.

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Anaesthetic method

After hospital ethics committee and patient approval 14 schizophrenic patients were admitted to the study. In all patients anaesthesia was induced with intravenous (i.v.) administration of droperidol 0.15–0.25 mg kg^{-1}, fentanyl 2–4 $\mu g\ kg^{-1}$ and ketamine 1.5–2.0 mg kg^{-1} in divided dose. The tracheal intubation was facilitated with either suxamethonium chloride 0.8 mg kg^{-1} or vecuronium bromide

Table 1. Pre-operative profiles of 14 schizophrenic patients

No.	Age (years)	Sex (M/F)	Antipsychotic drugs (daily dose)	Treatment (duration (years))	Surgical procedures
1	38	F	Haloperidol 3 mg Chlorpromazine 100 mg	2	Repair of the retinal detachment
2	48	F	Haloperidol 9 mg Oxypertine 60 mg	24	Removal of the mandibular sequestrum
3	56	M	Haloperidol 10 mg Chlorpromazine 150 mg Levomepromazine 100 mg	33	Left upper lobe lobectomy of the Lung
4	43	F	Haloperidol 2 mg Chlorpromazine 50 mg	21	Laparoscopic cholecystectomy
5	27	M	Haloperidol 3 mg Levomepromazine 1000 mg Bromperidol 5 mg	7	Skin grafting for burned tissues (2 times)
6	41	M	Sulpiride 200 mg Bromperidol 2 mg	2	Skin grafting for burned tissues (2 times)
7	38	M	Thioridazine 30 mg	19	Skin grafting for burned tissues (3 times)
8	65	F	Bromperidol 6 mg	18	Removal of the cataract
9	46	F	Chlorpromazine 100 mg	20	Vaginal hysterectomy
10	47	F	Haloperidol 2 mg Bromperidol 12 mg Propericiazine 30 mg	24	Radical mastectomy
11	42	M	Thioridazine 30 mg Pimozide 3 mg	24	Removal of the lung tumour
12	38	M	Levomepromazine 50 mg	7	Subtotal thyroidectomy
13	31	F	Nemonapride 12 mg	2	Treatment of dental caries
14	49	M	Levomepromazine 150 mg Bromperidol 18 mg	23	Nasal polypectomy

Mean $\pm$ SD: Age 43.5 $\pm$ 9.3 years; Treatment duration 16.1 $\pm$ 9.8 years.

0.1 mg kg^{-1} given i.v. Anaesthesia was maintained with a continuous infusion of ketamine 2 mg kg^{-1} hr^{-1} in combination with divided injections of fentanyl 8–15 μg kg^{-1} and droperidol 0.25–0.3 mg kg^{-1} total dose. Intra-operative muscle relaxation was maintained by i.v. vecuronium bromide as needed.

Post-anaesthetic follow up

Close observations were made in the recovery room during the immediate post-operative period at least 1 h after the trachea had been extubated. Anaesthetists routinely visited each patient three times during the first post-operative week and recorded each patient's condition including psychological state. Patient's charts throughout the first post-operative month were reviewed and each patient's post-operative psychological condition was also followed by one of the authors (HK) who consulted with the psychiatrist in charge of each patient. Presence or absence of exacerbation of psychosis, changes in antipsychotic drugs or other important events during the first post-operative month were recorded.

Results

The pre-operative profiles of the 14 schizophrenic patients are shown in Table 1. All the patients were using chronic phenothiazine derivatives or other antipsychotic drugs for at least the preceding 2 years. The average duration of the treatment was 16.1 $\pm$ 9.8 year. These drugs had been administered until the morning

Table 2. Anaesthetic and post-operative profiles of 14 schizophrenic patients

No.	Surgery duration (min)	Total fentanyl (μg)	Total ketamime (mg)	Readministration antipsychotic drugs (day)	Post-operative complications (day)	Discharge (day)	Remarks
1	226	700	615	0	–	17	
2	68	350	200	2	–	7	
3	336	950	870	1	–	36	WPW syndrome
4	128	400	280	2	Vomiting (1)	5	
5	314	1400	600	1	Died (12)	–	Septic shock
	393	750	870				
6	287	2000	1150	1	Died (14)	–	Multiple organ
	216	1100	800				Failure
7	182	700	560	0	–	–	Stay in burn unit
	85	900	380				
	157	750	420				
8	32	250	150	0	Constipation (2–6)	6	
9	120	400	320	1	Delayed recovery from Anaesthesia (90 min)	20	
10	257	550	650	0	–	26	
11	130	1000	700	1	–	8	
12	271	1350	820	0	–	9	
13	55	400	240	0	Mild anxiety (5hrs)	8	
14	53	750	340	0	–	8	

