Perioperative Management for Chronic Schizophrenic Patients

Akira Kudoh, MD, PhD

Department of Anesthesiology, Hirosaki National Hospital, Hirosaki, Japan

Schizophrenic patients are at increased risk for perioperative complications, as their biological response to stress is impaired. The increased complications are associated with physical disorders, antipsychotic or hazardous health behaviors, and interactions between antipsychotics and anesthetic drugs. Thus, anesthesiologists must not only be aware of the perioperative problems of these patients but must also learn how to manage their perioperative course.

(Anesth Analg 2005;101:1867–72)

Schizophrenia is a mental disease characterized by thought disorders, delusions, and hallucinations. It is the most common psychotic disorder, accounting for approximately 20% of all persons treated for mental illness. Schizophrenic patients are impaired in the biological response to stress, are at increased risk for medical illnesses such as cardiovascular and respiratory disease and diabetes mellitus (1), and present a variety of problems during anesthesia. Anesthesiologists may be confronted with the following problems: potential difficulties with patient communication, concomitant pathology associated with chronic schizophrenia, such as abnormalities of the endocrine, immune, and cardiovascular systems, and interactions between antipsychotic and anesthetic drugs. An increased mortality rate in the postoperative period for schizophrenic patients receiving chronic antipsychotic therapy has been demonstrated (2,3). Adverse responses during anesthesia include arrhythmias, hypotension, prolonged narcosis or coma, hyperpyrexia, postoperative ileus, and postoperative confusion (3). In addition, chronic schizophrenic patients lack pain sensitivity (4), and have pituitary-adrenal and autonomic nerve dysfunction (5,6), abnormalities of the immune system (7), and water intoxication (8). These alterations may influence postoperative outcome. This review provides a summary of perioperative problems and management for chronic schizophrenic patients.

Preoperative Problems and Management
Antipsychotics

Schizophrenia comprises paranoid, catatonic, disorganized, and undifferentiated subtypes (9). The subtypes of schizophrenia are defined by the predominant symptomatology at the time of evaluation and can change at subsequent evaluations. The presentation may include symptoms characteristic of more than one subtype (9). Antipsychotics used in the treatment of schizophrenia are determined by target symptoms, past responses, side effects, and patient preference (10). The antipsychotics include two major classes: dopamine receptor antagonists and serotonin-dopamine antagonists (10). Of dopamine receptor antagonists, haloperidol and fluphenazine tend to cause extrapyramidal symptoms or Parkinsonian syndrome and induce few autonomic actions such as ileus and hypotension. Chlorpromazine and thioridazine tend to cause confusion and hypotension (11). Serotonin-dopamine receptor antagonists produce fewer neurologic and endocrine adverse effects than do the dopamine receptor antagonists (10). Lanctot et al. (12) suggested that 21% of patients receiving antipsychotics had a serious side effect such as extrapyramidal symptoms, sedation or hypotension, and disturbances of the cardiovascular and autonomic nervous systems. Nearly half of schizophrenic patients have a comorbid medical condition owing to adverse effects of antipsychotic drugs and poor self-care such as increased smoking and alcohol consumption (1). Chronic schizophrenic patients have increased death rates resulting from cardiovascular disease, diabetes mellitus, tuberculosis, lung, kidney, and digestive diseases (2,13).

In the acute state such as hallucination or postoperative confusion, antipsychotics such as haloperidol are

administrated IM for treatment. A benzodiazepine may sometimes be needed to sedate the patients further (10).

Cardiovascular Disease

In one study, users of antipsychotics had a fivefold higher risk of myocardial infarction than control subjects (14). The increased incidence of cardiovascular disease in chronic schizophrenic patients is associated with increased body weight, diabetes mellitus, and frequent smoking (15). Weight gain is a common problem in patients receiving antipsychotics (16). Half of patients taking antipsychotics experience clinically significant weight gain (16). Schizophrenic patients are predisposed to developing diabetes mellitus because the antipsychotics can produce glucose intolerance by decreasing insulin action (2). Seventy-five percent of schizophrenics smoke compared with 26% of the general population (17). The frequent rate of smoking associated with schizophrenia may be related to the effect of nicotine on the neurobiology of schizophrenia because nicotine may alleviate psychotic symptoms in some patients (18).

