

I've missed a dose; what should I do?

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SYNOPSIS

More than 80% of patients occasionally miss a dose of their medication. Health practitioners ought to plan with their patients what to do if a dose is missed. Patients believe that this plan should be a required part of the information received when a medication is prescribed and dispensed. Consumer Medicine Information sheets, which are available for most commonly prescribed medications, contain a section on what to do if a dose is missed. The routine use of these sheets or similar advice may help patients to know what to do when they miss a dose.

Index words: Consumer Medicine Information, patient compliance.

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Introduction

Why **don't** consumers know what to do when they miss a dose of their medication? As health professionals we know that the vast majority of patients occasionally miss a dose of their medication. This unintentional non-compliance, and request for advice after the event, is very common in practice. In a study of 205 people, 90% rated having information on 'what to do if a dose is missed' as very important or important and only 1.5% did not want information on this topic.¹ A USA study² found that less than 50% of patients received this information.

Given our understanding of the difficulties around compliance with medication regimens, it must be our expectation that many patients will miss doses. Informing them about what to do about a missed dose at the time of prescribing, dispensing and administration would seem to be a logical step towards improved compliance.

Pre-emptive advice

Missed doses could be viewed within the framework of patient non-compliance, however the problems which arise often result because health professionals do not give enough information to allow the patient to safely use the medication. Teaching a patient what to do if a dose is missed and providing strategies to minimise the number of missed doses appears a sensible approach.³ Providing written information, that includes what to do if a dose is missed, improves people's self-administration of medicines, including corrective action when a dose is missed.⁴

In practice, giving information on what to do if a dose is missed should not be too onerous a task for medical practitioners or

pharmacists. Most of the commonly prescribed medications in Australia come with, or have available, a Consumer Medicine Information (CMI) sheet. All CMI sheets have a section entitled 'What to do if you miss a dose'. Giving patients a CMI sheet the first time they receive a medication, and using this material in discussion with patients at the time of prescribing and dispensing would prepare them for this eventuality.

Assessing the importance of a missed dose (Table 1)

The severity of the patient's condition, whether clinically significant breakthrough effects are likely to be observed, and the characteristics of the medication should be considered when deciding the most appropriate strategy following a missed dose. Vulnerable patients are easily recognisable in any practice and include those on medications of low therapeutic index*, or suffering from conditions which require constant maintenance of therapeutic concentrations (for example epilepsy and thromboembolic diseases requiring anticoagulation). On the other hand, for most people with hypertension or hypercholesterolaemia a single missed dose will be of little consequence.

The patients should be informed at the time of prescribing and dispensing, of strategies to minimise missed doses and to redeem the situation when a dose is missed. Highlighting the strategy as it appears on the CMI or writing out an action plan as a reminder to the patient may prove very useful.

While a pre-emptive approach is ideal it is recognised that requests for information about missed doses are common. Knowledge of a drug's half-life, a major determinant of the fluctuation in interdose concentrations at steady state, is useful for making recommendations on what to do if a dose is missed. Upon cessation of therapy, it takes four to five half-lives for the drug to be completely eliminated.

In general, medications, or their active metabolites, with a long half-life tend to create less problems when a dose is missed than medications with a short half-life. However, the clinical effect of some drugs is not related to the half-life. 'This usually occurs when the drug is acting via an irreversible

* The therapeutic index reflects the range of concentrations between the drug concentration which produces toxic effects and the drug concentration required for therapeutic effects. A narrow therapeutic index means only small increases in concentration can cause toxicity and small decreases in concentration can result in loss of efficacy.

Table 1

Examples of medications for which missed doses may be clinically important, and information for patients on what to do if a dose is missed

Medication	Information for consumers
Oral contraceptives	
Combined oral contraceptives	<p>If one or more tablets are missed from the inactive tablets, no additional contraceptive precautions are necessary, and tablet taking should be recommenced ignoring the missed tablet or tablets. However, if all the inactive tablets are missed and then the next pack is not started on time, start as soon as it is remembered. Additional contraception (such as a condom or a diaphragm) must be used for the next 7 days.</p> <p>If an active tablet is forgotten take it as soon as it is remembered, within 12 hours after the time that it is normally taken. Then take the next and subsequent tablets at the usual time.</p> <p>If there is a delay of more than 12 hours after the time that the tablet is normally taken, contraceptive protection in this cycle may be reduced. There is more risk in becoming pregnant if tablets are missed during the first week, or at the end of the current pack. Take the missed tablet as soon as it is remembered, even if this means taking two tablets at the same time. Any earlier missed tablets are left in the pack. Continue taking a daily tablet as usual, and use additional contraceptive precautions (except for the rhythm or temperature method) for the next 7 days. If these 7 days extend into the inactive section, skip the inactive section and start a new pack in the active area on the next day instead.</p>
Progestogen-only oral contraceptives	<p>For women using the progestogen-only pill the recommendation for the use of other methods of contraception is extended to 14 days if the dose is delayed by three hours or more.</p>
Anticonvulsants	
Acetazolamide	<p>If it is almost time for next dose (within 4 hours), skip the missed dose and take the next dose when it is due. Otherwise, take it as soon as it is remembered, and then go back to taking the medicine as usual.</p> <p>Do not take a double dose to make up for the missed dose. This may increase the chance of you getting an unwanted adverse effect.</p>
Carbamazepine	
Ethosuximide	
Phenytoin	
Tiagabine	
Topiramate	
Vigabatrin	
Lamotrigine	<p>Do not take a double dose to make up for the dose that you missed. (This drug has a long half-life.)</p>
Sodium valproate	
Digoxin	<p>If it is almost time for the next dose, skip the missed dose and take the next dose when it is due.</p>
Warfarin	<p>Otherwise, take it as soon as it is remembered, and then go back to taking the medicine as usual. Do not take a double dose to make up for the dose that you missed.</p>
Psychotropics	
Lithium	<p>If it is almost time for the next dose (within 2 hours), skip the missed dose and take the next dose when it is due. Otherwise, take it as soon as it is remembered, and then go back to taking the medicine as usual.</p> <p>Do not take a double dose to make up for the dose that you missed.</p>
Antidepressants other than monoamine oxidase inhibitors	<p>If it is almost time for the next dose, skip the missed dose and take the next dose when it is due. Otherwise, take it as soon as it is remembered, and then go back to taking the medicine as usual. Do not take a double dose to make up for the dose that you missed.</p>
Monoamine oxidase inhibitors	<p>Do not take an extra dose. Wait until the next day and take the normal dose then.</p>
Phenelzine	
Tranylcypromine	

