

Psychiatric patient and anaesthesia

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ABSTRACT

Many patients with psychiatric illnesses are prescribed long-term drug treatment, and the anaesthesiologist must be aware of potential interactions with anaesthetic agents. Psychotropic drugs often given in combination with each other or with other non-psychiatric drugs generally exert profound effects on the central and peripheral neurotransmitter and ionic mechanisms. Hence, prior intake of these drugs is an important consideration in the management of the patient about to undergo anaesthesia and surgery. This article highlights the effects of anaesthetics on patients taking antipsychotics, tricyclic antidepressants, monoamine oxidase inhibitors and lithium carbonate. The risk that should be considered in the perioperative period are the extent of surgery, the patient's physical state, anaesthesia, the direct and indirect effects of psychotropics, risk of withdrawal symptoms and risk of psychiatric recurrence and relapse.

Key words: Anaesthetic management, antidepressants, bipolar disorders, depression, schizophrenia

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INTRODUCTION

Psychiatric 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 behaviour and interactions between antipsychotics and anaesthetic drugs. Thus, the anaesthesiologist must not only be aware of the dose adjustment of the anaesthetic agents but also learn how to manage their perioperative course.^[1] For example, patients with hysteria require less anaesthetic agents than those with neurotic depression or anxiety state. Similarly, organic psychosis requires less than acute functional psychosis, which in turn require less than chronic psychosis.

Anaesthesiologists may be confronted with many potential difficulties, such as communication with patient, concomitant pathology associated in chronic psychiatric patients and abnormalities of the endocrine, immune and cardiovascular systems. An increased mortality rate in the post-operative period for psychotic patients receiving chronic antipsychotic therapy has been demonstrated. Adverse responses

during anaesthesia include arrhythmias, hypotension, prolonged narcosis or coma, hyperpyrexia, post-operative ileus and post-operative confusion. In addition, chronic psychotic patients lack pain sensitivity and have pituitary–adrenal and autonomic nervous dysfunction, abnormalities of the immune system and water intoxication. These alterations may influence the post-operative outcome.^[2-6] We will discuss some of the common psychiatric disorders and their management as follows.

DEPRESSION DISORDERS

Depression is the most common psychiatric disorder, affecting 10–20% of the population, and is characterized by sadness and pessimism. Its cause is multifactorial, but pharmacological treatment is based on the presumption that its manifestations are due to a brain deficiency of dopamine, norepinephrine and serotonin or altered receptor activities. Up to 50% of the patients with major depression hypersecrete cortisol and have abnormal circadian secretion.^[7]

Antidepressants can be divided into four groups: Tricyclic antidepressants (TCA), selective serotonin

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re-uptake inhibitors, atypical agents and monoamine oxidase inhibitors (MAOIs). Atypical antidepressants include venlafaxine and mirtazapine. Both these drugs should be continued throughout the perioperative period.

About 70–80% of the patients respond to antidepressant medications, and at least 50% who do not respond to antidepressant do respond favourably to electroconvulsive therapy (ECT). ECT is increasingly used for refractory and severe cases.

DISCONTINUATION SYNDROME

Abrupt cessation of antidepressants is associated with the risk of developing withdrawal symptoms, known as discontinuation syndrome. The common symptoms are nausea, abdominal pain and diarrhoea, sleep disturbance, somatic symptoms (sweating, lethargy and headache) and, finally, affective symptoms (low mood, anxiety and irritability). These reactions start abruptly within a few days of stopping the antidepressant, are short lived (a few days to 3 weeks) and end if the antidepressant is reintroduced.^[8,9]

TCA

Before the availability of selective serotonin reuptake inhibitors (SSRIs), TCAs were the most commonly used drugs for treating depression. Drugs in this group include amitriptyline, imipramine, desipramine, doxepin, nortriptyline and others. Desipramine and nortriptyline are used as tricyclic antidepressant as they are less-sedating. TCAs are thought to affect depression by inhibiting synaptic reuptake of norepinephrine and serotonin. However, they also affect other neurochemical systems including histaminergic and cholinergic systems. Consequently, they have a large range of side-effects, including postural hypotension, cardiac dysrhythmias, urinary retention, dry mouth, blurred vision and sedation.^[1,7,9]

Given chronically, these drugs decrease stores of noradrenergic catecholamines. They can cause changes on the ECG (changes in the T wave, widening of the QRS complex and prolongation of QT interval, bundle branch block or other conduction abnormalities, or PVCs). Ventricular arrhythmias and refractory hypotension may occur in higher doses.

