

Sex, drugs and alcohol

Drug interactions of concern to consumers

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SUMMARY

People often have misconceptions about interactions between alcohol and commonly prescribed drugs. Often there is insufficient evidence to support prohibiting alcohol, but the overall risk needs to be assessed for each individual.

Any drug which suppresses the central nervous system will exacerbate the immediate effects of alcohol and can be expected to increase the risk of alcohol-related harm. Alcohol should not be taken with drugs that can cause a disulfiram-like effect.

Combined hormonal contraceptives are less reliable if taken with drugs which can increase the rate of metabolism of oestrogens and progestogens. The interacting drugs include some antiepileptic drugs and the rifamycins, so action is required to maintain contraception.

Introduction

Patients often express concerns about interactions between their medicines and alcohol and any illicit drugs that they may consume. Doctors and pharmacists are also often asked about interactions, especially short courses of antibiotics, which might reduce the efficacy of oral contraceptives.

There are many misconceptions about which interactions are of clinical concern. While there is information about oral contraceptives and alcohol, it is not possible to predict the safety of consuming any illicit drug. The outcomes of illicit drugs interacting with prescribed medicines cannot be quantified.

Alcohol

Current Australian guidelines do not define 'social drinking' but make recommendations that for healthy people daily alcohol consumption should be limited to two standard drinks* and a maximum of four on a single occasion.¹ However, people asking about

alcohol and medicines will generally have some level of ill health. Questions of safety will therefore often need to be in the context of consuming a smaller volume of alcohol. A safer approach would be to think in terms of up to two standard drinks on one occasion – typically, 'Can I have a glass of wine (or beer) when I go out to dinner?'. This can often be addressed in terms of an individual's risk of additive sedation and the circumstances of the occasion, including the support available if the reaction to alcohol was more than expected.

The duration of additive sedation due to an alcohol-drug interaction will depend on the clearance rates of the two components. Blood alcohol concentrations will decline at a predictable rate, but the rate of inactivation of the interacting drug must be considered, for example with long- and short-acting benzodiazepines.

Alcohol (ethanol) is principally metabolised to acetaldehyde by alcohol dehydrogenase in the liver. Other enzymes, including cytochrome P450 (CYP) 2E1, contribute to this conversion and become more significant with higher concentrations of alcohol.² Acetaldehyde causes unpleasant symptoms such as headache, flushing and vomiting. These effects are more pronounced if the metabolism of acetaldehyde is inhibited by drugs such as disulfiram (which block aldehyde dehydrogenase). Regular alcohol consumption can induce elevated levels of CYP 2E1, but fortunately this does not result in any clinically significant interactions with other drugs used at therapeutic doses. Consumers can also be assured that metabolic interactions do not lead to elevated (or prolonged) blood alcohol concentrations.

The management of many chronic diseases will be assisted if patients limit their alcohol consumption, regardless of any additional risks from drug interactions. Regularly drinking alcohol may increase the risks in people with chronic diseases, especially if they take drugs which, for example, increase the risk of liver disease, gastric bleeding or falls. A modest level of alcohol consumption is safe in patients who take paracetamol. This is also the case with non-steroidal anti-inflammatory drugs, such as ibuprofen, however the overall long-term risk of gastric bleeding needs to be considered. Regular or occasional consumption of small amounts of alcohol should not affect warfarin control in the absence of liver disease.

* An Australian standard drink contains 10 g of ethanol, for example 375 mL of medium-strength (3.5%) beer or 100 mL of 12.5% wine

Antiepileptic drugs can increase sedation. Intoxication with alcohol can cause seizures, as can alcohol withdrawal syndrome.

The adverse effects of alcohol on illegal 'recreational' drugs only add to the hazards. Any attempt to advise a patient about the outcomes of an interaction between a medicine and an illicit drug will be undermined by a lack of certainty about the actual content of the illicit substance consumed. The possibility of toxic 'contaminants' in an illicit product may be of more concern than a possible pharmacological interaction.

Antimicrobials

Most antibiotics prescribed in general practice do not require abstinence from alcohol. Penicillins, cephalosporins, macrolides and tetracyclines do not present a hazard with alcohol, but the condition being treated may warrant avoiding alcohol.