Mean ± SD: Surgery duration 184 ± 106 min; Total fentanyl 817 ± 430 μg; Total ketamine 554 ± 272 mg.

of the operative day with or without premedication, and the administration of drugs restarted post-operatively in the evening of the operative day when patients were allowed by the surgeon, anaesthetist or psychiatrist to take drugs.

None of 14 patients experienced an adverse emergency reaction in the early post-operative period except one patient (no. 13) who transiently felt mildly anxious. Two patients died because of the complications of underlying severe disease (no. 5: septic shock, no. 6: multiple organ failure). Other post-operative complications included delayed recovery from anaesthesia (no. 9), vomiting (no. 4) and constipation (no. 8). Both respiratory and cardiovascular function were stable during and after DFK except in the case of one patient (no. 3) with Wolff Parkinson White syndrome who developed a supraventricular tachycardia associated with the mechanical stimulation of the heart when the internal jugular vein was cannulated. Verapamil 5 mg, lignocaine 60 mg and diltiazem 5 mg i.v. in divided dose converted the tachycardia to sinus rhythm. Summary of anaesthesia and important events during and after anaesthesia are shown in Table 2.

No alteration or exacerbation in the psychotic condition of the patients was observed within the first post-operative month.

Discussion

The present study reports that none of the schizophrenic patients experienced obvious adverse emergence reactions or psychological deterioration following ketamine anaesthesia. The reported incidence of psychological disturbances following ketamine in non-psychotic patients varies markedly from

less than 5 to over 30% [9]. When compared with thiopentone, ketamine was found to be associated with a significantly greater incidence of psychological abnormalities in the immediate post-operative period [10]. Psychological susceptibility may affect the incidence of emergence reaction following ketamine anaesthesia [11]. However, when compared with a general anaesthetic regimen including thiopentone, nitrous oxide and halothane, the degree of post-operative anxiety in non-psychotic patients was found to be similar to those patients who only received ketamine [12]. Although White *et al*. [9] noted that non-psychotic patients receiving droperidol combined with ketamine were at risk of disorientation during the recovery period, droperidol was reported to reduce the incidence of adverse emergence reactions [13]. These observations in non-psychotic patients would at least partly support the present findings in which no patient suffered obvious disorientation or excitement in the early post-operative period.

To our knowledge, only one clinical report described deterioration in psychosis following ketamine anaesthesia [2], though the author did not describe this in detail. However, Shipilenia [3] reported that ketamine was therapeutically effective in 29 schizophrenic patients who did not respond to conventional antipsychotic drugs. Antipsychotic drugs are most likely to exert their therapeutic effects by inhibition of dopamine binding at postsynaptic dopamine receptors [14]. Ketamine may also inhibit neuronal uptake of dopamine as well as noradrenaline and serotonin [15].

Although two patients died post-operatively of concomitant severe disease unrelated to schizophrenia associated pathophysiology or to anaesthetic complications, neither exacerbation of psychosis nor changes in administered antipsychotic drugs were reported during the 1 month post-operative period. Judged by this evidence, it is suggested that DFK may be given safely and effectively to schizophrenic patients.

Since Matsuki *et al*. [16] reported an extremely high post-operative mortality in chronic schizophrenic patients, hazards of anaesthesia and surgery including unexpected cardio-respiratory collapse and post-operative paralytic ileus in such patients have been well recognized [17,18]. Autonomic nervous dysfunction was also demonstrated in patients using long term treatment with antipsychotic drugs [19]. Peri-operative cardiovascular instability may develop frequently in such patients [20]. DFK has advantages in terms of the least adverse effects on respiratory, cardiovascular, hepatic and kidney function [8] and therefore it would be a suitable anaesthetic choice for such patients.

It is therefore concluded that DFK can be given safely and effectively to schizophrenic patients because of the low incidence of adverse emergence reactions and psychotic deterioration, furthermore it maintains cardiovascular stability. Nonetheless appropriate perioperative management is mandatory in order to reduce the risk of mortality and morbidity in these patients.

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