Commonly observed electrocardiographic changes caused by antipsychotic drugs are prolongation of the QT and PR intervals and T-wave changes. Prolongation of QT interval is a marker for the ability of antipsychotic drugs to cause torsade de pointes (19). All antipsychotic drugs have the potential for torsade de pointes and sudden death. Risks are substantially higher for thioridazine and droperidol (20). Torsade de pointes and sudden death occurs in 10 to 15 of 10,000 patients in populations taking antipsychotic drugs, which is almost twice as often as in normal populations (20). Minor cardiovascular adverse effects such as postural hypotension and tachycardia are extremely common in schizophrenic patients taking antipsychotics (21). Postural hypotension leads to syncope with risk of injury and is associated with an increased risk of hip fracture (22).

Paralytic Ileus

Paralytic ileus is often encountered in chronic schizophrenic patients. This condition is caused by the anticholinergic and noradrenergic effect of antipsychotic drugs (23). As paralytic ileus is associated with the postoperative prognosis, chronic schizophrenic patients should be checked preoperatively by abdominal radiographs.

Pain Insensitive

There are some reports on changes in pain responsiveness in schizophrenic patients, many of whom do not complain of pain after abdominal surgery (24). Schizophrenic patients have an increased incidence of silent myocardial infarction (25). It has been reported that chronic schizophrenic patients have an increased threshold of C-fiber function, as measured with quantitative thermal and pain sensation, and $A\sigma$ and $A\beta$ fiber function, as measured with sensory-nerve conduction and quantitative vibratory evaluations (26). A dysregulation of N-methyl-D-aspartate (NMDA) receptor transmission in schizophrenic patients may account for pain insensitivity (27). Schizophrenia is associated with NMDA receptor hypofunction (28). Pain insensitivity in schizophrenic patients may also be a result of antipsychotics, as most antipsychotics have analgesic effects (29). Pain insensitivity may have life-threatening consequences because pain insensitivity can delay the diagnosis and treatment of illness. Delays in the initial diagnosis and treatment of illness in schizophrenic patients are partly responsible for many postoperative complications (9).

Preoperative Discontinuation of Antipsychotics

There is little published information describing whether antipsychotic drugs used as chronic treatment for schizophrenia should be continued or discontinued before anesthesia. The preoperative use of antipsychotics makes schizophrenic patients more susceptible to the hypotensive action of general anesthesia (3). On the other hand, discontinuation of antipsychotics may increase episodes of psychotic symptoms such as hallucinations and agitation. One report studied the effects of discontinuation of antipsychotics before surgery on perioperative outcome in chronic schizophrenic patients (30). Postoperative confusion in chronic schizophrenic patients who discontinued antipsychotics 72 h before surgery was significantly more frequent than in patients who continued antipsychotics (31% versus 14%) (30). The frequency of hypotension and arrhythmias during anesthesia did not significantly differ between chronic schizophrenic patients who preoperatively discontinued and those who continued antipsychotics (16% versus 18%). Therefore, the authors suggested that patients with chronic schizophrenia should continue their antipsychotics preoperatively.

Intraoperative Problems and Management
Anesthetics

Whether general or regional analgesia is best suited for schizophrenic patients remains controversial. Bronchospasm and persistent hypotension during spinal anesthesia were reported in a chronic schizophrenic patient (31). One report suggested that enflurane is unsuitable for schizophrenic patients because enflurane caused hypotension, arrhythmias, seizures,

and malignant hyperthermia in combination with antipsychotics (32). On the other hand, several studies reported that no schizophrenic patients developed severe hypotension, arrhythmias, or seizures under isoflurane or sevoflurane anesthesia (30,33–35).

Hemodynamics

The use of antipsychotics contributes to increased heart rate in schizophrenic patients (36). Therefore, the heart rate during anesthesia tended to increase in schizophrenic patients (5,37).

