Antidepressants and antipsychotics: anaesthetic implications

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Abstract

According to the World Health Organization about 450 million people suffer from mental and behavioural disorders worldwide, whereas depression has a lifetime prevalence of between 10 and 20%. Antidepressants are broadly divided into four main groups: tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), atypical agents and monoamine oxidase inhibitors (MAOIs). Lithium is also occasionally used as an adjunct to treat refractive depression, but is more commonly used as a mood stabilizer in bipolar affective disorder. Antipsychotics are usually classified as 'conventional' antipsychotics or 'atypical' agents. The anaesthetist has to incorporate these agents in premedication and should anticipate their interactions with anaesthetic technique.

Keywords 5-Hydroxytryptamine; dopamine antagonists; monoamine oxidase inhibitors; noradrenaline re-uptake inhibitors; norepinephrine; selective serotonin re-uptake inhibitors

Royal College of Anaesthetists CPD Matrix: 1A02

Learning objectives

After reading this article, you should be able to understand the:

- basic pharmacology and drug interactions of the antidepressants, mood stabilizers and antipsychotics
- anaesthetic implications of these groups of drugs in patients undergoing anaesthesia
- effect of abrupt discontinuation of these groups of psychiatric drugs

Antidepressants

The amine hypothesis postulates that depression is associated with a functional deficit of neurotransmitter amines (5-hydroxytryptamine [5HT; serotonin], noradrenaline [NA] and dopamine [DA]) at critical central nervous system synapses. Antidepressants increase the levels of neurotransmitters by inhibiting the activity of the enzymes that break them down, blocking their re-uptake or enhancing neurotransmitter release from presynaptic terminals (Figure 1).

Tricyclic antidepressants (TCAs)

TCAs increase the level of both serotonin and noradrenaline by blocking their re-uptake into the brain cells. However, the secondary changes responsible for the pharmacological efficacy occur on chronic exposure and include up and down regulation of various receptors. The overdose toxicity of TCAs (Table 1) makes them used less often in patients with suicidal ideation.

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Anaesthesia for a patient on TCAs

TCAs should be continued throughout the perioperative period to prevent withdrawal symptoms. Sensitivity to the catecholamines is enhanced by TCAs, which may result in hypertension and arrhythmias when directly or indirectly acting sympathomimetics are used. Likewise, anaesthetics known to increase endogenous circulating catecholamines (e.g. pancuronium and ketamine) should be used with caution. The arrhythmogenic potential of TCAs is also potentiated in the presence of hypercapnia and volatiles, especially halothane. They also exaggerate the effects of anticholinergics and may precipitate anticholinergic syndrome. TCAs are highly protein bound and their levels may be enhanced by competing drugs, for example non-steroidal anti-inflammatory drugs (NSAIDs). TCAs are potent cytochrome P450 inducers.

Selective serotonin reuptake inhibitors (SSRIs)

Like the TCAs, there is a delay of 2–3 weeks before the patient's mood lifts but compared to TCAs, SSRIs have a lower side effect profile (Table 1) and are even relatively safer when taken in overdose.

Anaesthesia for a patient on SSRIs

SSRIs should be continued throughout the perioperative period to prevent discontinuation syndrome, which is characterized by symptoms which can be psychiatric (anxiety/confusion), gastrointestinal (nausea/vomiting), neurological (dizziness/tremor), or musculoskeletal (myalgia). SSRIs decrease platelet aggregation at high doses, and may increase surgical bleeding if combined with NSAIDs. They inhibit cytochrome p450 enzymes resulting in increased bioavailability of other drugs, such as warfarin, theophylline, phenytoin, benzodiazepines and TCAs.

Serotonin syndrome

This is a potentially fatal toxic reaction, which typically results from interactions between various serotonergic agents. The most common combination is an SSRI and a monoamine oxidase inhibitor, but the culprits may include TCAs, pethidine and tramadol or may also occur after overdose of SSRIs. The syndrome consists of behavioural symptoms (agitation and confusion), increased motor activity (muscle rigidity, hyperreflexia) and autonomic instability (hyperthermia, tachycardia, labile blood pressure and diarrhoea). Seizures, rhabdomyolysis, renal failure,

