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(CASE REPORT)

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Antipsychotics and anesthetic drugs

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Abstract

Psychiatric illness is common, affecting up to 10% of the population, with around 1% diagnosed with a major psychiatric disorder. An increased mortality rate in the postoperative period for schizophrenic patients receiving chronic antipsychotic therapy has been demonstrated. According to the Diagnostic and Statistical Manual of Disease, schizophrenia-associated psychotic disorders are characterized by disturbances in emotional, behavioral and cognitive arenas, impeding on nearly every aspect of life functioning in the form of thought disorders, delusions and hallucinations. Chronic schizophrenic patients lack pain sensitivity, and have pituitary-adrenal and autonomic nerve dysfunction, abnormalities of the immune system, and water intoxication. These alterations may influence postoperative outcome. 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. The increased complications are associated with physical disorders, antipsychotic or hazardous health behaviour and interactions between antipsychotics and anaesthetic drugs. Adverse responses during anaesthesia include arrhythmias, hypotension, prolonged narcosis or coma, hyperpyrexia, post-operative ileus and post-operative confusion. Although drug interaction probably remains the most potentially serious problem current evidence suggests that psychiatric medication need not be discontinued prior to anesthesia.

Keywords: Schizophrenia; Psychiatric medication; Mental health; Cognitive dysfunction

1. Introduction

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. The physical and psychological fragility of patients with psychiatric illness poses critical importance in the preoperative assessment, evaluation, and choice of premedication, which includes regular therapy, as well as concerns about polypharmacy with possible interactions of anesthetics, analgesics, and psychiatric medications. A considerable effort is to reduce risks for exacerbations or relapses of imminent illness in the postoperative period. Antipsychotic drugs are used in the treatment of psychoses such as schizophrenia and mania. They treat the acute symptoms of hallucinations and delusions and in the case of schizophrenia are used prophylactically often for long periods. Most drugs act by antagonism at the dopamine D2 receptors in the central nervous system. Neuroleptic or typical antipsychotics, chlorpromazine, haloperidol, trifluoperazine, which have a propensity to cause extrapyramidal side effects: acute dystonia, akathisia, parkinsonism and tardive dyskinesia. Atypical antipsychotics, clozapine, olanzapine, respiridone, amisulpride, quetiapine and aripirazole, which do not have a tendency to cause extrapyramidal side effects. An increased mortality rate in the post-operative period for psychotic patients receiving chronic antipsychotic therapy has been demonstrated. Approximately 70% of schizophrenic patients taking chronic antipsychotic drugs develop postoperative psychosis emergence or confusion. The cognitive dysfunction of schizophrenia is associated with an increased frequency of postoperative confusion. Postoperative psychosis emergence or confusion has been associated with adverse clinical and economic outcomes [1-7].

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2. Case report

A 53-year-old, 80-kg woman underwent a total hysterectomy due to cancer, who is in chronic schizophrenia. The operation was performed with a combination of epidural and general anesthesia. Naropaine 20 ml, 0.75 % was administered epidurally and 0.1 mg Fentanyl, 200 mg Propofol and 70 mg Esmeron were given intravenously. The patient was mechanically ventilated on a Drager ventilator and with a volume control ventilation model. Sevoflurane 2% was administered to maintain anesthesia. Fluid deficit was adjusted with Ringers Lactate. Intraoperatively, she developed persistent hypotension that was treated with phenylephrine. Awakening was delayed up to one hour after the inhaled anesthetic was discontinued. Reversal of residual muscle wasting was done with Bridion. The interaction with the patient's antipsychotic medications was particularly intense.

2.1. Interactions between antipsychotics and anesthetic drugs

2.1.1. Antipsychotics

2.1.2. Tricyclic antidepressants (TCA), selective serotonin 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. Abrupt cessation of antidepressants is associated with the risk of developing withdrawal symptoms. Selective serotonin reuptake inhibitors (SSRIs), TCAs: amitriptyline, imipramine, desipramine, doxepin, nortriptyline; were the most commonly used drugs for treating depression. They inhibit synaptic reuptake of norepinephrine and serotonin. Also affect neurochemical systems including histaminergic and cholinergic systems, thus they have a large range of side-effects, including postural hypotension, cardiac dysrhythmias, urinary retention, dry mouth, blurred vision and sedation. Given chronically, these drugs decrease stores of noradrenergic catecholamines, and can cause changes on the ECG, ventricular arrhythmias and refractory hypotension. 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. 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. Pancuronium, ketamine, meperidine and epinephrine containing solutions should be avoided. If hypotension occurs and vasopressors are needed, direct acting drugs such as phenylephrine are recommended. 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. Fluoxetine is inhibitor of certain hepatic cytochrome P-450 enzymes and their side-effects are headache, agitation and insomnia.This drug may increase the plasma concentration of drugs that depend upon hepatic metabolism for clearance, such as warfarin, theophylline, phenytoin and benzodiazepines. Cardiac antidysarrhythmic drugs are also metabolized by this enzyme system, and fluoxetine inhibition of the enzyme system may result in potentiation of their effects. SSRIs should be continued throughout the perioperative period to prevent discontinuation syndrome. The use of pethidine, tramadol, pentazocine and dextromethorphan should be avoided. 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 (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). These include SSRI, MAOI, TCAs, pethidine, tramadol and dextromethorphan. MAOIs, tranylcypromine and phenelzine, and moclobemide, act by inhibition of the metabolic breakdown of norepinephrine and serotonin by the MAO enzyme. The level of norepinephrine and serotonin is increased at the receptor site. All MAOIs are eliminated by hepatic metabolism. Opioids like morphine, fentanyl, alfentanyl and remifentanyl can all be used safely. Reactions occur in patients given pethidine and dextromethorphan, both of which inhibit serotonin reuptake. 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 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. 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. Therefore, dosages should be titrated. 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. Valproate is the drug of choice for treating acute episodes of Bipolar disorder. 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. 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. Lithium discontinuation is recommended. Lithium can be stopped at once because no withdrawal symptoms occur. 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. Neuroleptic or typical antipsychotics (chlorpromazine, haloperidol, trifluoperazine) cause extrapyramidal side-effects like acute dystonia, akathisia, Parkinsonism and tardive dyskinesia. Clozapine causes seizures and neutropenia [8-24].

3. Discussion

Schizophrenic patients are at increased risk for perioperative complications, as their biological response to stress is impaired. Antipsychotic medication should be continued perioperatively, as abrupt withdrawal may result in recurrence of psychotic symptoms. It may also increase the incidence of postoperative confusion, which is high in those suffering with schizophrenia. Opioids like pethidine and indirectly acting sympathomimetics are contraindicated in MAOI patients. Mood stabilisers are used to treat bipolar affective disorders which have a lifetime incidence of 1% in the UK. A manic or hypomanic episode is required for the diagnosis to be made. Some patients also suffer depressive episodes. Mood stabilisers include lithium and anticonvulsant drugs such as carbamazepine and sodium valproate. Mood stabilisers should not be stopped abruptly as there is a significant risk of relapse. The management of lithium poisoning is supportive, with correction of electrolyte imbalance and convulsions. Haemodialysis is required if renal failure is present, which may need to be repeated as tissue lithium enters the circulation. Cardiac risk factors are increased in patients taking long term antipsychotic drugs due to a combination of side effects and high smoking levels in these patients.

4. Conclusion

Patients with chronic schizophrenia should continue their antipsychotics pre-operatively as abrupt withdrawal may result in recurrence of psychotic symptoms. 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.

Compliance with ethical standards

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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