Hypotension caused by antagonistic effects of antipsychotics on α-adrenergic receptors is a symptom that occurs during and after anesthesia induction rather than during maintenance with inhaled anesthetics (23,38). Five to twenty percent of schizophrenic patients were reported to have episodes of profound hypotension during and after anesthesia induction (23,30). Schizophrenic patients treated with chlorpromazine are especially prone to develop hypotension after anesthesia induction (30). The risk factors for hypotension during anesthesia include increased age, use of antihypertensives, increased individual sensitivity to anesthetics, and the influence of the renin-angiotensin system. Therefore, it is important during anesthesia in schizophrenic patients to note the presence of risk factors and adjust anesthetic dose according to individual response.

Thermoregulation

Temperature regulation during anesthesia may be impaired in chronic schizophrenic patients because of the direct effect on hypothalamic thermoregulation caused by dopamine blockade with antipsychotics (39). One report showed that intraoperative core temperature in chronic schizophrenic patients was lower than in control patients. However, the frequency of postanesthesia shivering was not increased (40). Hypothermia may be an important factor affecting postoperative mortality and morbidity rates for schizophrenic patients. Kramer et al. (41) reported that 54 patients died from hypothermia associated with antipsychotic medication. Therefore, temperature monitoring and appropriate thermal management are especially helpful for chronic schizophrenic patients.

Ketamine

Ketamine has been thought to be unsuitable for schizophrenic patients because it can produce prolonged hallucinations or delirium after surgery (42). On the other hand, Ishihara et al. (43) reported that

14 chronic schizophrenic patients who were anesthetized with ketamine did not develop exacerbation of psychosis during the first postoperative month. We compared the frequency of postoperative confusion, or postoperative psychological state, between total IV anesthesia with ketamine, propofol, and fentanyl and anesthesia with sevoflurane, nitrous oxide, and fentanyl (44). The frequency of postoperative confusion in schizophrenic patients with total IV anesthesia with ketamine, propofol, and fentanyl was significantly less than that in schizophrenic patients with sevoflurane anesthesia (30% versus 54%) (44). The psychological state 4 days after surgery did not change compared to that before surgery or between patients treated with and without ketamine. Ketamine, when combined with propofol and fentanyl, is an appropriate anesthetic drug for chronic schizophrenic patients.

Endocrine Response

Schizophrenic patients have abnormalities in hypothalamic-pituitary-adrenal and autonomic nerve function, particularly in their response to stress (5,6). Use of antipsychotics decreases the plasma cortisol concentration (6). The plasma norepinephrine, adrenocorticotropic hormone (ACTH), and cortisol response to surgical stress in chronic schizophrenic patients was less than that in control patients (23,37). The decreased norepinephrine, ACTH, and cortisol response to surgical stress appears to be caused by antipsychotics.

Malignant Hyperthermia

There is an unusual side effect of the antipsychotics called neuroleptic malignant syndrome (NMS). This syndrome is characterized by acute increase of body temperature, muscle rigidity and autonomic nervous system instability. The prevalence of this disorder ranges between 0.02% and 2.4% of patients exposed to antipsychotics (38). The syndrome shares many clinical similarities with malignant hyperthermia (MH), which is triggered by inhaled anesthetics and succinylcholine. However, NMS is more benign than MH. The relationship between NMS and MH is important, but remains unclear. Abnormality in the Ca^{2+} release channel (ryanodine receptor) of the sarcoplasmic reticulum is considered to be the cause of MH. Miyatake et al. (45) reported that MH-susceptible mutations of the ryanodine receptor gene were not detected in NMS patients. Adnet et al. (46) suggested that there was no association between NMS and MH based on halothane-caffeine contracture studies. When patients with a history of NMS require anesthesia, it is unclear whether they should be anesthetized with the same precautions as patients susceptible to MH or not.

Postoperative Problems and Management

Psychological State

Molnar and Fava (47) suggested that surgical stress worsens the psychotic symptoms after surgery in schizophrenic patients. We also evaluated the preoperative and postoperative psychiatric state using Positive and Negative Syndrome Scale, which is a widely used method for the assessment of symptoms of schizophrenia (48). However, the psychological state before and after surgery did not significantly change in schizophrenic patients (48).

