62 - Interactions between illicit drugs and prescr

Interactions between illicit drugs and prescribed psychotropic drugs

Addictions and substance misuse CHAPTER 4 Interactions between illicit drugs and prescribed psychotropic drugs Interactions between drugs of misuse and prescribed psychotropics are common, not least because of the high rates of psychotropic prescribing in such patients.1 Information on adverse interactions is derived largely from case reports and theoretical assumptions and rarely from systematic investigation. A summary of major interactions can be found in Table 4.25. In all patients who misuse illicit drugs: ■ ■Infection with hepatitis B and C is more common. The associated liver damage may lead to a reduced ability to metabolise other drugs and increased sensitivity to adverse effects. ■ ■Infection with HIV is relatively common.2,3 Antiretroviral drugs are involved in pharmacokinetic interactions with a number of prescribed and non-prescribed drugs.4 For example, ritonavir can decrease the metabolism of ecstasy and precipitate toxicity, and a number of antiretrovirals can increase or decrease methadone metabolism.5 ■ ■Prescribed drugs may be used in the same way as illicit drugs (i.e. erratically and not as intended). Large quantities of prescribed drugs should not be given to out-patients. ■ ■Additive or synergistic effects of respiratory depressants may play a contributory role in deaths from overdose with methadone or other opioid agonists.6 Caution is needed in prescribing sedative medicines such as benzodiazepines and gabapentinoids.

Table 4.25 Interactions between illicit drugs and psychotropics. Cannabis Heroin/methadone6 Cocaine, amfetamines, ecstasy, MDA, 6-APD Alcohol Ketamine7 General considerations ■ ■Usually smoked in cigarettes (induces CYP1A2) ■ ■Can be sedative ■ ■Dose-related tachycardia ■ ■THC/CBD inhibit CYP3A4, CYP2C19 and CYP2D68,9 ■ ■Can produce sedation/ respiratory depression ■ ■QTc prolongation with methadone (see section on methadone earlier in this chapter) ■ ■Stimulants (cocaine can be sedative in higher doses) ■ ■Arrhythmia possible ■ ■Cerebral/cardiac ischaemia with cocaine – may be fatal ■ ■MDMA inhibits CYP2D6/CYP3A4 ■

■Hyperthermia/dehydration with ecstasy10 ■ ■Sedative ■ ■Liver damage possible ■ ■Induces various enzymes ■ ■Sedative readily causes unconciousness ■ ■Onset of effects may be rapid if snorted or injected Older antipsychotics ■ ■Antipsychotics reduce the psychotropic effects of almost all drugs of abuse by blocking dopamine receptors (dopamine is the neurotransmitter responsible for 'reward') (e.g. haloperidol and MDMA11) ■ ■Patients prescribed antipsychotics may increase their consumption of illicit substances to compensate ■ ■Patients who have taken ecstasy may be more prone to EPSEs ■ ■Cardiotoxic or very sedative antipsychotics are best avoided, at least initially. Sulpiride is a reasonably safe first choice ■ ■Methamphetamines increase risk of EPSEs with haloperidol12 Second- generation antipsychotics ■ ■Risk of additive sedation ■ ■Cannabis smoking in tobacco can reduce plasma levels of olanzapine and clozapine via induction of CYP1A213 ■ ■Clozapine might reduce cannabis and alcohol consumption14 ■ ■Outcome of THC/CBD inhibition of CYP1A2 unknown ■ ■Risk of additive sedation ■ ■Case report of methadone withdrawal being precipitated by risperidone15 ■ ■Isolated report of quetiapine increasing methadone levels, especially in those with slowed CYP2D6 hepatic metabolism16 ■ ■Antipsychotics may reduce craving and cocaine-induced euphoria17–21 ■ ■Olanzapine may worsen cocaine dependency22 ■ ■Clozapine may increase cocaine levels but diminish subjective response23 ■ ■Increased risk of hypotension with olanzapine (and possibly other beta-blockers) ■ ■Increased sedation ■ ■Possible interaction between risperidone and ketamine24

Antidepressants ■ ■Tachycardia has been reported (monitor pulse and take care with TCAs25) ■ ■Complex, unpredictable effects of CYP induction (tobacco) and CYP inhibition (THC/CBD) ■ ■Avoid very sedative antidepressants ■ ■Some SSRIs can increase methadone plasma levels26 (citalopram is SSRI of choice but note the small risk of additive QTc prolongation) ■ ■Case report of serotonin syndrome occurring when sertraline prescribed with methadone for a palliative care patient27 ■ ■Avoid TCAs (arrhythmia risk) ■ ■MAOIs contraindicated (hypertension) ■ ■Combining moclobemide and MDMA can be fatal28 ■ ■SSRIs may increase plasma concentrations of MDMA29 but reduce subjective effects30 ■ ■Risk of SSRIs increasing cocaine levels, especially fluoxetine31 ■ ■Concomitant use of SSRIs or aripiprazole and lamotrigine with cocaine or other stimulants (especially MDA and 6-APD) could precipitate a serotonin syndrome32,33 ■ ■SSRIs may enhance subjective reaction to cocaine34 ■ ■Avoid very sedative antidepressants ■ ■Avoid antidepressants that are toxic in overdose ■ ■Impaired psychomotor skills (not SSRIs) ■ ■Inhibitors of CYP3A4 (e.g. fluoxetine/ paroxetine) will lengthen ketamine half--life ■ ■Beware hypertension with SNRIs and reboxetine Anticholinergics ■ ■Misuse is likely. Try to avoid if at all possible (by using a second-generation drug if an antipsychotic is required) ■ ■Can cause hallucinations, elation and cognitive impairment Lithium ■ ■Very toxic if taken erratically ■ ■Always consider the effects of dehydration (particularly problematic with alcohol or ecstasy) Carbamazepine/ valproate ■ ■Carbamazepine may decrease THC concentrations via induction of CYP3A435 ■ ■Carbamazepine decreases methadone levels36 (danger if carbamazepine stopped suddenly) ■ ■Valproate seems less likely to interact ■ ■Monitor LFTs ■ ■Carbamazepine decreases ketamine plasma concentrations via CYP3A4 induction Benzodiazepines ■ ■Monitor level of sedation ■ ■Oversedation (and respiratory depression possible) ■ ■Concomitant use can lead to accidental overdose ■ ■Possible pharmacokinetic interaction (increased methadone levels) ■ ■Oversedation (if high doses of cocaine have been taken) ■ ■Widely used after cocaine intoxication ■ ■Future misuse possible ■ ■Oversedation (and respiratory depression) possible ■ ■Widely used in alcohol detoxification ■ ■Oversedation and respiratory depression Gabapentinoids ■ ■Monitor level of sedation ■ ■Large increase in risk of death in overdose37,38 ■ ■Does not reduce cocaine use39 ■ ■Oversedation and respiratory depression possible ■ ■No

interaction reported24 6-APD, 6-(2-aminopropyl)benzofuran; CBD, cannabidiol; EPSEs, extrapyramidal side effects; MAOIs, monoamine oxidase inhibitors, MDA, 3,4--methylenedioxyamphetamine; MDMA, 3,4-methylene dioxymethamphetamine; TCAs, tricyclic antidepressants; THC, tetrahydrocannabiniol.

Revision #1
Created 2026-01-04 20:16:19 UTC by Omar Ayman
Updated 2026-01-04 20:16:19 UTC by Omar Ayman