Management of anaesthesia for a patient on TCA

Patients being treated with TCA may have altered

responses to drugs administered during the perioperative period. Increased availability of neurotransmitters in the central nervous system can result in increased anaesthetic requirements. TCAs may result in increased response to intraoperatively administered anticholinergics, and those that cross the blood–brain barrier, such as atropine, may cause postoperative confusion. Likewise, increased availability of norepinephrine at the post-synaptic nervous system can be responsible for exaggerated blood pressure responses following administration of indirect acting vasopressors such as ephedrine. The most important interaction between anaesthetic agents and tricyclic antidepressant drugs is an exaggerated response to both indirect acting vasopressors and sympathetic stimulation. Pancuronium, ketamine, meperidine and epinephrine containing solutions should be avoided. There are two hazardous drug interaction risks to be avoided: The direct effect on the cardiac system and the interactions with anaesthetic drugs regulating the cardiovascular system.^[7,9]

Chronic therapy with tricyclic antidepressant drugs depletes cardiac catecholamines, potentiating the cardiac depressant effects of anaesthetic agents. During anaesthesia and surgery, it is important to avoid stimulating the sympathetic nervous system. If hypotension occurs and vasopressors are needed, direct acting drugs such as phenylephrine are recommended. The dose should probably be decreased to minimize the likelihood of an exaggerated hypertensive response.

SSRIs

SSRIs comprise the most widely prescribed class of antidepressants, and are the drugs of choice to treat mild to moderate depression. SSRIs block reuptake of serotonin at the pre-synaptic membranes, with relatively little effect on adrenergic, cholinergic, histaminergic or other neurochemical systems. As a result, they are associated with few side-effects. Examples include fluoxetine, paroxetine and sertraline.

Among SSRIs, fluoxetine is a potent inhibitor of certain hepatic cytochrome P-450 enzymes. Their principal side-effects are headache, agitation and insomnia. As a result, this drug may increase the plasma concentration of drugs that depend upon hepatic metabolism for clearance, such as warfarin, theophylline, phenytoin and benzodiazepines. Some cardiac antidysrhythmic drugs are also metabolized by this enzyme system, and fluoxetine inhibition of the enzyme system may result in potentiation of their effects.^[1,7,9]

SSRIs should be continued throughout the perioperative period to prevent discontinuation syndrome. Avoid the use of pethidine, tramadol, pentazocine and dextromethorphan.

Serotonin syndrome

Serotonin syndrome is a potentially life-threatening adverse drug reaction that results from increased serotonin levels in the brain stem and spinal cord. A large number of drugs have been associated with the serotonin syndrome. These include SSRI, MAOI, TCAs, pethidine, tramadol and dextromethorphan.

Clinical features of this syndrome include changes in behaviour (agitation and confusion), increased motor activity and autonomic instability (hyperthermia, tachycardia, labile blood pressure and diarrhoea). Seizures, rhabdomyolysis, renal failure, arrhythmias, coma and death may occur.

MAOIs

They are used for resistant cases of depression due to the incidence of side-effects. The irreversible MAOIs, tranylcypromine and phenelzine, and the selective and reversible MAOIs, moclobemide, act by inhibition of the metabolic breakdown of norepinephrine and serotonin by the MAO enzyme. Therefore, the level of norepinephrine and serotonin is increased at the receptor site. All MAOIs are eliminated by hepatic metabolism.^[1,7,9]

Interactions between MAOIs and anaesthetic drugs

Hazardous interactions in both reversible and irreversible MAOIs and anaesthesia have been reported. There are two distinct types of reaction that can occur between MAOIs and opioids.