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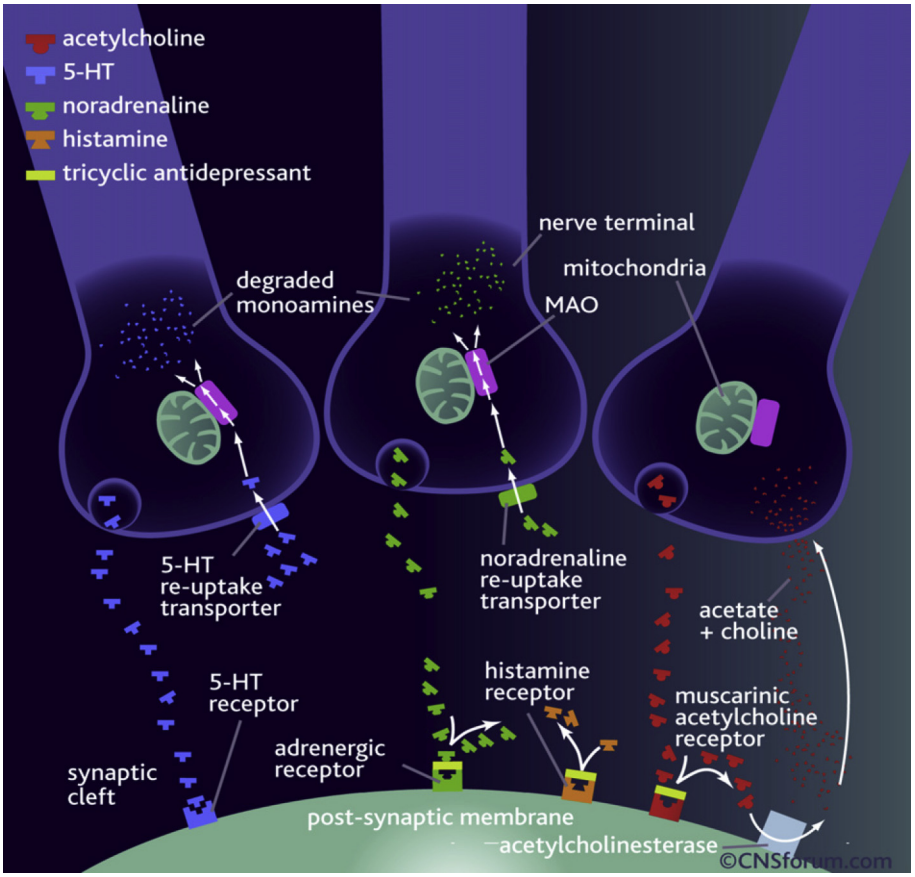

Figure 1 The mechanism of action of antidepressants. 5-HT, 5-hydroxytryptamine; MAO, monoamine oxidase. (Reproduced with kind permission of the CNS Forum, the Ludbeck Institute.)

arrhythmias and coma may also occur, confusing the diagnosis with the neuroleptic malignant syndrome.

Monoamine oxidase inhibitors (MAOIs)

MAOIs are mainly classified on the basis of reversibility of the block. Non-selective irreversible MAOIs (e.g. tranylcypromine) may result in accumulation of tyramine, which causes hypertensive crisis. Moclobemide, the only reversible inhibitor of MAO-A (RIMAs) available in the UK, selectively inhibits MAO-A, so that the response to tyramine (metabolized mainly by MAO-B) is less severe and most patients do not need the same level of dietary restriction.

Anaesthesia in a patient on MAOIs

Pethidine and dextromethorphan inhibit serotonin re-uptake and may cause serotonin syndrome when co-administered with an MAOI. These agents can also potentiate the depressive effects of all the opioids. Indirect sympathomimetics can displace endogenous noradrenaline in higher concentration causing hypertensive surges whereas direct-acting sympathomimetics may have an enhanced effect due to receptor hypersensitivity and should be used cautiously. Similarly pancuronium should be avoided as it releases stored noradrenaline. Phenelzine decreases plasma cholinesterase concentration and prolongs the action of suxamethonium. MAOIs also decrease dose requirements of thiopentone. Local anaesthetics containing adrenaline should be avoided making felypressin a suitable alternative.

Discontinuation of the MAOI for 2 weeks may replenish the enzyme stores but will make the patient vulnerable to relapse, especially after the first week. The decision merits discussion with the patient and their psychiatrist and should be based on individual risk assessment.

Newer antidepressants

Venlafaxine may block both serotonin and noradrenaline depending on the dose and hence may cause hypertension in a dose-dependent fashion. It can also potentiate warfarin. Mirtazapine promotes noradrenergic and serotonergic neurotransmission via a-2 antagonism. Both venlafaxine and mirtazapine should be continued throughout the perioperative period.

Mood stabilizers

Mood stabilizers are used to treat bipolar affective disorders which have a lifetime prevalence of 0.3–1.5% in the UK. Mood stabilizers include lithium and anticonvulsant drugs such as

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