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Drugs and complementary medicine interactions

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Polypharmacy raises the issue of adverse drug interactions and complementary medicines must be taken into account when assessing this risk.

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Adverse drug reactions are a constant concern for all practitioners, and reasonably so. Increasingly we are faced with potentially conflicting data in terms of who needs what medications and at what cost. Add to this the fact that many patients prefer to use 'natural' agents, as opposed to the so-called manmade, synthetic alternatives and we have a potential catastrophe. The magnitude of the problem seems massive; however, there are some simple ways that practitioners can reduce the risks of adverse drug interactions in a practical and relatively simple way. The problem rests with the patient's mistaken belief that complementary medicines are more natural and therefore safer.

This short article is not intended to be a comprehensive review of herb–drug interactions. Instead it is meant to serve as a reminder to be aware of the potential for interactions between prescribed and complementary medicines.

RED FLAGS FOR ADVERSE INTERACTIONS

From a pharmacological perspective, there are several 'red flags' for adverse drug interactions. Common sense tells us that the more medications a patient is taking, the greater the potential for the occurrence of adverse interactions. The risk of adverse drug interactions has been shown to increase exponentially with the number of agents being used, with risk increasing most sharply after eight medications are being used by the same patient.[1] At this level of medication use, the risk of adverse interactions is almost 100%. This includes the use of natural or complementary medicines. Often the use of complementary medicines is not reported by patients; it is estimated that almost 50% of Australians use complementary medicines and prescription agents concomitantly.[2]

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There are several areas where the risks of adverse interactions are relatively obvious, and can include both individual patient factors and iatrogenic factors. The usual risks associated with the extremes of age, polypharmacy, high doses and high-risk drugs (e.g. warfarin) and when new agents are added to an already full medication regimen warrant careful attention. These risks apply equally to complementary medicines and prescription agents. For example, the use of prescription antiplatelet agents with the addition of complementary medicines with known antiplatelet activity such as garlic, ginger and Korean ginseng may leave patients open to an increased risk of bleeding.[3]

Another source of risk is the cytochrome P450 (CYP450) pathway. There is only so much a single enzyme pathway can cope with – overload it and there will be consequences.

RULES OF POLYPHARMACY

- **Rule 1:** Do not overload any single major enzyme metabolic pathway. Two drugs competing for metabolism will not be metabolised as quickly as if there were no competition. Overloading is likely to result in drug accumulation and toxicity.
- **Rule 2:** Saturation of the metabolic pathway of a drug will cause it to accumulate or use an alternative metabolic pathway, which may increase the risk of toxicity. The classic example of this is paracetamol – overload the usual metabolic pathway and the drug will be metabolised via an alternative toxic pathway.
- **Rule 3:** Addition of an enzyme inducer or inhibitor to a drug that relies on consistent clearance will change its concentration and likely its effect. This is the case with the addition of phenytoin or St John's wort to quetiapine. Preparations containing starfruit may also inhibit the metabolism of many of the CYP3A4, 3A5 and 3A7 metabolised drugs, the major classes of which include antiretrovirals, benzodiazepines, calcium channel blockers and several of the HMG Co-A reductase inhibitors.[4]
- **Rule 4:** If the patient was clinically stable and now is not, look for the cause. This applies as much to patients on warfarin as it does to those on metoprolol. Could the change in INR be due to the new antibiotic or the gastroenteritis that had developed over the past five days? Is it the new Chinese herbal medication the patient started taking? If the patient's blood pressure was stable on metoprolol and now is not, did he just start using sildenafil? A good rule of thumb is to consider any new agents, including complementary medications.
- **Rule 5:** Get into the habit of asking patients about alternative or complementary medication use. One of the most frequently used examples is St John's wort. This plant contains several chemicals, including those thought to be responsible for the antidepressant action, which may cause potentiation of the serotonergic effects of selective serotonin reuptake inhibitors, pethidine and tramadol[5] and has CYP450-inducing effects that may lead to alteration of INR.[3]

Australians Moses and McGuire provide a detailed list of major interactions between 'conventional' agents and complementary and alternative medicines, many of which illustrate the principles outlined above.[6] There are also several useful internet-based sources of information on complementary medicine interactions (see the box on this page). The strength of evidence is steadily increasing in this area, although case studies and small case series remain the most common source of evidence for interactions between prescription agents and complementary medicines.

USEFUL RESOURCES

- Natural Medicines Comprehensive Database: http://naturaldatabase.therapeuticresearch.com
- Natural Standard: www.naturalstandard.com
- The Integrative Medicine Gateway: www.imgateway.net
- MedicinesComplete: www.medicinescomplete.com
- Prescribe Guide: http://prescribeguide.com
- NPS: www.nps.org.au

CONCLUSION

Complementary medicines have a place in our pharmacological landscape. This article is intended to act as an aide memoire to remind us all to consider the potential for interactions with any therapeutic regimen. It is important that we allow and encourage our patients to report all of the agents they take, including complementary medicines. MT

REFERENCES

1. Cadieux RJ. Drug interactions in the elderly. How multiple drug use increases risk exponentially. Postgrad Med 1989; 86: 179-186.
2. MacLennan AH, Myers SP, Taylor AW. The continuing use of complementary and alternative medicine in South Australia: costs and beliefs in 2004. Med J Aust 2006; 184: 27-31.
3. Myers SP. Interactions between complementary medicines and warfarin. Aust Prescr 2002; 25: 54-56.
4. Cytochrome P450 drug interaction table. Indiana University; 2009. Available online at: http://medicine.iupui.edu/clinpharm/ddis/ (accessed May 2012).
5. Moses GM, McGuire TM. Drug interactions with complementary medicines. Austr Prescr 2010; 33: 177-180.
6. Rossi S, ed. Australian medicines handbook 2012. Adelaide: Australian Medicines Handbook; 2012.

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