There are sufficient reports of disulfiram-like reactions with metronidazole to warrant abstinence during therapy. However, the actual danger of the alcohol contained in one or two standard drinks is low. There is no direct evidence with tinidazole but, as with metronidazole, treatment courses are usually short and any risk of an interaction is easily avoided.

Griseofulvin is normally dispensed with an ancillary warning label for alcohol. This is based on a report of an adult who had a severe reaction after consuming a can of beer and one hour later taking his regular dose of griseofulvin.³ Given the limited evidence and the extended periods of treatment required with griseofulvin, it would be reasonable if patients wanted to test their tolerance to small amounts of alcohol rather than abstain.

Psychotropic drugs

Additional sedation can be anticipated when alcohol is consumed by patients taking benzodiazepines, antipsychotics, sedating antidepressants (especially tricyclics) and many antiepileptic drugs. This potential may not preclude modest levels of alcohol consumption, however some patients who need these drugs may have a history of alcohol abuse. There is also a profound risk if patients overdose with sedative drugs and alcohol. Beverages with a high tyramine content, including some beers and red wine, present an additional hazard with non-selective monoamine oxidase inhibitors (phenelzine, tranylcypromine).

Hormonal contraceptives

Drugs which increase the metabolism of oestrogens and progestogens can reduce the efficacy of oral contraceptives. This occurs when the activity of metabolising enzymes (principally CYP 3A4) in the

liver and intestinal mucosa is increased by 'inducing' drugs. These include the complementary medicine St John's wort which can potentially lead to a failure of oral contraception.⁴ Although not an enzyme inducer, griseofulvin can potentially reduce the efficacy of hormonal contraceptives. Examples of drugs which can reduce the effectiveness of oral contraceptives are listed in the Box.

Box Drugs which can reduce the effectiveness of oral contraceptives⁵

carbamazepine	oxcarbazepine	rifampicin
griseofulvin	phenobarbitone	rifabutin
modafinil	phenytoin	St John's wort

Women taking enzyme-inducing drugs may need to consider other methods of contraception, such as a levonorgestrel intrauterine device, depot medroxyprogesterone or a copper intrauterine device.

Depot medroxyprogesterone remains effective when used with enzyme-inducing drugs whereas etonogestrel implants are unreliable (based on reported failures over a shorter period of use).⁶ The efficacy of the levonorgestrel intrauterine device is due mainly to local release of progestogen and any increased metabolism in the liver would not be expected to reduce its effectiveness. Vaginal rings (containing ethinylloestradiol and etonogestrel) depend on systemic release of oestrogen and progestogen and cannot be considered a safe option in the presence of enzyme-inducing drugs.

After ceasing an enzyme-inducing drug it may take four weeks for enzyme activity to return to baseline and reliable methods of contraception should be used during this period.⁷

Contraceptive hormones can also affect the metabolism of other drugs. This can be clinically significant with antiepileptic drugs such as lamotrigine.

Antimicrobials

Guidelines published in the UK and USA no longer recommend additional contraceptive precautions when non-enzyme inducing antibiotics are taken with oral contraceptives, regardless of the duration of therapy.^{7,8} This applies to commonly prescribed drugs such as penicillins, cephalosporins, macrolides, tetracyclines, trimethoprim and azole antifungals. These recommendations reflect the limited evidence of contraceptive failure associated with antibiotics which do not induce liver enzymes. The theory that oral antibiotics could interrupt enterohepatic reabsorption of oestrogens has not been substantiated.

Additional contraceptive precautions may be warranted if the antibiotic or infection causes

vomiting or diarrhoea. This is particularly important with progestogen-only oral contraceptives.

Enzyme-inducing antimicrobials include rifampicin, rifabutin, efavirenz, nevirapine, ritonavir and tipranavir. Women must use a reliable form of contraception with these drugs. There are no data on the effects of short courses of rifampicin on hormonal contraceptives. Additional methods of contraception should be used if rifampicin is taken for prophylaxis of meningitis due to *Neisseria meningitidis* or *Haemophilus influenzae*. Four weeks of additional cover will be required even after two days of exposure to rifampicin. Also, an active pill should be taken each day during the course and for seven days after the last rifampicin dose.⁵

Enzyme-inhibiting antibiotics, such as erythromycin and fluconazole, can increase oestrogen and progestogen concentrations, but have limited potential to cause adverse effects. The duration of antibiotic therapy will rarely warrant reducing the dose of oral contraceptive.