mechanism (for example aspirin's effect on platelets), via an indirect mechanism (for example the effect of warfarin on blood coagulation), when the drug is a pro-drug (in which case it is the half-life of the active species that is important) or when the drug is converted to an active metabolite which has a long half-life.⁵

Missing several consecutive doses raises additional problems. For example, for drugs with long half-lives it can take a

significant time to re-establish therapeutic concentrations when regular dosing resumes unless loading doses are given (for example digoxin). Drugs with short half-lives will lose therapeutic effect rapidly. Further, drugs with first-dose effects, for example an ACE inhibitor in combination with diuretics, may also present clinical problems when normal dosing is resumed. Overall, surprisingly few studies have examined the clinical significance of a missed dose.

Missed doses of the oral contraceptive pill have been well studied. Women taking the pill need to be aware of the risk associated with missed doses and of what to do when a dose is missed (Table 1). Given the complexity of this information, and the risk of an unwanted pregnancy, it is important that any verbal counselling is supported with appropriate written material. Where a CMI sheet is available this can be used during the consultation. If no CMI sheet is available for the prescribed product, written notes based on the recommendations in the Australian Medicines Handbook are useful.⁶

Conclusion

For the vast majority of patients an occasional missed dose will have little impact on the outcome of therapy. Most CMI sheets include statements such as:

- If you forget to take one or more doses: take your next dose at the normal time and in the normal amount. Do not take any more than your doctor prescribed.
- If you miss one dose, skip it and continue with your normal schedule.

Having this knowledge when starting therapy may be a simple way to alleviate much patient anxiety and in some cases avoid unwanted clinical consequences.

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Conflict of interest: none declared

Self-test questions

The following statements are either true or false (answers on page 23)

5. Patients who miss a dose of warfarin should take a double dose when the next dose is due.
6. Contraception becomes unreliable if a progestogen-only contraceptive pill is missed by more than three hours.

Book review

Therapeutic Guidelines: Palliative care. North Melbourne: Therapeutic Guidelines Limited; 2001. 308 pages. Price (postage not included): \$33, students \$25.30.

Peter Keppel, General Practitioner, Yarrawonga, Vic. 'Palliative care is active care.'

This statement rings true to me, having worked in a small rural town for over 16 years, in which the care of the dying is a large part of my practice. Whether it is severe chronic obstructive pulmonary disease, intractable congestive cardiac failure (less often seen now with newer drugs) or cancer, the process always involves a brief introduction, then breaking bad news, then a terminal phase in which shifting goals are negotiated and renegotiated.

The book attempts a lot more than a list of pharmacological options. It opens with general chapters covering principles of palliative care, ethical issues, communication, loss and grief, and analgesic guidelines. It makes the point that general practitioners are by default the co-ordinators of care, as well as being the gatekeepers to the health system. The place of self-care among providers is recognised.

With regard to pain management, the approach is one of identifying different types of pain, e.g. nociceptive (superficial somatic, deep somatic, skeletal muscle, visceral colicky, visceral constant) or neuropathic, rather than the traditional three stage 'ladder' approach.

The emotional, spiritual and social aspects of pain are not ignored. I particularly found useful the approach to delirium and confusion. The problems of the elderly demented patient are dealt with rather briefly, given the large cohort of these people now ageing. No mention is made of the practical problems accessing the newer antipsychotics because of the Pharmaceutical Benefits Scheme prescribing restrictions. The dose of morphine in terminal severe chronic obstructive pulmonary disease patients is stated to be 1 mg 4 hourly, increasing as needed. In my experience this is usually nowhere near enough.

There are useful chapters on medical oncology describing some newer regimens for particular cancers.

The book has been found useful by our active and busy palliative care team. It would not be sufficient on its own to answer all questions on the subject, but is written in a compassionate style, showing the wisdom of experience. There is extensive cross-referencing within the text. There is no list of other texts for reference that I could find.