Ileus

Postoperative paralytic ileus is frequently encountered in chronic schizophrenic patients who undergo abdominal surgery and is a serious side effect in these patients (9,23,33). The frequency of postoperative ileus in chronic schizophrenic patients who underwent abdominal surgery was 28%, significantly more than the 5% in control patients who underwent abdominal surgery (23,33). Postoperative ileus after abdominal surgery is believed to be caused by sympathetic hyperactivity brought on by surgical stress (49). Epidural local anesthetics improve intestinal motility through blockade of both the spinal reflex and stress-related sympathetic hyperactivity. Whether epidural analgesia with local anesthetics minimizes postoperative ileus was studied in chronic schizophrenic patients who underwent lower abdominal surgery (33). The frequency of patients who did not pass flatus and feces for more than 120 h postoperatively was significantly less in chronic schizophrenic patients with epidural analgesia (33). Postoperative pain scores and postoperative plasma norepinephrine concentrations were significantly smaller in chronic schizophrenic patients with epidural analgesia. Thus, epidural analgesia with local anesthetics improved intestinal motility in chronic schizophrenic patients through both pain relief and inhibition of the sympathetic efferents.

Confusion

Schizophrenic patients are at greater risk of developing postoperative confusion than are normal patients (9). Postoperative confusion occurred in 28% of schizophrenic patients during the first 3 days after surgery, which was significantly more than the rate of 6% in control patients (34). Postoperative confusion in schizophrenic patients may be associated with increased cortisol (50) and norepinephrine (51) because psychological disturbances in schizophrenic patients have been extensively related to hypersecretion of cortisol (52). We studied the relationship between postoperative confusion and plasma norepinephrine

or cortisol response to surgery in chronic schizophrenic patients (34). Plasma norepinephrine and cortisol concentrations during and after surgery in such patients with postoperative confusion were significantly larger than those of chronic schizophrenic patients without confusion. We hypothesized that inhibiting the secretion of norepinephrine and cortisol with epidural injection of local anesthetics may contribute to a decrease in the occurrence of confusion in chronic schizophrenic patients. We studied the effect of epidural anesthesia on the frequency of postoperative confusion in chronic schizophrenic patients (35). However, epidural anesthesia did not decrease the frequency of postoperative confusion. On the other hand, the study showed that increased plasma interleukin-6 (IL-6) during and after surgery was involved in developing postoperative confusion in these patients. Thus, controlling inflammatory cytokines, as well as norepinephrine and cortisol concentrations, during and after anesthesia may be important on inhibiting the frequency of postoperative confusion in chronic schizophrenics.

Pain

Postoperative pain in chronic schizophrenic patients was studied (26) because pain responsiveness in such patients is impaired (24,25). Postoperative pain scores of chronic schizophrenic patients were significantly lower than those of control patients in the early period after surgery and postoperative analgesic consumption for pain relief was also reduced approximately 60% in chronic schizophrenic patients compared with control patients (26). Thus, chronic schizophrenic patients appear to be less sensitivity to postoperative pain. However, as postoperative pain is an important risk factor for postoperative confusion, adequate postoperative pain relief is needed in schizophrenic patients for preventing postoperative confusion.

Sudden Death

Sudden death in chronic schizophrenic patients is five times more frequent compared with the general population (53). Use of antipsychotics may be associated with sudden unexpected death. Cardiac arrhythmias such as QTc prolongation are the most common cause of sudden death in schizophrenic patients (19). Other potential causes of sudden death are aspiration resulting from excessive sedation, heat stroke, and NMS (54). Matsuki et al. (2) demonstrated an increased mortality rate in the postoperative period in schizophrenic patients receiving chronic phenothiazine therapy. They reported that 11 of 12 schizophrenic patients receiving chronic phenothiazine therapy died within the first 12 postoperative days and the deaths were attributable to a variety of causes, including cardiac complications, respiratory arrest, and complications

after a paralytic ileus. They proposed that the adverse effects were related to phenothiazine overdosing. Chute et al. (55) speculated that the etiology of sudden death may be the result of an imbalance between sympathetic and parasympathetic discharge resulting from an agitated mental state. Laposata et al. (56) described that agitated delirium in schizophrenic patients is associated with sudden death. Thus, when these patients develop postoperative confusion or agitation, one should consider the possibility of their sudden death.

