Check suitability, minimise sue-ability!

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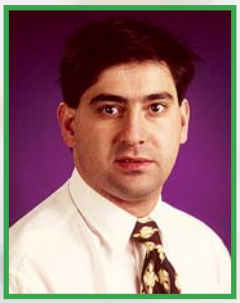

In the last issue of Australian Family Physician we discussed how to individualise drug therapy once a P-drug had been chosen for prescribing. In this issue we will look at the use of checking whether the drug is, in fact, suitable for the patient or not, before prescribing it.

BACKGROUND Having chosen which drug to prescribe, the suitability of the medication needs to be checked before the prescription is written.
OBJECTIVE This article discusses what checking for suitability means and how it differs from specific considerations that a patient may have.
DISCUSSION A drug is unsuitable for a patient if it is very likely to cause a predictable adverse reaction, and its prescription, in the absence of extenuating circumstances, would be difficult to defend. A simple example is anaphylaxis to penicillins. It is important to distinguish between patients for whom certain drug therapy is unsuitable, and others who have specific considerations, where the drugs can still be prescribed, but where additional steps need to be undertaken either in prescribing or monitoring. Examples of each of these will be discussed.

The issue of suitability causes much concern for prescribers. Frequently prescribing is deemed inappropriate because a medication is prescribed to a patient for whom it is clearly not suitable. It is important, initially, to distinguish between checking suitability and individualising therapy, as there is often confusion about this issue. A very simple example is flucloxacillin: any patient with previous allergic reaction to any penicillins is not suitable for flucloxacillin. A patient with underlying liver disease can be prescribed flucloxacillin, but may need closer monitoring of their liver function tests to look for flucloxacillin induced cholestasis. This is because, although they are no more likely to develop this reaction, the outcome can be more severe in such patients.

George (see Case history) would be a very difficult case to manage, and many general practitioners would understandably refer him to a specialist for management. Many practitioners would feel that a beta blocker would be contraindicated in George because of his diabetes and probable airways disease and would opt for a calcium channel blocker for his hypertension instead.

Case history – George

George is 74 years old and has recently been discharged from hospital with an acute myocardial infarct, complicated by cardiac failure. He has a past history of diabetes (from which he has no complications) and hypertension, and you have seen him a few times with wheeziness and bronchitis during winter.

His current medications are:

Aspirin 100 mg

Gliclazide 160 mg twice per day

Metformin 1000 mg three times per day

Trandolapril 4 mg per day

Bendrofluazide 5 mg per day

He had a number of blood tests performed in hospital that revealed his creatinine was 0.08 mmol/L and his HbA_1C was 6.4%.

On the last three occasions that you have seen him, he has been persistently hypertensive with a mean blood pressure of 150/95. The discharge letter from the hospital advised to 'commence a beta blocker if his blood pressure remained high'.

Some may also feel that his cardiac failure represents a contraindication to beta blocker therapy.

The fact is, that none of these conditions are a specific contraindication to beta blockers. As we have discussed in previous issues of AFP, such patients are simply at a higher than average risk of adverse reactions, but are also particularly likely to benefit from beta blocker therapy and by carefully individualising their therapy. By monitoring these patients appropriately, it is possible to minimise the risk and maximise the benefit of such medications.

The best way to think of it is to consider how predictable the adverse reaction is and whether it can be avoided in any way: prescribing a beta blocker to someone with a systolic blood pressure of 85 mmHg, or a heart rate of 45 is very likely to make them more unwell! But this is not necessarily the case with chronic obstructive pulmonary disease (COPD), diabetes, and heart failure. Beta blockers have been shown to reduce the mortality rate of patients with heart failure by approximately 30% provided that therapy is commenced at a low dose, and is titrated carefully.[1,2] Cardioselective beta blockers such as atenolol and metoprolol have been shown to have little impact on worsening respiratory function in patients with chronic obstructive lung disease,[3] and there is evidence that postmyocardial infarction patients with COPD who are treated with such agents have a better outcome than those who are not.[4,5] Similarly with diabetes, the impact of beta blocker therapy may be a slight deterioration of blood sugar control, as well as a loss of hypoglycaemic awareness. This can be dealt with by altering the hypoglycaemic medications so as to reduce the risk of this complications, and needs to be weighed up against the considerable mortality benefit of beta blockers in patients such as George with hypertension, cardiac failure, and who are postmyocardial infarction.

Table 1 lists the actual contraindications to beta blockers. As can be seen, these are conditions where the patient has a very high likelihood of clinical deterioration, regardless of how carefully they are dosed, or how their condition is otherwise managed. The adverse outcomes of the prescriptions, here, are very predictable. A medication should only be prescribed in the presence of a contraindication under the following circumstances:

- a clear indication
- the absence of viable alternatives, and
- with the full consent of the patient.

In other cases, the prescription of a drug to a patient for whom it is not suitable may not have any immediate adverse outcomes. This can give rise to a false sense of security, but the possible consequences may be so dire that they are best avoided. A good example here is the prescription of COX-2 inhibitors or NSAIDs to patients with heart failure. Although, a patient may not necessarily feel worse in the next few days, given that the likely complication is hospitalisation with acute pulmonary oedema or acute renal failure, it is best avoided!

So when you are checking the suitability of a drug before prescribing it, you are really checking to make sure that it is unlikely that the patient is going to have a very predictable adverse outcome as a result of the prescription. As can be seen from Table 1 often the differences between the contraindications that preclude the drug's prescription and the specific considerations that mean they have to be prescribed carefully can be quite subtle.