Antiepileptic and psychotropic drugs

Enzyme-inducing drugs such as phenytoin, carbamazepine, oxcarbazepine and phenobarbitone can cause failure of oral contraceptives. Topiramate is a weaker inducer and a change in contraception may only be required with doses of more than 200 mg

daily.⁷ Lamotrigine can cause slight reductions in progestogen concentrations, but this should not lead to a reduction in the efficacy of combined oral contraceptives.⁷ However, ethinylloestradiol can increase the clearance of lamotrigine and reduce control of seizures. Combined oral contraceptives may therefore be unsuitable for women taking lamotrigine for epilepsy.

Conclusion

The potential significance of interactions depends on both the drugs involved and an individual's susceptibility to suffering an adverse outcome. Clinicians often appeal for drug interaction alerts to define a severity rating. However, the severity of the outcome will usually depend as much on a patient's medical risk as on the drugs in question. The best approach is to identify a potential problem and then assess its significance for the patient. Practical advice on clinically significant interactions can be found in the Australian Medicines Handbook,⁵ and guidelines for managing interactions with contraceptives are provided in Contraception: an Australian clinical practice handbook⁹. If in doubt seek advice from a pharmacist or a medicines information centre. <

Conflict of interest: none declared



SELF-TEST QUESTIONS

True or false?

1. Additional contraception is needed by women who take oral contraceptives, when they are prescribed a short course of penicillin.
2. Patients should not drink alcohol while being treated with metronidazole.

Answers on page 67

REFERENCES

1. National Health and Medical Research Council. Australian guidelines to reduce health risks from drinking alcohol. Canberra: NHMRC; 2009.
2. Jang GR, Harris RZ. Drug interactions involving ethanol and alcoholic beverages. *Expert Opin Drug Metab* 2007;3:719-31.
3. Fett DL, Vukov LF. An unusual case of severe griseofulvin-alcohol interaction. *Ann Emerg Med* 1994;24:95-7.
4. Murphy PA, Kern SE, Stanczyk FZ, Westhoff CL. Interaction of St. John's Wort with oral contraceptives: effects on the pharmacokinetics of norethindrone and ethinyl estradiol, ovarian activity and breakthrough bleeding. *Contraception* 2005;71:402-8.
5. Rossi S, editor. Australian Medicines Handbook 2013. Adelaide: Australian Medicines Handbook Pty Ltd; 2013.
6. Implanon: interactions and failure of contraception. *Aust Adv Drug React Bull* 2007;26:14-5.
7. Faculty of Sexual and Reproductive Healthcare. Clinical Guidance: drug interactions with hormonal contraception. London, UK: Royal College of Obstetricians and Gynaecologists; 2011 (updated 2012 Jan).
8. Centers for Disease Control and Prevention. U.S. Medical Eligibility Criteria for contraceptive use, 2010. *MMWR Morb Mortal Wkly Rep* 2010;59:1-86.
9. Sexual Health and Family Planning Australia. Contraception: an Australian clinical practice handbook. 3rd ed. Family Planning New South Wales, Family Planning Queensland, Family Planning Victoria; 2012.

Dental note

Sex, drugs and alcohol

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Amongst the misconceptions, or 'urban legends', that exist in dental practice is the potential for an unwanted pregnancy because of an interaction between the antibiotics we prescribe and oral contraceptives. The lack of evidence for this interaction has resulted in a change in overseas guidelines and we should be advising our patients accordingly.

Dentists should discuss with patients potential problems with any adverse reaction to prescribed

medicines, particularly diarrhoea or vomiting. If they develop any reaction or are otherwise concerned, they should be told to cease the drug and contact us as the prescribing clinician, or their doctor, as soon as possible.

Of particular note for dentists is the interaction between alcohol and metronidazole. We should warn our patients of this possibility and recommend that they abstain from alcohol.