CASE REPORT

Schizophrenia and anaesthesia

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SUMMARY

Administering anaesthesia for elderly patients with chronic schizophrenia has always been a great challenge to anaesthetists. These patients will usually be on multiple antipsychotic drugs for many years and may lead to delayed awakening, cardiovascular instability, arrhythmias and sudden cardiac death during general anaesthesia. This case report is about the perioperative anaesthetic management of an elderly schizophrenic patient undergoing removal of femur implant. This article will explore important drug interactions and available options for a successful anaesthesia.

BACKGROUND

Schizophrenia is the most common mental disorder, accounting for approximately 20% of all mental illnesses. Patients usually present with thought disorders, delusions and hallucinations. Schizophrenic patients also have an impaired response to stress, and that increases the risk for chronic medical illnesses such as cardiovascular, respiratory and endocrine diseases. Anaesthesiologists may be confronted with potential difficulties when communicating to patients and some uncooperative patients may present with an aggressive behaviour.

This case report discusses the anaesthetic management of an elderly catatonic schizophrenia patient with a history of neuroleptic malignant syndrome (NMS), who presented for an elective surgery.

CASE PRESENTATION

An 82-year-old man, weighing 62 kg with a height of 165 cm, was admitted to the surgical ward for removal of implant from his right femur. He has a history of schizophrenia, hypertension and dyslipidaemia, and was planned for general anaesthesia. He was diagnosed with catatonic schizophrenic 40 years ago and had a history of NMS due to antipsychotic drugs, which had been managed symptomatically then. He was under psychiatric follow-up and was on tablet risperidone 4 mg once a day.

With a blood pressure of 110/62 mm Hg, the patient was agitated, uncooperative and violent when approached by healthcare providers, making all physical examination, insertion of intravenous catheter and urinary catheter impossible. Preoperative blood investigations were within normal limits. His ECG was normal, and his echocardiogram ejection fraction was 65% with no other abnormality detected. His psychiatrist was not keen to increase the dose of antipsychotic medication or to add any newer medication at the moment due to history of NMS.

Due to the absence of close family members, an informed consent was taken from two medical consultants in the operating theatre. Anaesthesia was induced with a mixture of oxygen-sevoflurane as an intravenous access was not obtained due to his uncooperativeness. Monitors were attached for pulse rate, blood pressure, ECG, oxygen saturation, temperature and end-tidal carbon dioxide. Two 20 G intravenous access lines were inserted on both upper extremities after loss of unconsciousness.

Intravenous fentanyl, propofol and rocuronium were administered during induction of anaesthesia. Airway was secured with endotracheal tube size 7.0. Anaesthesia was maintained with oxygen-sevoflurane mixture. Injection dexamethasone was given for prevention of postoperative nausea and vomiting. During anaesthesia, the patient's blood pressure, pulse rate and oxygen saturation were within normal limits. Adequate precautions were taken to maintain normothermia. Estimated blood loss during the surgery was <500 mL. Intravenous paracetamol and tramadol were administered for postoperative analgesia. The entire operation lasted 2 hours 30 min, with no untoward events intraoperatively. Anaesthesia was reversed with intravenous neostigmine and glycopyrrolate.

In the postoperative recovery room, oxygen was given with Hudson's mask at 5 L/min. When the patient woke up, he was agitated and attempted to pull out his intravenous access and surgical dressings. However, a single bolus of intravenous fentanyl 50 μg was administered and the patient remained calm after that. He was in the recovery room for 2 hours.

OUTCOME AND FOLLOW-UP

Tablet diclofenac 50 mg and soluble tablet tramadol 50 mg were given every 8 hours for pain relief for the next two weeks after surgery. The patient was discharged back to the psychiatric hospital for further nursing care.

DISCUSSION

Administering anaesthesia to schizophrenics poses a great challenge because of the presence of an impaired biological response to stress and an increased risk for medical illnesses involving the cardiovascular and respiratory system.[1] Preoperatively, anaesthetists may be confronted with difficulties in patient communication, cooperation and obtaining informed consent similar to what we had experienced. Concomitant medical conditions associated with elderly and chronic schizophrenics as well as interaction between antipsychotics and anaesthetic agents have to be considered, especially

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antipsychotic agents, which are serotonin and dopamine receptor blockers.

