

Psychiatric effects of drugs for other disorders

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Abstract

Many drugs used therapeutically for non-psychiatric disorders can cause neuropsychiatric reactions. A wide range of such effects are reported including sedation, sleep disturbance, anxiety, depression, mania, psychosis, cognitive disturbance and delirium. The reactions are usually dose-related but may occur at therapeutic doses or on drug withdrawal after chronic use. They are more common in elderly or ill patients or those with a psychiatric history and may be unpredictable or paradoxical. Some of the more common psychiatric effects of drugs used for non-psychiatric disorders are reviewed briefly here. They include, among others, dopaminergic and antimuscarinic drugs for parkinsonism; digitalis and β -adrenoceptor antagonists for cardiovascular disorders; cannabinoid receptor antagonists for obesity; corticosteroids for endocrine disorders, asthma and allergic conditions; and anti-infective drugs for bacterial, parasitic and viral infections.

Keywords adverse drug reactions; corticosteroids; dopaminergic drugs; neuropsychiatric reactions; opioids; side effects

Neuropsychiatric effects account for up to 30% of adverse drug reactions (ADRs). Many of these ADRs, ranging from anxiety states to delirium, are caused by therapeutically administered non-psychiatric drugs, and many drugs can cause a variety of psychiatric effects. The incidence of such reactions is not always known because the information usually depends on selected patient groups or individual reports. In general, psychiatric ADRs are more common in elderly or ill patients and in those with a psychiatric history. Other factors include metabolic status, drug interactions and personality. The ADRs are usually dose-related, and can occur at therapeutic doses and with plasma concentrations in previously normal individuals with no innate vulnerability. They may also occur on drug withdrawal. The mechanisms are often complex and vary between drugs and clinical situations. Management may be simple if the cause is known, but patients who are taking several different drugs may need careful assessment. A selection of the more common ADRs is given here.

Parkinson's disease and parkinsonism

Dopaminergic and antimuscarinic agents – dopaminergic drugs can cause depression, agitation, paranoid psychosis, mania,

What's new?

- Rimonabant, a cannabinoid CB₁ receptor antagonist, is effective for weight loss in obesity but carries a 2.5-fold risk of depression and a threefold risk of anxiety compared with placebo
- Nabilone, a synthetic cannabinoid receptor agonist similar to tetrahydrocannabinol (THC), and sativex, a plant-derived agent containing THC and cannabidiol, alleviate pain in spastic disorders and neuropathic pain; psychiatric side-effects are minimized by using modest doses and/or combination with opioids or other analgesics
- Abrupt withdrawal of baclofen may cause serious psychiatric reactions, especially delirium, and after chronic use the drug should be withdrawn gradually over several weeks
- Isotretinoin has not been shown to increase the risk of depression or suicide in adolescents treated for severe acne but remains under suspicion of causing rare paradoxical reactions

hypomania and excessive daytime sleepiness. The incidence of psychiatric problems was 20% in one series of 908 patients treated with levodopa for Parkinson's disease.¹ Delirious states occurring with bromocriptine can be serious, involving confusion, aggressiveness, florid delusions and hallucinations, which can last for weeks after discontinuation of the drug. Similar effects have been reported with apomorphine, lisuride, pergolide and selegiline. These effects are usually dose-related but are exacerbated by antimuscarinic agents, which are often used concomitantly in Parkinson's disease and can also cause delirium. In addition, they may cause dementia, and contribute to cognitive impairment in patients with Parkinson's disease.

Management of psychiatric symptoms in parkinsonism involves withdrawal or dose reduction of the offending drug. The psychiatric effects of dopaminergic agents may limit the dose that can be administered, which may still be subtherapeutic, particularly in elderly patients and those with post-encephalitic disease, and the appearance of symptoms may be delayed. Delirium caused by anticholinergic drugs or amantadine can be reversed rapidly with intravenous physostigmine (see also pages 463–466). Benzodiazepines may be helpful, but antipsychotic drugs with antimuscarinic effects should be avoided.

Other medical conditions – bromocriptine has caused schizophreniform or manic reactions when used for post-partum suppression of lactation and in the treatment of pituitary tumours.¹ Use of mydriatic eye drops containing antimuscarinics has been associated with delirium, hallucinations and amnesia (Table 1).