Type I (excitatory) reactions occur in patients given pethidine and dextromethorphan, both of which inhibit serotonin reuptake. The features are those of serotonin syndrome. Therefore, pethidine and dextromethorphan remain contraindicated. Other opioids like morphine, fentanyl, alfentanil and remifentanyl can all be used safely.

Type II (depressive) reaction, which is very rare, is thought to be due to MAO inhibition of hepatic enzymes resulting in enhanced effects of all opioids. It is reversed by naloxone.

Indirect acting sympathomimetics may precipitate potentially fatal hypertensive crisis and are absolutely

contraindicated with any MAOIs. Direct acting sympathomimetics (adrenaline, noradrenaline and phenylephrine) may have an enhanced effect due to receptor hypersensitivity. Therefore, dosages should be titrated. Phenelzine decreases plasma cholinesterase concentration and prolongs the action of suxamethonium. Pancuronium should be avoided as it releases stored noradrenaline.

MAOIs may cause a reduction in the hepatic metabolism of barbiturates, resulting in reduction of dose requirement of thiopentone. Propofol and etomidate can be used safely. Ketamine should be avoided as it causes sympathetic stimulation. Local anaesthetics containing adrenaline should be used with caution. Benzodiazepines, inhalational anaesthetic agents, anticholinergic drugs and non-steroidal anti-inflammatory drugs can be used safely in patients taking MAOIs.^[1,7,9]

Anaesthesia for a patient on MAOIs

The decision to stop MAOIs therapy pre-operatively for elective surgery should be made in advance on an individual basis after discussion between the anaesthesiologist, psychiatric team and patient. Although continuation of MAOIs carries risks, by careful anaesthetic technique, these risks can be minimized and must be balanced against the risks of relapse and discontinuation syndrome.

If the MAOI is to be stopped, the doses should be reduced gradually and with regular psychiatric review. Cancellation of surgery should be avoided and treatment restarted as soon as possible post-operatively. In a patient on MAOIs or in the emergency situation, benzodiazepine premedication can be given and sympathetic stimulation should be avoided. Adequate hydration of the patient should be ensured. Hypotension should be treated initially with intravenous fluids and then with cautious doses of phenylephrine. Pethidine and indirect acting sympathomimetics are absolutely contraindicated.^[1,7,9]

BIPOLAR DISORDERS

Bipolar disorder is characterized by marked mood swings from depressive episodes to manic episodes with normal behaviour in between these episodes. Valproate is the drug of choice for treating acute episodes. Mood stabilizers are used to treat bipolar affective disorders. Lithium and valproate remain a mainstay of treatment. In some cases, olanzapine and

other antipsychotics are also used in the beginning of treatment to control excitement and agitation.

Lithium inhibits the release of thyroid hormones and results in hypothyroidism. Lithium is eliminated by the kidneys and, therefore, if renal function is compromised or there is dehydration, lithium levels rise dramatically. Toxic blood concentration produces confusion, sedation, muscle weakness tremors and slurred speech. Cardiac problems may include sinus bradycardia, sinus node dysfunction, AV block, T wave changes, hypotension and ventricular irritability. Lithium toxicity occurs when levels are >1.5 mmol/L, and is exacerbated by dehydration, diuretics and renal impairment.^[7,9]

Lithium carbonate is used to treat manic depression, but it is more effective in preventing mania than in relieving depression. Lithium prolongs neuromuscular blockade and may decrease anaesthetic requirements because it blocks brainstem release of norepinephrine, epinephrine and dopamine.^[7,9]

Drug interactions with lithium

Thiazide diuretics reduce the clearance of lithium by the kidneys. Non-steroidal anti-inflammatory drugs may increase the lithium levels up to 40%, which can result in toxicity. Angiotensin converting enzyme inhibitors not only reduce the excretion of lithium but may also cause renal failure.