Antidepressants such as phenelzine (Nardil), isocarboxazid (Marplan) and tranylcypromine (Parnate) are all irreversible inhibitors of monoamine oxidase-A (MAO-A) and monoamine oxidase-B (MAO-B). Chronic usage of such medication may lead to pronounced effects on the metabolism of endogenous (serotonin, dopamine and norepinephrine) and exogenous (tyramine) monoamines. Selegiline, on the other hand, is a selective MAO-B inhibitor. Since serotonin is deaminated by MAO-A, the risk of serotonin syndrome is lower in patients taking selegiline.[2] If the monoamine oxidase inhibitor (MAOI) is planned to be discontinued prior to anaesthesia, the doses should be titrated down gradually and regular psychiatric review will be necessary. The extent of surgery, patient's physical state, mode of anaesthesia, the risk of withdrawal symptoms and psychiatric illness relapse should be considered when doing so.

All phenylpiperidine opioids (meperidine, methadone, tramadol) are weak serotonin reuptake inhibitors and may lead to serotonin syndrome caused by excessive serotonergic stimulation of the 5-HT1A receptor.[2] Serotonin syndrome will present with confusion, fever, diaphoresis, shivering, ataxia, myoclonus, hyper-reflexia and possible death. Benzodiazepine premedication can be served and may help to avoid possible sympathetic stimulation. However, pethidine (meperidine) and indirect acting sympathomimetics (eg, ephedrine) would be best avoided.

An uncommon, life-threatening side effect of these antipsychotic agents is NMS, characterised by an acute increase in body temperature, muscle rigidity, fever, autonomic nervous system instability (unstable blood pressure, diaphoresis) and sudden changes in mental status (agitation, delirium or coma). These symptoms may last from hours to weeks. NMS is caused by a sudden, marked reduction in dopamine activity, either from withdrawal of dopaminergic agents or from blockade of dopamine receptor D_2 and D2-like (D3 and D4) receptors in the hypothalamus, nigrostriatal and spinal pathways, which results in abnormal thermoregulation and muscle rigidity.[3] Prevalence is between 0.02% and 2.4%.[4] Causative drugs of NMS include butyrophenones (eg, haloperidol and droperidol), phenothiazines (eg, promethazine and chlorpromazine), atypical antipsychotics (eg, clozapine, olanzapine, risperidone and ziprasidone), antiemetic (eg, metoclopramide), amoxapines, lithium, desipramine, phenelzine and abrupt reduction or withdrawal of levodopa or carbidopa for Parkinson's disease.[5 6] NMS was first described by Delay and Colleagues in 1960[7] after the introduction of neuroleptics into medical practice. It was described as 'akinetic hypertonic syndrome'. Differential diagnoses to be considered are serotonin syndrome, encephalitis, toxic encephalopathy, status epilepticus, heat stroke, malignant hyperthermia (MH), cocaine use and amphetamine overdose.[8] It is interesting to know that MH and NMS share the same pathophysiology. Hence, the possibility of developing MH should be considered when administering general anaesthesia to patients with chronic schizophrenia with risk of NMS.[9 10] Therefore, drugs such as droperidol, succinylcholine, haloperidol and metoclopramide should be used with caution.

We used volatile induction and maintenance of anaesthesia with sevoflurane. In the recent years, there has been particular interest in anaesthesia for the elderly, in which sevoflurane has demonstrated to provide a greater cardiovascular stability compared with propofol.[11 12] Sevoflurane also produced a lesser reduction in left ventricular mechanical performance.[13] The anaesthetic agent employed is probably less important than the manner of its use, but inhalational induction may be the technique of choice when trying to provide a stable induction in elderly patients with a questionable cardiovascular reserve.

Patients on antipsychotics may often have an increased heart rate and a risk of hypotension. We also kept in mind other adverse responses such as arrhythmias, prolonged QT, silent MI, hypotension, hyperpyrexia, prolonged narcosis, water intoxication and glucose intolerance. Drugs with minimal haemodynamic alteration should be preferred and titrated accordingly.