ACE inhibitors and renal failure

A good example is the use of angiotensin converting enzyme (ACE) inhibitors. Many clinicians feel that chronic renal failure is a contraindication to ACE inhibitor therapy. However, it is these very patients that are most likely to benefit from these agents; when ACE inhibitors are prescribed to patients with chronic renal failure, many patients have a slight initial deterioration in their renal function, eg. increase in serum creatinine of 0.02–0.05 mmol/L. However, in the long term, such patients have a slower rate of renal decline than if they were not on an ACE inhibitor. A smaller percentage of patients do have a more dramatic creatinine rise, and this is why ACE inhibitors need to be commenced at a low dose and monitored carefully in patients with underlying renal impairment. These latter patients may have underlying renal artery stenosis as the reason for their renal impairment, which explains the sudden deterioration of renal function.

If an ACE inhibitor is prescribed to a patient with known bilateral renal artery stenosis or a previous history of acute renal failure on ACE inhibitor therapy, they will have a predictable deterioration in their renal function.

Keeping informed

One of the frustrating issues in this area, as seen with the beta blockers in the heart failure example, is that occasionally yesterday's contraindication is today's indication! That is why keeping up-to-date with sources such as Australian Prescriber and the Australian Medicines Handbook (AMH) is so important. The latter is particularly useful as it has contraindications for the drug class, and each drug is listed with specific considerations and what to do in those circumstances.[6]

MIMS is a frequently used source of such information as well, however, there is no obligation on the part of the pharmaceutical company to keep their product information up-to-date once their drug is approved, and often their contraindications and precautions tend to be too over inclusive.

Two issues that are regularly listed in the AMH as specific considerations are pregnancy and lactation. The other useful source of similar information is the 'Prescribing medicines in pregnancy' booklet which is published by ADEC. Appendix B of that publication lists useful resources in each state that can be contacted for more specific information.

Table 1. Examples of contraindications and specific considerations

Drug class	Contraindication	Specific considerations	Individualising and monitoring required when specific considerations exist
ß-blocker	Uncontrolled asthma, hypotension, bradycardia (45–50 bpm), second or third degree heart block	COPD	Check for reversibility, start low dose, monitor respiratory function
		Diabetes	Monitor BSLs more closely, alter hypoglycemic medication to reduce risk of hypoglycaemia
		Heart failure	Optimise other medication, start low, monitor for worsening CCF
Ace inhibitors	Acute renal failure on commencement, clinically significant renal artery stenosis	Chronic renal failure	Start low, monitor BP, K+ and renal function
SSRIs	Use with another serotonergic agent	Past history of bipolar disorder	Start with low dose, observe for evidence of mania
Typical antipsychotics	Seizure disorder, Parkinson disease	Postural hypotension	Use lowest dose and observe for postural hypotension
Warfarin	Falls, confusion, noncompliance, inability to have INRs measured	Variable INRs, use of interacting medication	Monitor INRs, bleeding closely, check INR about a week after introduction of new medication
Oral bisphosphonates	Delayed oesophageal emptying, hypocalcaemia	Reflux disease	Inform patient of administration instructions and to be aware of worsening symptoms, odynophagia
Aspirin/NSAIDs	Aspirin hypersensitivity, previous aspirin/NSAID induced ulcer	Asthma	Ensure adequate asthma control with inhaled corticosteroids
Allopurinol	Use with azathioprine	Vasculitis	Start at low dose and adjust for renal function
		Precipitation of acute gout	Prophylaxis with colchicine or low dose anti-inflammatory
Systemic steroids	Active infection	Long term osteoporosis	Prophylaxis with other medications in high risk patients
Digoxin	Heart block	Chronic renal failure	Prescribe lowest dose, monitor levels and evidence of toxicity
Flucloxacillin	Penicillin allergy	Underlying chronic liver disease	Monitor LFTs more frequently, and use as short a course as possible
Cefaclor	Cephalosporin allergy, severe penicillin allergy, eg. anaphylaxis	Child with repeated previous exposure to cefaclor	Inform parents of possibility of serum sickness and to present as soon as possible if reaction occurs
Aminoglycosides	Family history of aminoglycoside induced deafness	Renal impairment	Give dose appropriate for renal function, and use assays to guide dosing. Cease if unable to achieve adequate peak or evidence of retention or toxicity

Drug interactions

Another frequent source of confusion about the suitability of medications is concerns about drug interactions. Frequently practitioners avoid prescribing quite useful medications because of the concern that the possibility of drug interactions represents a contraindication to the medication's use. A good example here is warfarin. Frequently practitioners do not use certain first line medications because their prescribing software reports an interaction with warfarin, so they resort to prescribing agents which may be less preferred and which they are not as familiar with (ie. not on their P-drug list) because the same alerts do not come up with these. It is important to appreciate that a medication is not suitable for use with warfarin if the patient cannot have an international normalised ratio (INR) measurement performed, not because it has been reported to have a drug interaction. This is because, even if the drug is not listed as having an interaction with warfarin, the patient's INR may still be altered significantly for a number of reasons. These can include incorrect information about the drug's interactions, alterations in physiology as a result of the condition for which the drug is being prescribed, eg. worsening heart

failure, pneumonia, exacerbation of chronic obstructive airways disease, alterations in diet due to the illness, eg. diarrhoea, vomiting, or co-medication with paracetamol or other over-the-counter medications, eg. vitamins all of which can alter the INR. Hence, a good rule is to always check the INR after the introduction of a new regular medication at about a week, regardless of what the prescribing software says, and if the patient cannot have an INR, then they really should not be on warfarin.

Conclusion

Checking drug suitability protects the patient and the practitioner from predictable adverse reactions and is a vital and often forgotten step in the prescribing process. It is a good rule to peruse the patients active problem list, as well as medications each time a new prescription is written to check for suitability issues.

In the next issue of AFP, we will look at the requirements for a valid prescription, as well as how to inform patients about the prescription they are receiving.

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