Management of bipolar cases

Lithium's direct effects cause hazardous risks in surgery. This is specifically true when haemodynamic instability occurs and renal excretion becomes impeded through interference with sodium and potassium metabolism. Therefore, lithium discontinuation is recommended. Lithium can be stopped at once because no withdrawal symptoms occur. Taking a half-life of 24–36 h into account, lithium should be discontinued 72 h before surgery.

Sodium depletion decreases renal excretion of lithium and can lead to lithium toxicity. To prevent significant renal absorption of lithium, it is reasonable to administer sodium-containing IV fluids during the perioperative period. Stimulation of urine output with thiazide diuretics must be avoided. ECG monitoring should be done to monitor various cardiac abnormalities due to lithium. The association of sedation with lithium suggests that anaesthetic requirement may be decreased in these patients. Duration of both depolarizing and non-depolarizing

muscle relaxants may be prolonged in the presence of lithium; therefore, neuromuscular monitoring should be used.

In the post-operative period, when the patient has normal ranges of potassium, sodium and creatinine, is haemodynamically stable, able and allowed to drink, lithium should be restarted, with control of blood levels within 1 week. This is most important because the psychiatric risk of recurrence or relapse is hazardous.^[1,7,9] The only reason not to stop lithium is minor surgery with local anaesthesia.

SCHIZOPHRENIA

It is the major psychotic mental disorder. It is characterized by abnormal reality testing or thought process. This disorder has multifactorial aetiology and is thought to be related to an excess of dopaminergic activity in the brain. Its exact aetiology is yet to be established. Antipsychotic drugs used are classified into two groups:

Neuroleptic or typical antipsychotics (chlorpromazine, haloperidol, trifluoperazine) cause extrapyramidal side-effects like acute dystonia, akathisia, Parkinsonism and tardive dyskinesia.

Atypical antipsychotics (clozapine, olanzapine, risperidone, amisulpiride, quetiapine and aripiprazole), which do not have a tendency to cause extrapyramidal side-effects. They act via the D2 receptor blockade, but also act on other receptors like histamine (H1), serotonin (5HT₂), acetylcholine (muscarinic) and alpha adrenergic receptors. Clozapine causes seizures and neutropenia. Weight gain, postural hypotension and gynaecomastia are also very common with antipsychotic drugs.

The pre-operative use of antipsychotics makes schizophrenic patients more susceptible to the hypotensive action of general anaesthesia.^[3] On the other hand, discontinuation of antipsychotics may increase the episodes of psychotic symptoms such as hallucinations and agitation. Therefore, patients with chronic schizophrenia should continue their antipsychotics pre-operatively as abrupt withdrawal may result in recurrence of psychotic symptoms.^[10]

Anaesthetic problems and management in patients with schizophrenia

Antipsychotic drugs remain the only effective treatment for controlling this disease. For the anaesthesiologists, important effects of antipsychotic drugs include

α -adrenergic blockade causing postural hypotension, prolongation of QT intervals, seizures, hepatic enzyme elevation, abnormal temperature regulation, sedation and Parkinsonism-like manifestations. Drug-induced sedation may decrease anaesthetic requirement.

Anaesthetics, whether general or regional anaesthesia, whatsoever are best suited for schizophrenic patients remains controversial. Bronchospasm and persistent hypotension during spinal anaesthesia were reported in a chronic schizophrenic patient.^[11] Lanctot *et al.*^[12] suggested that 21% of the patients receiving antipsychotics had a serious side-effect, such as extrapyramidal symptoms, sedation or hypotension, and disturbances of the cardiovascular and autonomic nervous systems. Minor cardiovascular adverse effects such as postural hypotension and tachycardia are extremely common in schizophrenic patients taking antipsychotics.^[13] The heart rate during anaesthesia tends to increase in schizophrenic patients due to the use of antipsychotic drugs.^[5,14] Schizophrenic patients treated with chlorpromazine are especially prone to develop hypotension after anaesthesia induction.^[10] The risk factors for hypotension during anaesthesia include increased age, use of antihypertensives, increased individual sensitivity to anaesthetics and the influence of the renin-angiotensin system. Therefore, it is important during anaesthesia to note the presence of risk factors and adjust the anaesthetic dose according to individual response. Ketamine should probably be avoided as antipsychotics decrease the seizure threshold.^[7,9]