Schizophrenic patients have higher pain thresholds due to hypo-functioning *N*-methyl D-aspartate receptors[14] and a decreased conduction by C fibres. As postoperative pain may present as a risk for confusion, therefore controlling inflammatory cytokines, norepinephrine and cortisol levels during and after anaesthesia is imperative. Laposata *et al* noted that agitated delirium in schizophrenics is associated with sudden death.[15] Chute *et al* speculated that the aetiology of this sudden death may be due to an agitated mental state resulting in imbalances between sympathetic and parasympathetic discharge.[16] For this reason, antipsychotic medication should be continued perioperatively as an abrupt withdrawal may result in recurrence of psychotic symptoms[17] and an increased incidence of postoperative confusion. However, these medications must be given with precaution as these drugs may potentiate the hypotensive and sedative effects of general anaesthetic agents.[18]

Hypothermia may itself precipitate cardiac events. Therefore, normothermia should be maintained by adequate warming. All inhalational anaesthetic agents are relatively safe with the exception of enflurane, which carries a higher risk of hypotension, arrhythmias, seizures and malignant hyperthermia in schizophrenic patients who are taking antipsychotics.[19] All routinely using intravenous induction anaesthetic agents are acceptable in patients except ketamine as it may cause prolong hallucinations and delirium after surgery.[20] However, interestingly a study done by Kudoh concluded that the frequency of postoperative confusion in schizophrenic patients with ketamine, propofol and fentanyl was significantly less than sevoflurane anaesthesia (30% vs 54%).[21]

For perioperative pain management, opioids and non-steroidal anti-inflammatory drug may be routinely used. Our patient was already taking oral tramadol 50 mg occasionally in the ward prior to surgery. No adverse effects were noted during that time. Therefore, we chose tramadol as our analgesic. Tramadol works directly on the brain's central nervous system. Long-term abuse may create many adverse effects, including seizures and serotonin syndrome. Tramadol addiction can also increase the risk of schizophrenia because it alters the brain's chemistry, which leads to other mental health disorders like depression, anxiety disorders, bipolar disorder and psychosis.

Ondansetron, an anti-emetic, may cause QT interval prolongation.[22] Metoclopramide, on the other hand, may cause extra pyramidal side effects (EPS).[23] It is best to avoid these medication in schizophrenic patients. Paralytic ileus is another complication caused by the anticholinergic and noradrenergic effects of antipsychotic drugs. A high index of suspicion should be present during the perioperative period. However, epidural analgesia in abdominal and lower limb surgery can reduce the incidences of postoperative paralytic ileus and should be incorporated in appropriate surgeries.[24]

Surgical stress may also worsen the psychotic symptoms and postoperative delirium after surgery in schizophrenic patients.[1] It is believed to be due to hypersecretion of cortisols and norepinephrine. Administration of intravenous haloperidol 0.5–2 mg is preferable to reduce this problem. Haloperidol antagonises the D_2 receptors in the higher nervous pathway, leading to

restoration of hippocampal function and reversing hallucination.[25] However in hypoactive delirium, it can worsen the symptoms due to dopamine deficiency. Intravenous haloperidol is less likely to produce extrapyramidal symptoms compared with intramuscular or oral haloperidol.[26] The side effects of haloperidol includes torsades de pointes, MH and EPS.

Fatal water intoxication may also occur in chronic schizophrenic patients as a result of vasopressin hypersecretion.[27] Sudden death in chronic schizophrenic patients is five times more frequent compared with the general population.[28]

In summary, the goal of the anaesthesiologist is to prevent perioperative mortality, physical morbidity, withdrawal problems and acute or relapse of psychiatric illness. Selective serotonin reuptake and tricyclic antidepressant should be continued throughout perioperative period. Careful consideration is required for patients on MAOIs. Pethidine and indirectly acting sympathomimetics are absolutely contraindicated in patients on MAOIs.

Learning points

- Since schizophrenia is not an uncommon psychiatric problem, performing anaesthesia for patients with schizophrenia is inevitable.
- A sound knowledge of pharmacology and drug interaction is of utmost important especially in patients with schizophrenia.
- Neuroleptic malignant syndrome is an uncommon but life-threatening condition which must always be remembered when anaesthetising patients with schizophrenia.

Contributors All authors have contributed sufficiently to the project and have met all criteria to be included as authors.

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