Immune System

Increased rates of infectious disease have been demonstrated in schizophrenic patients (57). This may be a consequence of dysregulation of the immune system. Frequent rates of postoperative wound infection and pneumonia have been found in these patients (3). One study demonstrated that postoperative plasma IL-6 and IL-8 responses to surgery in chronic schizophrenic patients were significantly less than in control patients (58). The depressed cytokine response to surgical stress in chronic schizophrenic patients appeared to be related to antipsychotics and their pituitary-adrenal dysfunction. The suppressed immune response to surgery may lead to local and systemic infections and delayed wound healing.

Antidiuretic Hormone

Life-threatening water intoxication often occurs in chronic schizophrenic patients. Water intoxication is associated with vasopressin hypersecretion as a result of chronic administration of antipsychotics (8). The plasma vasopressin and atrial natriuretic peptide response to surgical stress in these patients was more intense than in control patients (59), and their plasma aldosterone response to surgery was less than in control patients (59). These findings suggest that these patients may develop postoperative water intoxication because of abnormal secretion of vasopressin, aldosterone, and atrial natriuretic peptide during anesthesia.

In conclusion, chronic schizophrenic patients are at increased risk for developing various perioperative complications. The prevention of perioperative complications is an important task for the clinician. Continuation of antipsychotic drugs before anesthesia and total IV anesthesia with ketamine, propofol, and fentanyl can decrease the incidence of postoperative confusion. Epidural analgesia with local anesthetics during and after anesthesia can decrease the occurrence of postoperative ileus in chronic schizophrenic patients.

References

1. Goldman LS. Medical illness in patients with schizophrenia. J Clin Psychiatry 1999;60(suppl 21):10–15.
2. Matsuki A, Oyama T, Izai S, et al. Excessive mortality in schizophrenic patients on chronic phenothiazine treatment. Agressologie 1972;13:407–18.
3. Kudoh A, Kimura F, Murakawa T, et al. Perioperative management of patients on long-term administration of psychotropic drugs [in Japanese]. Masui 1993;42:1056–64.
4. Dworkin RH, Clark WC, Lipsitz JD, et al. Affective deficits and pain insensitivity in schizophrenia. Motivation Emotion 1993; 17:245–76.
5. Kudoh A, Murakawa T, Ishihara H, et al. Autonomic nerve function and plasma catecholamine levels of perioperative patients treated with antipsychotic drugs [in Japanese]. Masui 1992;41:320–5.
6. Wik G. Effects of neuroleptic treatment on cortisol and 3-methoxy-4-hydroxyphenylethyl glycol levels in blood. J Endocrinol 1995;144:425–9.
7. Naudin J, Capo C, Giusano B, et al. A differential role for interleukin-6 and tumor necrosis factor in schizophrenia? Schizophr Res 1997;26:227–33.
8. Goldman MB, Robertson GL, Luchins DJ, et al. Psychotic exacerbations and enhanced vasopressin secretion in schizophrenic patients with hyponatremia and polydipsia. Arch Gen Psychiatry 1997;54:443–9.
9. Herz MI, Marder SR. Schizophrenia. Comprehensive treatment and management: diagnosis, course and outcome, and epidemiology. Philadelphia: Lippincott Williams Wilkins, 2002:21–34.
10. Sadock BJ, Sadock VA. Schizophrenia. In: Kaplan and Sadock's synopsis of psychiatry: behavioral sciences/clinical psychiatry, 9th ed. Philadelphia: Lippincott Williams Wilkins, 2003:471–504.
11. Zayas EM, Grossberg GT. Treatment of psychosis in late life. J Clin Psychiatry 1998;59(suppl 1):5–10.
12. Lanctot KL, Best TS, Mittman N, et al. Efficacy and safety of neuroleptics in behavioral disorders associated with dementia. J Clin Psychiatry 1998;59:550–61.
13. Baxter DN. The mortality experience of individuals on the Salford Psychiatric Case Register: I. All-case mortality. Br J Psychiatry 1996;168:772–9.
14. Davidson M. Risk of cardiovascular disease and sudden death in schizophrenia. J Clin Psychiatry 2002;63(suppl 9):5–11.
15. Kawachi I. Physical and psychological consequence of weight gain. J Clin Psychiatry 1999;60(suppl 21):5–9.
16. Baptista T. Body weight gain induced by antipsychotic drugs: mechanisms and management. Acta Psychiatr Scand 1999;100: 3–16.
17. de Leon J, Diaz FJ, Rogers T, et al. Initiation of daily smoking and nicotine dependence in schizophrenia and mood disorders. Schizophr Res 2002;56:47–54.
18. Glassman AH. Cigarette smoking: implications for psychiatric illness. Am J Psychiatry 1993;150:546–53.
19. Haddad PM, Anderson IM. Antipsychotic-related QTc prolongation, torsade de pointes and sudden death. Drugs 2002;62: 1649–71.
20. Glassman AH, Bigger JT Jr. Antipsychotic drugs: prolonged QTc interval, torsade de pointes, and sudden death. Am J Psychiatry 2001;158:1774–82.
21. Buckley NA, Sanders P. Cardiovascular adverse effects of antipsychotic drugs. Drug Saf 2000;23:215–28.
22. Ray WA, Griffin MR, Schaffner W, et al. Psychotropic drug use and the risk of hip fracture. N Engl J Med 1987;316:363–9.
23. Kudoh A, Ishihara H, Matsuki A. Pituitary-adrenal and parasympathetic function of chronic schizophrenic patients with postoperative ileus or hypotension. Neuropsychobiol 1999;39: 125–30.
24. Katz E, Kluger Y, Ravinovici R, et al. Acute surgical abdominal disease in chronic schizophrenic patients: a unique clinical problem. Isr J Med Sci 1990;26:275–7.