Skeletal muscle relaxants such as baclofen used for chronic spastic conditions often cause sedation, and sometimes cause anxiety and agitation with insomnia. Other reported symptoms include euphoria, nightmares, confusion and hallucinations. The UK Committee on Safety of Medicines has warned that serious side effects can occur on abrupt withdrawal of baclofen,

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Disorders and drugs

Parkinson's disease, parkinsonism

Dopaminergic agents (e.g. levodopa, bromocriptine, amantadine, apomorphine, lisuride, selegiline)

Antimuscarinic agents (benzatropine, biperiden, orphenadrine, procyclidine, benzhexol)

Chronic spastic conditions

Skeletal muscle relaxants (baclofen, dantrolene, tizanidine)

Cardiovascular disorders

Digitalis preparations (digoxin, digitoxin)

Diuretics (causing potassium loss) (thiazides, frusemide, bumetadine, torasemide)

β -adrenoceptor antagonists (e.g. propranolol, atenolol, metoprolol, oxprenolol, sotalol)

Antiarrhythmic agents (e.g. lignocaine, procainamide, mexiletine)

Calcium channel blockers (e.g. nifedipine, diltiazem)

Angiotensin-converting enzyme inhibitors (e.g. enalapril, imidapril, quinapril, ramipril)

Obesity

Cannabinoid CB₁ receptor antagonist (rimonabant)

Endocrine disorders

Glucocorticoids (e.g. prednisolone, betamethasone, dexamethasone, triamcinolone)

Oestrogens and progestogens (contraceptives, hormone replacement therapy, treatment of menstrual abnormalities)

Male sex hormones and anabolic steroids (e.g. testosterone, nandrolone, stanozolol)

Pain syndromes

Opioids (e.g. morphine, diamorphine, pethidine, dihydrocodeine, tramadol, pentazocine, nalbuphine, buprenorphine)

Non-steroidal anti-inflammatory drugs (e.g. ibuprofen, diclofenac, piroxicam, celecoxib)

Cannabinoids (nabilone)

Gastrointestinal disorders

H₂ receptor antagonists and proton pump inhibitors (e.g. cimetidine, ranitidine, omeprazole)

Bacterial, parasitic and viral infections

Antibiotics (e.g. chloramphenicol, streptomycin and related drugs, cephalosporins, isoniazid, cycloserine, quinolones)

Antimalarials (mefloquine, chloroquine, mepacrine, quinine)

Antivirals (aciclovir and related drugs, zidovudine and related drugs)

Interferons (alpha and beta interferons)

Acne vulgaris

Isotretinoin

Psychiatric effects

Delirium, depression, agitation, paranoid psychosis, mania, somnolence

Exacerbate effects of dopaminergic agents; confusion and dementia

Anxiety, agitation, insomnia, nightmares, euphoria, confusion, hallucinations, withdrawal effects

Delirium, depression, hallucinations, psychosis

May exacerbate toxic effects of digitalis preparations

Sleep disturbance, nightmares, hypnogogic or hypnogenic hallucinations, depression, delirium

Psychotic reactions, depression

Psychotic reactions, depression

Confusion, depression, nervousness, sleep disturbance

Depression, anxiety

Euphoria, mania, depression, psychosis, violent behaviour

Depression, premenstrual tension-like symptoms, changes in libido

Depression, anxiety, changes in libido; mania, psychosis, aggression and withdrawal symptoms with high doses of anabolic steroids

Dysphoria, depression, psychosis (especially mixed agonists/antagonists), withdrawal symptoms

Nervousness, depression, drowsiness, insomnia; may aggravate depression and other psychiatric disorders

Sedation, euphoria, depression, cognitive impairment, psychosis

Depression, somnolence, insomnia, agitation, confusion, hallucinations

Delirium, psychosis; sleep disorders, hallucinations, convulsions

Anxiety, panic, insomnia, nightmares, dysphoria, mania, psychosis, delirium

Drowsiness, hallucinations, delusions, depression, insomnia, anxiety

Depression and suicidal behaviour

Possible depression, psychosis

Table 1

which should be discontinued by gradual dose reduction over several weeks.² If necessary delirium may be alleviated by reinstatement of baclofen and unremitting spasticity (e.g. constant severe hypertonus) by other agents including dantrolene and/or benzodiazepines.²

Cardiovascular disorders

Digitalis preparations can cause delirium, depression, hallucinations and psychosis. The effects are usually dose-dependent and the likelihood of psychiatric toxicity increases progressively

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