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] Antipsychotics can produce glucose intolerance by decreasing insulin action.^[2] Commonly observed electrocardiographic changes caused by antipsychotic drugs are prolongation of the QT and PR intervals and T wave changes. Torsades de pointes and sudden death occurs in 10–15 of 10,000 patients taking antipsychotic drugs, which is almost twice as often as in normal populations.^[17] Paralytic ileus is caused by the anticholinergic and noradrenergic effect of antipsychotic drugs.^[18]

There are some reports on changes in pain responsiveness in schizophrenic patients, many of whom do not complain of pain after abdominal surgery. Pain insensitivity in schizophrenic patients may also

be a result of antipsychotics, as most antipsychotics have analgesic effects.^[19]

Temperature regulation during anaesthesia may be impaired in chronic schizophrenic patients because of the direct effect on hypothalamic thermoregulation caused by dopamine blockade with antipsychotics.^[20] Therefore, temperature monitoring and appropriate thermal management are especially helpful for chronic schizophrenic patients. Schizophrenic patients have abnormalities in the hypothalamic-pituitary-adrenal and autonomic nerve function, particularly if there is no response to stress. Use of antipsychotic decreases the plasma cortisol concentration.

Post-operative problems and management

Molnar and Fava^[21] suggested that surgical stress worsens the psychotic symptoms after surgery in schizophrenic patients. Schizophrenic patients are at greater risk of developing post-operative confusion than are normal patients. It is associated with increased cortisol^[22] and norepinephrine,^[23] because psychological disturbances in schizophrenic patients have been extensively related to hypersecretion of cortisol. Increased rate of infectious disease have been demonstrated in schizophrenic patients. This may be a consequence of dysregulation of the immune system. 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.^[6]

NEUROLEPTIC MALIGNANT SYNDROME

Neuroleptic Malignant Syndrome is a rare but potentially life-threatening, neurological disorder that is most often caused by an adverse reaction to neuroleptic or antipsychotic drugs. The incidence is estimated to range from 0.02 to 2.4% with conventional antipsychotics. It causes acute hyperthermia, muscular rigidity, altered mental status, elevated creatinine phosphokinase and autonomic dysfunction. Awareness of diagnosis, cessation of medication, early medical intervention and consideration of specific remedies can reduce morbidity and mortality when Neuroleptic Malignant Syndrome occurs.^[7,24]

Patients should be treated in the intensive care unit. Dantrolene is used along with supportive treatment. Despite the clinical similarities with malignant hyperthermia, there is no proven association between the two conditions.

Tramadol and psychiatric drugs

The use of tramadol in patients taking antipsychotic drugs is of particular interest as tramadol may itself cause psychiatric symptoms, e.g. altered mood (elation or dysphoria), hallucinations, confusion, sleep disturbance and nightmares. Tramadol may precipitate the serotonin syndrome when combined with antidepressant medication, which raise the level of this transmitter.

When combined with antipsychotics, selective serotonin re-uptake inhibitors or TCA, tramadol reduces the seizure threshold. Carbamazepine induces the metabolism of tramadol and, therefore, co-administration of these drugs leads to reduced efficacy of tramadol.^[25]

CONCLUSION

The focus of the anaesthesiologist should be on risk management to prevent perioperative mortality, physical morbidity, withdrawal problems and acute or long-term relapse of psychiatric illness, thereby preventing last minute cancellation of surgery. Selective serotonin re-uptake and TCA should be continued throughout the perioperative period to avoid discontinuation syndrome. Careful planning is required for patients on MAOIs. Opioids like pethidine and indirectly acting sympathomimetics are absolutely contraindicated in patients on MAOIs. Mood stabilizers and antipsychotic drugs should be continued throughout the perioperative period to avoid the risk of relapse. The prevention of perioperative and post-operative complications is an important task for the anaesthesiologist.

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