25. Dworkin RH. Pain insensitivity in schizophrenia: a neglected phenomenon and some implications. Schizophr Bull 1994;20:235–48.
26. Kudoh A, Ishihara H, Matsuki A. Current perception thresholds and postoperative pain in schizophrenic patients. Reg Anesth Pain Med 2000;25:475–9.
27. Javitt DC, Zukin SR. Recent advances in the phencyclidine model of schizophrenia. Am J Psychiatry 1991;148:1301–8.
28. Olney JW, Farber NB. Glutamate receptor dysfunction and schizophrenia. Arch Gen Psychiatry 1995;52:998–1007.
29. Patt RB, Proper G, Reddy S. The neuroleptics as adjuvant analgesics. J Pain Sympt Manag 1994;9:446–53.
30. Kudoh A, Katagai H, Takazawa T. Effect of preoperative discontinuation of antipsychotics in schizophrenic patients on outcome during and after anesthesia. Eur J Anaesth 2004;21:414–6.
31. Sawada N, Higashi K, Yanagi F, et al. Sudden onset of bronchospasm and persistent hypotension during spinal anesthesia in a patient on long-term psychotropic therapy [in Japanese]. Masui 1997;46:1225–9.
32. Vohra SB. Convulsions after enflurane in a schizophrenic patients receiving neuroleptics. Can J Anaesth 1994;41:420–2.
33. Kudoh A, Katagai H, Takazawa T. Effect of epidural analgesia on postoperative paralytic ileus in chronic schizophrenia. Reg Anesth Pain Med 2001;26:456–60.
34. Kudoh A, Takahira Y, Katagai H, Takazawa T. Schizophrenic patients developed postoperative confusion have increased norepinephrine and cortisol secretion. Neuropsychobiol 2002;46:7–12.
35. Kudoh A, Takase H, Takahira Y, et al. Postoperative confusion in schizophrenic patients is affected by interleukin-6. J Clin Anesth 2003;15:455–62.
36. Rechlin T, Claus D, Weis M. Heart rate variability in schizophrenic patients and changes of autonomic heart rate parameters during treatment with clozapine. Biol Psychiatry 1994;35:888–92.
37. Kudoh A, Kudo T, Ishihara H, et al. Depressed pituitary-adrenal response to surgical stress in chronic schizophrenic patients. Neuropsychobiol 1997;36:112–6.
38. Casey DE Side effect profiles of the new antipsychotic agents. J Clin Psychiatry 1996;57(2 suppl):40S–5.
39. Young DM. Risk factors for hypothermia in psychiatric patients. Ann Clin Psychiatry 1996;8:93–7.
40. Kudoh A, Takase H, Takazawa T. Chronic treatment with antipsychotics enhances intraoperative core hypothermia. Anesth Analg 2004;98:111–5.
41. Kramer MR, Vandijk J, Rosin AJ. Mortality in elderly patients with thermoregulatory failure. Arch Intern Med 1989;149:1521–3.
42. Dundee JW, Wyant G. Intravenous anaesthesia, 2nd ed. Edinburgh: Churchill Livingstone, 1988:152.
43. Ishihara H, Kudoh H, Murakawa T, et al. Uneventful total intravenous anaesthesia with ketamine for schizophrenic surgical patients. Eur J Anaesthesiol 1997;14:47–51.
44. Kudoh A, Katagai H, Takazawa T. Total intravenous anaesthesia with ketamine decrease incidence of postoperative psychosis emergence in schizophrenic patients. J Clin Anesth 2002;14:107–10.
45. Miyatake R, Iwahashi K, Matsushita M, et al. No association between the neuroleptic malignant syndrome and mutations in the RYR1 gene associated malignant hyperthermia. J Neurol Sci 1996;143:161–5.
46. Adnet PJ, Krivosic-Horber RM, Adamantidis MM, et al. The association between the neuroleptic malignant syndrome and malignant hyperthermia. Acta Anaesthesiol Scand 1989;33:676–80.
47. Molnar G, Fava GA. Intercurrent medical illness in the schizophrenic patients. In: Stoudemire A, Fogel BS eds. Principles of medical psychiatry. Orland: Grune & Stratton Inc, 1987:451.
48. Igarashi Y, Hayashi N, Yamashina M, et al. Interrater reliability of the Japanese version of the Positive and Negative Syndrome Scale and the appraisal of its training effect. Psychiatry Clin Neurosci 1998;52:467–70.
49. De Winter BY, Boeckxstaens GE, De Man JG, et al. Effect of adrenergic and nitrergic blockade on experimental ileus in rats. Br J Pharmacol 1997;120:464–8.
50. O'Keeffe ST, Devlin JG. Delirium and the dexamethasone suppression test in the elderly. Neuropsychobiol 1994;30:153–6.
51. van der Mast RC. Pathophysiology of delirium. J Geriatr Psychiatry Neurol 1998;11:138–45.
52. Ceskova E, Drybcak P, Hrobar P, et al. The changes of biological markers and treatment efficacy in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 2001;25:323–35.
53. Ruschena D, Mullen PE, Burgess P, et al. Sudden death in psychiatric patients. Br J Psychiatry 1998;172:331–6.
54. Tueth MJ. Emergencies caused by side effects of psychiatric medications. Am J Emerg Med 1994;12:212–6.
55. Chute D, Grove C, Rajasekhara B, et al. Schizophrenia and sudden death. A medical examiner case study. Am J Forensic Sci 1999;20:131–5.
56. Laposata EA, Hale P Jr, Poklis A. Evaluation of sudden death in psychiatric patients with special reference to phenothiazine therapy: forensic pathology. J Forensic Sci 1988;33:432–40.
57. Felker B, Yazel JJ, Short D. Mortality and medical cormorbidity among psychiatric patients: a review. Psychiatr Serv 1996;47:1356–63.
58. Kudoh A, Sakai T, Ishihara H, et al. Plasma cytokine response to surgical stress in schizophrenic patients. Clin Exp Immunol 2001;125:89–93.
59. Kudoh A, Kudo M, Ishihara H, Matsuki A. Increased plasma vasopressin and atrial natriuretic peptide in chronic schizophrenic patients during abdominal surgery. Neuropsychobiol 1998;37:169–74.